INTESTINAL OBSTRUCTION.

III. THE DEFENSIVE MECHANISM OF THE IMMUNIZED ANIMAL AGAINST DUODENAL LOOP POISON.*

BY G. H. WHIPPLE, M.D., H. B. STONE, M.D., AND B. M. BERNHEIM, M.D.

(From the Hunterian Laboratory of Experimental Pathology, Johns Hopkins Medical School, Baltimore.)

In previous communications (1, 2, 3) we pointed out the value of closed duodenal or intestinal loops in the study of some of the obscure features of intestinal obstruction. The closed loop may be likened to a volvulus in which there has been no vascular disturbance or obstruction, and the clinical picture in the two conditions may be identical. The closed loop usually employed in our work is produced in dogs by heavy ligatures placed just below the pancreatic duct and again just beyond the duodenojejunal junction combined with a posterior gastro-enterostomy. The intoxication which develops from the condition must be limited to two factors, bacterial growth and epithelial activity, as other factors such as gastric and pancreatic juice, bile, and products of food digestion are excluded.

Our published experiments show that dogs with closed duodenal loops will die in about two days from acute intoxication, and further that a substance can be isolated from the closed loops, which, if injected into a normal dog, will cause similar but more intense signs of intoxication. The picture is one of severe and fatal shock,—low blood pressure and temperature, vomiting and diarrhea with extreme splanchic congestion. Moreover, this toxic substance can be extracted from the mucosa of the closed duodenal loops and destruction of the mucosa prevents its appearance in the loops, indicating that the epithelium is essential to its production. The loop in question can be excised without any intoxication resulting therefrom.

* Received for publication, November 29, 1913.
Some of our early experiments led to the conclusion that a normal dog which had been injected intravenously with a sublethal dose of this toxic material became relatively immune, and could withstand much larger doses given by subsequent injection with little intoxication. This immunity can be demonstrated with little difficulty in spite of the varying reaction of normal dogs to the toxic material obtained from the duodenal loops. It was also noted that healthy dogs immunized by injection of the toxic substance can survive operation and the production of a closed duodenal loop for a period of six days or longer. The average duration of life in a non-immune dog after production of a closed duodenal loop is two days, the maximum four days. Further, the immune dogs do not show the early signs of intoxication which are so evident in the untreated dogs.

It seemed likely that this immunity might be explained by the presence of the protective ferments which appear in the blood after the injection of proteids and peptones (Abderhalden (4)). Repeated injection of sublethal doses of the poisonous material from duodenal loops showed that the blood after a suitable period was free from any ferments capable of dissolving various peptones as tested by means of the polariscopic method. The material injected was obtained from closed loops, digested for many days at 38° C., heated to 70° C. for one half hour, centrifugalized, and filtered (Gooch crucible). It seems clear that the cleavage had been sufficient to destroy all peptones. Additional evidence is supplied by the observation that guinea pigs cannot be sensitized by the material so that the anaphylactic reaction may later be elicited. Guinea pigs sensitized by the blood of a closed loop dog will not react to the duodenal loop fluid prepared as outlined above.

Evidence is submitted below to show that the poison found in the closed loop of the dog or cat, and in the human intestine in acute obstruction, may be the same. The poisons have the same toxic effects and may all be used to immunize dogs against subsequent lethal doses of the material from a closed duodenal loop. Further it is noted that a dog (No. O-66) which recovered from a simple obstruction was extremely resistant to the intoxication of a closed

---

1 These observations were made by Dr. E. K. Marshall.
Intestinal Obstruction.

duodenal loop, exactly like a dog which had been immunized with loop poison. This fact surely indicates that a poison is absorbed under these conditions, and also that the poison present in simple obstruction and in the closed loop may be identical.

The poison found in the closed loops is a resistant body (1). It is evident that the immune dog develops new power or increases its normal capacity to destroy this poison. The experiments below show that the immune serum is inert but that the protective agent resides in the organ cells and extracts. The liver, spleen, and lungs are very active in destroying the duodenal loop poison when a mixture is incubated for a few hours or days. The clear filtrate from the digested immune liver can destroy the poison after autolysis for hours, indicating possibly some ferment as the active agent.

Normal tissues act on the poison very slowly, and weeks may be required to show any definite destruction of the toxin. Normal liver acts more quickly than other normal organs, but is far weaker than the immune liver. This fact may be taken as evidence of the method of defense of the body against this poison. This protective body or ferment is not a stable factor, but may disappear; so too the acquired immunity of dogs may vanish after a period of weeks or months.

METHOD.

The method will be given here in outline; the full account will be found in previous publications. The material obtained from the duodenal loop is allowed to undergo autolysis with chloroform and toluol for several days at 38° C., after which it is heated at 60° to 70° C. for one half hour or longer, centrifuged at high speed for several minutes, and the supernatant fluid filtered through filter paper or asbestos (Gooch crucible). The filtrate may be faintly acid or alkaline. Unless otherwise stated the material obtained from the intestinal loops or mucosa is treated in this manner before injection. The operative technique has been described and illustrated in a former publication. It was found that intraperitoneal injection of this material caused some inflammation and that subsequent operation was not infrequently followed by peritonitis, resulting from the slight soiling of the peritoneum during the production of the gastro-enterostomy. Intravenous injection is much more satisfactory when it is desired to produce an immunity.

EXPERIMENTAL OBSERVATIONS.

DOG IMMUNIZED TO DUODENAL LOOP FLUID. LETHAL DOSE. SURVIVED.

Dog O-31.—Mongrel hound, male.
Jan. 29, 1913. 12 M. Intravenous injection of 20 c.c. of duodenal fluid (dog
G. H. Whipple, H. B. Stone, and B. M. Bernheim.

O-12). 1 P. M. Muscular tremors and intoxication but no vomiting. 3 P. M. Repeated attacks of vomiting. Dog looks rather sick.


Feb. 1. 2 P. M. Intravenous injection of 15 c.c. of duodenal fluid (dog S-51-54). This duodenal fluid, 20 c.c. in amount, was fatal to a 15 pound dog in four and one half hours. 4 P. M. Repeated vomiting and much fluid diarrhea.

Feb. 2. Dog has recovered completely and has a good appetite.

Feb. 4. Dog in good condition; weight 25½ pounds. 3 P. M. Intravenous injection of 20 c.c. of duodenal fluid (dog S-51-54). 3.30 P. M. Vomiting and much fluid feces. 4.30 P. M. Dog improving. Pulse is much stronger; no vomiting.

Feb. 6. Dog is in good condition; weight 21½ pounds. 10.30 A. M. Temperature 38.2° C. Ether anesthesia and kymograph observation. Intravenous injection of duodenal fluid, 30 c.c. (dog O-26). This fluid, 30 c.c., was fatal in seven hours to a dog weighing 25 pounds. The kymograph record (dog O-26) shows initial drop in blood pressure as usual, followed by a slow secondary drop always seen in fatal poisoning. At the end of the kymograph record the temperature was 37.3° C. Following recovery from ether, vomiting and diarrhea were marked. 12.30 P. M. Temperature 39.6° C. 2.30 P. M. Dog has vomited and had some dark fluid feces; appears much intoxicated but can walk about. 4 P. M. Temperature 39.7° C.

Feb. 7, 10 A. M. Dog is rather sick, but this is due to an extensive phlegmon developing about the neck wound involving the region of the shoulder. Temperature 39° C. 12 M. Bled from carotid. Ether anesthesia.

Autopsy.—Performed at once. There is an extensive area of inflammation at the root of the neck. Thorax and lungs negative. Liver rather pale. Gastrointestinal tract normal. Blood serum from this dog used below to show the absence of ferments capable of destroying duodenal poison. This serum together with a normal control showed no ferment activity after digestion with peptone and gelatin, with the polariscope method (Abderhalden).

INCREASED RESISTANCE TO DUODENAL LOOP FLUID.

Dog D-38.—Small pup; weight 10 pounds.

Jan. 16. Intravenous injection of duodenal loop fluid from a cat. This caused considerable intoxication, vomiting but no diarrhea.

Jan. 23. Dog is noisy and active.

Jan. 24, 10 A. M. Duodenal fluid, 20 c.c. (dog O-11), given intraperitoneally. 12 M. Frothy vomitus below cage, but no diarrhea.

Jan. 25. Dog is better, but abdomen is tender.

Jan. 28. Dog in good condition; weight 10 pounds. 10.30 A. M. The duodenal fluid was standardized. 20 c.c. killed a dog weighing 10½ pounds in four hours, with typical signs of acute intoxication, the experiment being done at the same time with this experiment. A kymograph record (dog D-38) was taken during this intravenous injection of 32 c.c., which is a 50 per cent. increase above the known lethal dose. The fluid caused a profound drop in blood pressure followed by a slow rise and slowing of pulse.

12.30 P. M. Dog badly shocked. Passes a little fluid feces. Pulse just palpable. Respiration slow; appears fatally poisoned. 3 P. M. Dog is badly shocked.
but has improved slightly, and the diarrhea has ceased. 4 p. m. Passes a large amount of fluid feces rich in mucus and bile. Bile-stained vomitus abundant. Pulse is much stronger. 6 p. m. Condition about the same.

Jan. 29, 9 a.m. Found dead.

Autopsy.—Beginning peritonitis over a large intussusception involving the middle portion of the small bowel. Thorax negative. Viscera are not much congested. Jejunum contains a good deal of fluid. The mucosa is perhaps slightly pinker than normally. It is probable that this dog would have survived this large dose of toxic material but for the intestinal intussusception, brought on undoubtedly during the active peristalsis which always follows the injection of this poisonous material.

The preceding experiments (dogs O-31 and D-38) show that a considerable grade of immunity may be established against the loop poison even by a single sublethal dose. Other experiments given below bring out the same point (dog O-51). The following experiment (dog O-43) shows again the increasing immunity following sublethal doses of the poison; and it appears that it is transient and may drop to a low level or disappear completely after a period of many weeks.

IMMUNITY TO DUODENAL LOOP FLUID DISAPPEARS IN THREE MONTHS.

Dog O-43.—Strong fox-terrier, male; weight 25½ pounds.
Feb. 17, 11 a.m. Duodenal fluid, 10 c.c., given intravenously (dog O-33-34). 12 m. Dog looks shocked. 2 p. m. No diarrhea; no vomitus. Dog improving.
Mar. 19, 11 a.m. Duodenal fluid (X), 14 c.c., given intravenously. 10 c.c. of this fluid had poisoned fatally within four hours a normal dog weighing 25 pounds. 4 p. m. Much vomiting and profuse diarrhea. The fluid stools are rich in mucus, as seen in fatal poisoning. 5 p. m. Pulse is weak, but dog is evidently recovering.
Mar. 20. Dog has recovered completely.
Mar. 24. 12 m. Duodenal fluid, 20 c.c., given intravenously (dogs O-33 and O-34). 14 c.c. of the fluid poisoned a dog fatally in six hours (dog O-38; weight 21 pounds). 3 p.m. Dog has vomited repeatedly. Much fluid diarrhea, but does not look badly shocked. 5 p.m. Diarrhea continues with tenesmus and bloody mucus. Animal looks sick.
Mar. 29. Dog in normal condition.
Apr. 12. Dog in fairly good condition; weight 22 pounds. 12 m. Duodenal fluid (X), 14 c.c., given intravenously. 2 p.m. Dog has had a little diarrhea; no vomiting. Pulse fair. 8 p.m. Dog eats and looks well. Pulse fair. 8 p.m. Dog eats and looks well. Pulse normal. The poisoning is obviously much less marked at this time than in the previous month.
July 25. Dog has mange, but is in fair condition; weight 22½ pounds. 11 a.m. Dog given a lethal dose of duodenal fluid, 150 c.c. (dog O-52). This fluid had been boiled and filtered and tested on a normal dog (No. O-101), weighing
24 pounds. The same amount of fluid used, 150 c.c., caused in the control dog fatal intoxication in eight hours with typical findings of an acute intoxication. 12.30 P.M. Dog has had one fluid stool and shows a slow deep respiration. 2.30 P.M. Dog is severely shocked and more soft feces are passed. 5 P.M. Diarrhea continued. Dog is very sick and died shortly after this observation.

Autopsy.—July 26, 9 A.M. Heart contained blood clots. Lungs show a great deal of edema. Liver, spleen, and stomach normal. Duodenum shows a mottled pink and red mucosa. Ileum mucosa is pale and the small bowel contains a great deal of fluid feces. Kidneys show a moderate grade of chronic nephritis. The resistance of this dog to duodenal poisoning at this time was not above normal and very much less than during the period three months earlier, when lethal doses of poison were survived with relatively little intoxication.

IMMUNITY WITH DOG AND HUMAN MATERIAL.

Dog O-90.—Black and tan male; weight 10 1/2 pounds.

May 24. Duodenal fluid, 50 c.c., (dog O-77) given intravenously. This caused some vomiting and diarrhea, but the dog made a good recovery.

June 24. Weight 11 pounds. 3 P.M. Human obstruction fluid (3921), 50 c.c., given intravenously. This did not cause severe intoxication, and it was slightly toxic to normal dogs.

June 25, 9 A.M. Dog is active and lively.

June 26, 12 M. Dog is in good condition; weight 10 1/2 pounds. Human obstruction fluid (jejunum 3759), 30 c.c., given intravenously. This fluid was very toxic, 30 c.c. being fatal to dog O-82 in five hours. Weight 13 1/4 pounds. 4 P.M. A few soft stools but no diarrhea. No vomiting. No evidence of shock.

June 27. Dog is active and hungry.

The preceding experiment (dog O-90) and one cited below (dog S-90), as well as other observations, show that the poisonous material present in the closed duodenal loops is similar to that present in human intestinal obstruction. Examples need not be multiplied but it can be stated that animals can be immunized against the duodenal loop poison of their own species (e.g. dog) by the material obtained from the closed loops of other species (e.g. cat), or from intestinal obstruction in man.

INTESTINAL OBSTRUCTION RELIEVED GIVES IMMUNITY TO CLOSED DUODENAL LOOP FLUID.

Dog O-66.—Yellow mongrel, male; weight 14 pounds.

Mar. 28. Ether anesthesia and operation; simple intestinal obstruction. Small intestine closed by ligature midway between the pylorus and ileocecal valve.

Mar. 31. Dog is dull and sick.

Apr. 1. Intravenous injection of a mixture containing ascitic fluid and organ extracts from immune dog.

Apr. 3. Dog seems slightly better.
Intestinal Obstruction.

Apr. 4. Dog has passed feces and is obviously improving. The ligature has probably cut through and established the continuity of the intestinal tract.

Apr. 5. Dog has had diarrhea and appears in good condition.

Apr. 10. Dog appears normal; weight 133/4 pounds.

Apr. 11. Exploratory operation under ether anesthesia. The ligature has cut through, and the lumen of the small gut was practically normal at this point, but the intestine above the site of ligation is definitely dilated and its walls are hypertrophied. A closed duodenal loop was done in the usual manner, together with a posterior gastro-enterostomy.

Apr. 12. Dog shows no evidence of intoxication.


Apr. 15. Dog has distemper with purulent discharge from nose. Pulse is good and strong. Weight 113/4 pounds. 4 P. M. Given intravenously ascitic fluid, 500 c.c., from dog 12-44 (experimental passive congestion).


Apr. 17. Dog eats a little food and is stronger. No evidence of intoxication. Weight 10 1/2 pounds.

Apr. 18. Dog is in fair condition; weight 10 1/2 pounds.

Apr. 19. Dog is improving and passed a solid stool. Weight 12 pounds.

Apr. 21. Condition remains the same. There is evident distemper. Temperature 39.1° C. Weight 12 pounds.

Apr. 22, 11 A. M. Weight 12 1/4 pounds. Ether anesthesia, exploratory laparotomy. The upper ligature had cut through, and the lower ligature was intact. The lumen here was completely obstructed. Gastro-enterostomy perfect. The loop was decidedly thickened and dilated, but contained only 30 to 50 c.c. (estimated). The duodenal loop was again isolated by means of cutting across the bowel and inverting the ends, as has been described in previous papers. Such dogs died as a rule within twenty-four hours and rarely survived thirty-six hours.

Apr. 23, 3 P. M. Dog curled up quietly. Weight 11 1/2 pounds. Temperature 39.3° C.

Apr. 24, 12 M. Dog looks sick. Pulse is weak. Temperature 38.1° C. Weight 11 1/2 pounds. 5 P. M. Died.

Autopsy.—Performed at once. The peritoneal cavity contains 200 c.c. of purulent, foul smelling fluid. There was an abscess at the lower end of the duodenal loop which had ruptured, causing general peritonitis. Thorax, heart, lungs, spleen, and liver negative. Stomach collapsed. Small intestine collapsed and contracted tightly around the root of the mesentery. The loop is small and contains thick, tenacious paste. Its mucosa, except for that covering the inverted ends, is normal.

The preceding experiment (dog O-66) is worthy of careful study and analysis. A simple obstruction of the small intestine presented the usual picture of intoxication, which was somewhat relieved by an injection of a solution of organ extracts from an immune dog. We shall not discuss this point here, and merely state that by about the fifth or sixth day there was improvement. It
was obvious that the obstruction had been relieved by the cutting through of the ligatures.

An exploratory operation two weeks after the first operation showed that the obstruction had been completely relieved, but the jejunum was dilated and hypertrophied. It may be supposed that this dog had been immunized by absorption from his own mucosa during the simple obstruction.

At this time a closed duodenal loop was made as usual and it is noteworthy that the dog appeared in no way intoxicated during the next few days, although he received no fluid infusions and no treatment of any kind, except on the fourth day. The closed loop was present for eleven days, and at this time a second exploratory operation showed an enlarged and thickened duodenal loop containing fluid. The lower ligature was intact and the upper had cut through allowing the escape of fluid on the application of pressure. In rare instances in very vigorous dogs we have observed the cutting out of a ligature with leakage of the loop fluid into the bowel above or below. These animals die, but may survive four or five days. The loop in this dog was securely closed the first few days and later became partly drained. It should be recalled that the majority of untreated dogs with duodenal loops draining externally die in three to six days.

There is no escape from the conclusion that this dog had a strong immunity toward the intoxication resulting from a closed duodenal loop, and the immunity developed as a result of a preceding simple intestinal obstruction, which emphasizes the fact that the intoxication of simple obstruction is similar or probably identical with that developing in association with a closed duodenal loop.

**IMMUNIZED DOG WITH CLOSED DUODENAL LOOP. KILLED AFTER SIX DAYS.**

Dog S-50.—Strong adult male; weight 15 pounds.

May 14. Dog was given intraperitoneally 30 c.c. of material obtained from the closed duodenal loop mucosa of dog S-20. This caused very little intoxication.

May 15. Dog seems normal.

May 17. 11 a.m. Dog was given 28 c.c. of material obtained from a closed duodenal loop (dog S-38). This likewise gave little indication of intoxication.

May 18-21. Dog is normal and eats well.

May 22, 12 M. Dog was given intraperitoneally duodenal loop fluid, 30 c.c. of clear filtrate, prepared as usual, obtained from dog S-11. 2 P.M. Dog had some diarrhea but no vomiting.
Intestinal Obstruction.

May 29, 3 P. M. Ether anesthesia and operation as usual with isolation of closed duodenal loop.

May 30, 1 P. M. Temperature 38° C. Dog eats; no vomiting and no diarrhea.

May 31, 10 A. M. Temperature 38.8° C. Dog eats well and seems in excellent condition. 5 P. M. Temperature 39° C. Dog refused food.

June 1, 10 A. M. No vomiting and no diarrhea, but refused food. Temperature 39° C. Given milk by stomach tube. 5 P. M. Temperature 38.6° C. Condition about the same.

June 2, 12 M. Dog has considerable diarrhea and drinks water eagerly; pulse good. Temperature 37° C. Given milk again by stomach tube, which was followed by vomiting. Dog has lost considerable weight and strength.

June 3, 10 A. M. Dog lies quietly in the cage. Temperature 36° C. Dog has had some diarrhea, the fluid being streaked with a little blood. Pulse is slow but of good volume and tension. 2 P. M. Temperature 37.5° C. Given 200 c.c. of salt solution subcutaneously, as animal will not retain fluids given by the stomach.

June 4, 10 A. M. Dog appears improved. Temperature 37.5° C. The pulse is strong and full. No diarrhea, and stools are pasty. 12 M. Given milk by stomach tube. 2.30 P. M. Pulse strong. Temperature 37° C. Given ether and bled from carotid. The blood pressure was good at this time. Blood showed a good deal of hydremia, giving about four fifths by volume of serum after centrifugalization. The dry weight of the blood at this time was 12.4 and 12.3 per cent., in parallel determinations.

Autopsy.—Performed at once. Heart, lungs, thorax, and peritoneal cavity normal. Spleen is pale and fibrous. Pancreas and kidneys are normal. The stomach contains bile-stained fluid and milky curds. The mucosa is normal. Small intestine shows a pale normal mucosa, in which hookworms are rather numerous. The duodenal loop is large and flabby. Its ends are closed tightly and it contains about 150 c.c. of canary yellow, purulent material. The mucosa is slightly swollen and pinkish, but intact throughout. Three hookworms are alive and active and adherent to the mucosa.

Microscopical Examination.—Spleen is atrophic. Kidneys, liver, duodenal loop, jejunum, and stomach mucosa are all normal.

Immunized Dog with Closed Duodenal Loop. Killed after Four Days.

Dog S-90.—Old mongrel, female; weight 12½ pounds.

July 16, 3 P. M. Ether anesthesia and intravenous injection of fluid obtained from a case of human intestinal obstruction. This material had undergone autolysis in the usual way for several days, was heated at 60° to 70° C. for two hours, centrifuged, and filtered. 20 c.c. of this broth-like filtrate were given intravenously and the ether removed at once. The duration of the anesthesia was only about ten minutes. 5 P. M. Pulse is just palpable and dog appears much shocked. Dog has vomited twice and passed one semifluid stool. 8.30 P. M. Pulse is good and dog is much improved. No diarrhea.

July 17, 9 A. M. Dog will not eat.

July 18, 10 A. M. Dog appears rather sick; in the afternoon ate some food and seems better.

July 22, 3 p. m. Ether anesthesia and operation as usual with isolation of a closed unwashed duodenal loop.

July 23, 9 a.m. Temperature 39° C. Dog is active. 5 p.m. Temperature 38.9° C.

July 24, 2 p.m. Rectal temperature 38.4° C. Dog drinks water but will not eat.

July 25, 1 p.m. Rectal temperature 38.4° C. Dog has lost weight and strength and refuses food.

July 26, 10 a.m. Rectal temperature 38.7° C. Pulse is good. 3 p.m. Rectal temperature 38.6° C. Dog is fairly strong, but has lost a good deal of weight. Given ether and bled from carotid. The pulse pressure is strong, and there is no indication of a severe intoxication. It is probable that this animal would have lived one or two days longer.

Autopsy.—Performed at once. Peritoneal cavity, thorax, heart, and lungs are all normal. Spleen and kidneys are normal. Liver is pale brownish in color, but otherwise normal. The duodenal loop is not distended. The ends are tightly closed. It contains about 10 c.c. of pasty, creamy material, which sets into a sort of jelly on contact with water. This is squeezed out and the mucosa scraped off as usual. The mucosa is normal and intact throughout. There are no ulcers and no submucous hemorrhages. Stomach and duodenum above the ligature contain bile-stained fluid. The mucosa is pale and intact. The small intestine contains bile-stained fluid, and its mucosa is pale and intact. The gut is uniformly constricted throughout.

The two preceding experiments (dogs S-51 and S-90) show a type of immunity which develops following the injection of the toxic material in sublethal doses. The results are the same whether material from closed loops in dogs or from intestinal obstruction in man is used to immunize the animals. The dogs with the closed loops do not show the usual acute signs of intoxication seen in dogs not previously injected. They survive often far beyond the maximum period for untreated dogs with closed loops. Hence the poison found in the closed loops is the cause of the intoxication resulting from their experimental production. A similar poison is found in human intestinal obstruction and presumably is concerned with the intoxication found in this condition.

The two next experiments (dogs S-72 and S-70) illustrate some of the difficulties in the work with the closed-loop dogs. The immunity following repeated doses of the poison will protect effectively against the loop intoxication, but not against peritonitis. The closed loops may behave very differently under various conditions. At times in a fatal case the loop will be found collapsed and containing only a few cubic centimeters of thick, pasty material. These cases are favorable for immunity work. If an immunity is
Intestinal Obstruction.

established in such a dog the animal may live more than double the usual period, but in most animals there is a rapid accumulation of fluid in the loop which produces tension and favors injury and ulceration of the mucosa which may effect a perforation. Perforation, of course, causes peritonitis with rapid death, and adds a confusing factor to the picture.

IMMUNIZED DOGS WITH CLOSED DUODENAL LOOP. DEATH IN FOUR DAYS WITH PERITONITIS.

Dog S-72.—Strong adult fox-terrier, male; weight 22 pounds.

June 21, 11 A.M. Dog was given 22 c.c. of duodenal loop fluid obtained and prepared as usual (dog S-65). This was injected intraperitoneally and caused no pain. 1 P.M. Dog has vomited once, but there is no diarrhea.

June 22. Dog is perfectly normal and eats well.

June 24, 5 P.M. Dog given intraperitoneally 25 c.c. of duodenal fluid (dog S-51).

June 25, 9 A.M. Dog is normal.

June 27, 3 P.M. Ether anesthesia and operation with isolation of closed duodenal loop in the usual way with washing out of contents of loop.

June 28. Dog is quiet and refuses food.

June 30, 10 A.M. Dog is in good condition. Pulse strong. Rectal temperature 38.5° C. Muscular tremors are noted. 4 P.M. Temperature 39° C. Given one half pint of milk. 5 P.M. Dog has vomited milk and bile-stained material. Small amount of soft blood-tinged feces are passed. Dog seems obviously intoxicated.

June 30, 12 M. Dog again given milk with one egg by stomach tube. Weight 19 pounds. Rectal temperature 40° C. Pulse strong and regular. 1 P.M. Dog vomited bile-stained coagulum.

July 1, 9 A.M. Condition about the same. Temperature 39° C. 11 A.M. Dog is given milk which is vomited at once, and later a little water which is also vomited immediately. 2 P.M. Pulse is slow and weak. Temperature 38.8° C. 2.15 P.M. Death. Blood obtained a few minutes after death showed dried weight of 22.3 and 22.4 per cent., in parallel determinations.

Autopsy.—Performed at once. Thorax, heart, lungs, and spleen are all normal. The peritoneal cavity contains some purulent, turbid fluid, about 20 c.c. in amount. The serous surfaces are injected and covered with tiny ecchymoses. It is found that there had been leakage from the lower puncture wound and lower ligature which had cut into the gut wall. Jejunum shows a mottled, pinkish mucosa with little injection. The ileum is quite normal and contains soft yellow feces, and fecal material slightly stained with blood. Liver is considerably injected. Kidneys and stomach are normal. The loop contains about 20 c.c. of slate-colored, thick material having a fecal odor. The mucosa is intact throughout and normal except for a little injection.

Dog S-70.—Small pup, male; weight 11 pounds.

June 20, 11.30 A.M. Ether anesthesia with kymograph observation. The material was obtained from the intestinal mucosa (dog S-66), a case of simple
intestinal obstruction. The intestinal mucosa, washed and scraped off, was allowed to undergo autolysis for six days, heated at 65° C. for one hour, centrifuged, and filtered. 55 c.c. of this clear filtrate caused the usual drop of the blood pressure with return to normal. 12.20 P.M. Dog removed from kymograph. 1 P.M. Dog passed a semifluid stool. 2.30 P.M. Dog is weak. Diarrhea persists.

June 21, 9 A.M. Dog is quite sick. Pulse is fair, and diarrhea continues.

June 23. Condition is normal. Dog is normal; weight 11½ pounds. 12.30 P.M. Ether anesthesia and kymograph observation. The material was obtained from dog S-46 (drained duodenal loop). 90 c.c. of this material was given intravenously, causing an initial drop of blood pressure followed by a rise above normal. 1 P.M. Dog removed from kymograph. 3 P.M. Dog is much shocked; vomiting and diarrhea are marked. 5 P.M. Dog is quite sick. Muscle tremors are marked.

June 25, 9 A.M. Dog is normal; weight 11½ pounds. 12.30 P.M. Ether anesthesia and kymograph observation. The material was obtained from dog S-46 (drained duodenal loop). 90 c.c. of this material was given intravenously, causing an initial drop of blood pressure followed by a rise above normal. 1 P.M. Dog is much shocked; vomiting and diarrhea are marked. 5 P.M. Dog is quite sick. Muscle tremors are marked.

June 27, 9 A.M. Dog seems well.

July 11, 3 P.M. Dog in excellent condition. Ether anesthesia and operation as usual, with isolation of closed unwashed duodenal loop.

July 12, 9 A.M. Dog seems well. 4 P.M. Condition the same.

July 13, 9 A.M. Dog has vomited. Rectal temperature 38.5° C. Pulse is strong. 4 P.M. Dog has passed solid and semifluid feces. 9 P.M. Pulse regular and strong.

July 14, 10 A.M. Dog seems pretty well. Temperature 38.3° C. Pulse regular, but tension is poor. Vomit is present under the cage, and partly digested food is present in it. 5 P.M. Dog is very weak and toxic. Pulse is of low tension. Given 200 c.c. of water and vomited immediately. Temperature 38.2° C.

July 15, 9 A.M. Pup is very toxic. Pulse is weak. Rectal temperature 39.4° C. Vomited at once water given by stomach tube. Muscle tremors are present. 9.30 A.M. Death.

Autopsy.—Performed at once. Thorax and heart are normal. Lungs show a few small patches of consolidation along the edges of the left lower lobe. Spleen is negative. Liver is congested. The peritoneal cavity contains a little thin, purulent material, about 5 c.c. in amount. The surfaces are injected and show scattered ecchymoses. The leak from which the peritonitis developed is about the upper ligature where a tiny perforation and pocket of pus is found. The loop is not distended and contains only 20 c.c. of rather thick fluid. The mucosa is quite intact, slightly injected, and shows no ulcers and no hemorrhage. The stomach contains bile-stained fluid. The jejunum shows a pinkish red mucosa, with definite injection of the villi. Considerable fluid is present. The ileum shows a very faint pinkish mucosa. The large intestine and kidneys are normal.

IMMUNE SERUM INACTIVE TO DUODENAL LOOP POISON.

Dog O-37.—Mongrel hound; weight 21 pounds. This dog (see history above) was given repeated injections of duodenal loop fluid and survived a known lethal dose. The blood after defibrination was centrifuged and 65 c.c. of blood serum were obtained. The red blood cells were then washed with salt solution, centrifuged, and the washings added to the serum, making 130 c.c. in all.
To this was added duodenal loop fluid (dog O-26), 30 c.c., an amount which was known to be a lethal dose as tested on other animals. This mixture of immune dog serum and duodenal fluid together with chloroform and toluol was incubated for twenty hours at 38° C., and after heating and filtration was injected intravenously into dog O-37, a mongrel Irish terrier, male, weighing 13½ pounds.

Feb. 2, 9 a.m. Ether anesthesia and kymograph record during injection. There was no immediate depression of blood pressure and obviously the incubation with serum neutralizes or destroys this substance, causing the acute primary drop in blood pressure. There was a remarkable secondary fall in blood pressure coming on after about twenty minutes accompanied by great slowing of pulse. The dog passed fluid feces at the end of fifteen minutes and vomited before coming out of the anesthesia. 1.30 p.m. Death.

Autopsy.—The findings are in every respect typical of acute poisoning by the duodenal loop fluid.

**IMMUNE SERUM DOES NOT DESTROY DUODENAL LOOP POISON.**

Dog 12-34.—Small pup; weight 9 pounds.

Jan. 9. Intravenous injection of material from closed intestinal loop of cat. This caused a moderate grade of intoxication with diarrhea.

Jan. 14. Complete recovery. Ether anesthesia and bleeding from carotid. The blood serum gave negative results for the ferments described by Abderhalden, with peptone and the polariscope method. The remaining blood was then defibrinated and 70 c.c. of serum were obtained.

Autopsy.—Normal organs throughout. Blood, 70 c.c., plus duodenal fluid (dog O-11), 50 c.c., were placed in the incubator with toluol and chloroform for twenty-four hours at 39° C. There was slight turbidity at the end of this time. The fluid was heated to 45° C. for one half hour, centrifuged, and filtered. This mixture, 115 c.c., was given intravenously to dog O-23, a strong adult fox terrier, weighing 16 pounds. 10.30 a.m. Ether anesthesia and kymograph record during the entire period of injection. There was no sudden drop in blood pressure and no marked drop during the period of observation (one half hour). A well marked erythema of the skin appeared over the legs and abdomen. 2 p.m. Dog is prostrated and has vomited. 3.30 p.m. Death.

Autopsy.—The findings were typical of acute poisoning by duodenal loop fluid, described and illustrated in previous publications (2).

Dog 0-22.—Small pup; weight 7 pounds.

Jan. 11, 12 m. Human mucosa (3782). Autolysis for twelve weeks. Heated at 95° C. for thirty minutes; no precipitate; filtered. 95 c.c. intravenously gave little evidence of severe intoxication. 2.30 p.m. Dog appears fairly well. No diarrhea.

Jan. 12. Dog is normal.

Jan. 20. Bled for ferment tests. The Abderhalden tests with this blood serum were negative, as above, for the presence of protective ferments. Blood serum, 50 c.c., was combined with blood serum of dog 12-30 to be used later.

Dog 12-30.—Fox-terrier, male; weight 14½ pounds.

Jan. 11. Human intestinal contents treated as above (dog O-22). 40 c.c. given intravenously caused little reaction.
Jan. 12. Dog is normal.

Jan. 20. Ether anesthesia and bleeding. This blood serum was tested with negative result for the Abderhalden ferments. The blood serum (110 c.c.) combined with that of dog 0-22 (50 c.c.) was added to duodenal loop fluid of dog O-11 (50 c.c.). This mixture was incubated together with chloroform and toluol for 22 hours at 39°C, then heated for one half hour at 60°C, and filtered. This clear brown fluid, 205 c.c., was given intravenously to dog O-27, a fox terrier, weighing 12 pounds.

Dog O-27.—Jan. 21, 12 M. Ether anesthesia. Kymograph observation showed a slow transient drop during injection, with a tendency to return to normal within thirty minutes. 3 P. M. Pulse is good. No evidence of shock. Has passed one solid stool. 8 P. M. Found dead, but quite warm. Fluid feces and vomitus abundant under cage.

Autopsy.—Performed at once. Heart still fibrillating. Blood clots slowly. Lungs show patches of hemorrhagic edema. Spleen is greatly enlarged. Liver is huge and deep purple in color, and very tense. Mesenteric vessels are greatly dilated. Stomach contains a little fluid and shows a pale mucosa. Duodenum shows engorgement of the villi, but is contracted. The small intestine contains much blood-tinged fluid. The mucosa is not deep purple, but is mottled pink and red.

The three preceding experiments (dogs O-31, 12-34, and 12-30) show that the serum of dogs immunized by sublethal doses of the poison will not neutralize or destroy the duodenal loop poison. This contrasts strikingly with the observations given below dealing with immune organs and organ extracts which can destroy this poison when the mixture is incubated for a short space of time. The protective ferments described by Abderhalden play no part in this reaction and were absent in all cases examined.

LIVER, SPLEEN, AND LUNGS OF IMMUNE DOG DESTROY DUODENAL LOOP POISON.

Dog O-31.—Mongrel female; weight 15½ pounds.

Mar. 15. Duodenal loop fluid digested with mucosa of immune dog. The filtrate was given intravenously with little evidence of intoxication.

Mar. 16. Dog is normal.

Mar. 19. Duodenal fluid (X), 20 c.c., given intravenously. This caused a little vomiting and a slight amount of diarrhea, but no grave intoxication. The dog has evidently a considerable grade of resistance as this amount of fluid contains more than enough toxin to kill a normal dog weighing 25 pounds.

Mar. 20. Dog rather weak, but is recovering.

Mar. 22. Dog is normal, and eats as usual. Weight 13 pounds. Ether anesthesia, bleeding, and perfusion with 0.9 per cent. salt solution to wash out all the blood from the organs which are normal in all respects. The following extracts and emulsions were made with the addition of a standardized duodenal loop fluid, of which 10 c.c. was fatal to a normal dog weighing 25 pounds in a period of four hours.
Intestinal Obstruction.

(1) Duodenal loop fluid (X), 20 c.c., plus washed mucosa from small intestine, 50 c.c. Dilution with water, toluol, and chloroform; autolysis for five days; heated at 60° C. for one hour. This fluid mixture caused fatal and typical intoxication in a period of ten hours (dog O-64 below). It is probable that some of the poison was destroyed.

(2) Duodenal fluid (X), 20 c.c., plus whole spleen ground up with sand and made up to a thin emulsion with water, toluol, and chloroform. Autolysis for three days. Heated at 60° C. for two hours followed by centrifugation. This fluid mixture caused no acute intoxication (dog O-63 below) and the poison had been destroyed.

(3) Duodenal loop fluid (X) plus liver, 250 gm., ground up with sand, extracted in Buchner press, and about 80 c.c. of the thick juice obtained. This was diluted to 190 c.c., centrifugated, and filtered, giving 160 c.c. of buff colored filtrate. 50 c.c. of this liver juice plus 15 c.c. of duodenal fluid (X) given at once intravenously into a normal dog. The mixture had stood only a few moments before the injection. This caused a fatal and typical intoxication after four hours (dog O-56).

(4) Duodenal fluid (X), 20 c.c., plus liver juice, 50 c.c., prepared as in (3), plus toluol and chloroform. Autolysis for forty-four hours, heated at 60° C. for one half hour, and centrifugated, giving a clear odorless broth. The entire amount was given intravenously to dog O-57 (see below) and caused no evidence of intoxication. Recovery was immediate, showing complete destruction of poison.

(5) Duodenal fluid (X), 20 c.c., plus both lungs ground to a thin paste with sand, water, chloroform, and toluol. Autolysis for sixty-six hours, heated at 60° C. for one half hour, centrifugated, and filtered, giving a clear, odorless, pale amber colored fluid. The entire filtrate, 125 c.c. in amount, was given intravenously to dog O-61 with but slight evidence of intoxication.

(1) Dog O-64.—Male pup; weight 10½ pounds.
Mar. 27, 12.30 P. M. Intravenous injection of a fluid mixture of immune dog's mucosa digested with duodenal loop fluid. Autolysis for five days and preparation for injection in the usual manner. This caused great and prolonged drop in blood pressure with the appearance of diarrhea within thirty minutes. 4 P. M. Dog is cool and badly shocked. Much fluid feces. 10 P. M. Dog is moribund and cool.
Mar. 28, 9 A. M. Autopsy shows typical picture of acute poisoning with duodenal loop fluid.

(2) Dog O-63.—Adult fox-terrier, male; weight 10 pounds.
Mar. 27, 12 M. Intravenous injection of fluid mixture of spleen emulsion from immune dog plus duodenal fluid (X), 20 c.c. Autolysis for three days and preparation as usual. This clear broth, 75 c.c. in amount, gave only a slight drop in blood pressure (kymograph). 4 P. M. One semifluid stool; no vomiting. No evidence of intoxication.
Mar. 28. Dog looks rather sick. No diarrhea. 1 P. M. Dog is quite sick; etherized.

Autopsy.—Extensive bronchopneumonia with hemorrhage and edema of both lungs. Liver shows areas of necrosis and hemorrhage. There is only a slight congestion of the intestinal mucosa. It is unlikely that much of the intoxication was due to the duodenal loop poison. Death was probably due in great measure...
to the acute pneumonia associated with aspiration of vomitus at the time of anesthesia.

(3) Dog O-56.—Fox-terrier, male; weight 14 pounds.
Mar. 22, 4 P.M. Intravenous injection of a fresh mixture of duodenal loop fluid (X), 15 c.c., plus fresh Buchner press liver juice, 50 c.c., of immune dog. Kymograph observation and ether anesthesia. This caused a marked drop in blood pressure with slow recovery. Marked polypnea. 5 P.M. Dog appears greatly shocked. 10 P.M. Found dead and rather cold. Much feces and vomitus below cage.

Mar. 23, 9 A.M. Autopsy showed typical evidence of acute poisoning with duodenal loop fluid. The splanchnic engorgement and congestion are very intense.

(4) Dog O-57.—Small bulldog; weight 14½ pounds.
Mar. 24, 10:30 A.M. Intravenous injection of fluid mixture, duodenal loop fluid (X), 20 c.c., plus Buchner press liver juice of immune dog, 50 c.c. Mixture autolyzed for forty-four hours at 38°C, diluted, heated, and treated in the usual way for injection. This clear broth-like, odorless fluid gave a slight drop, followed by rapid return to normal blood pressure (kymograph). 12 M. No vomiting; slight diarrhea. Dog does not appear poisoned.

Mar. 25. Dog is normal.

(5) Dog O-6t.—Small female; weight 11¾ pounds.
Mar. 25, 12 M. Intravenous injection of fluid mixture, duodenal loop fluid (X), 20 c.c., plus emulsion of lungs from immune dog O-51. Mixture incubated for sixty-six hours at 38°C and treated in the usual way for injection. This clear fluid, 125 c.c., the total filtrate, caused little reaction on the part of the blood pressure. 2 P.M. Dog is sick, but only one stool is passed.
Mar. 26. Dog is well.

The preceding experiment (dog O-51) brings out interesting points. The dog was immunized by means of a mixture of a standard loop fluid digested with immune mucosa which had destroyed most of the poison; yet the dog developed a high grade of immunity as shown four days later when the animal survived a lethal dose of standard duodenal fluid.

Many of the immune organs were washed free from blood and ground to a paste which was combined with a lethal dose of the duodenal loop fluid, diluted with water to a thin paste, and allowed to autolyze at 38°C for two to five days with chloroform and toluol. The filtrate was then tested on normal dogs by intravenous injection. The spleen and lung emulsion destroyed the poison. The liver juice (Buchner press), diluted and filtered, also destroyed it rapidly. The intestinal mucosa destroyed some of the poison but a part remained even after five days' digestion. A fresh mixture of liver juice and loop poison gave fatal intoxication, showing that
Intestinal Obstruction.

the reaction is not prompt or does not take place in the blood stream. This result serves as a control. If the protective action resides in a single type of cell, it is the endothelial cell that may be concerned, but it is of course possible that various body cells may develop the reaction or produce the ferment.

Liver, Spleen, and Mucosa of Immune Dog Destroy Duodenal Loop Poison.

Dog O-32—Mongrel, male; weight twenty pounds.

Jan. 30. Duodenal fluid (dog O-12), 15 c.c., given intravenously. This caused vomiting, but no diarrhea.

Feb. 1. Duodenal fluid (dog S-51), 15 c.c., intravenously. This caused vomiting and dog appears somewhat poisoned.

Feb. 4. Dog appears fairly well; weight 18 pounds. Duodenal fluid (dog S-51), 20 c.c., injected intravenously. This caused vomiting but no diarrhea.

Feb. 11, 10 A.M. Duodenal fluid (dog O-26), 26 c.c., given intravenously. 11.30 A.M. Considerable vomitus, but no diarrhea.


Autopsy.—Performed at once. The organs are practically normal. The mucosa of the small intestine is washed and scraped off carefully. The spleen is cut and ground up with sand and mixed with the mucosa.

The spleen-mucosa mixture was then added to 30 c.c. of duodenal loop fluid (dog O-26). This fluid had been tested and was known to be a lethal dose (compare dog O-31) for an animal of 13 pounds weight. This mixture, together with chloroform and toluol diluted to a thick emulsion by water, was incubated at 39° C. for three days. The mixture was then heated at 60° C. for one hour, centrifugized, but not filtered. The turbid, rather soupy fluid, 100 c.c. in all, was given intravenously to dog O-42, a small female fox-terrier, weighing 11½ pounds. The injection caused a great drop in blood pressure with rapid return to normal after each injection.

Feb. 15, 2.30 P.M. Kymograph. 4 P.M. Dog seems quite well.

Feb. 16. Dog is normal.

The liver obtained from the immune dog O-32, normal in gross, weight about 300 gm., was minced and ground up with sand and combined with duodenal loop fluid (dog O-26), 32 c.c. This was a known lethal dose of loop fluid (dog O-31). The mixture was diluted suitably with 0.9 per cent. salt solution, and then chloroform and toluol were added. This mixture of immune liver tissue and duodenal fluid incubated for twenty-four hours at 40° C. was then centrifugized, without heating, giving a cherry red, rather turbid fluid. The total amount, 85 c.c., given intravenously had a powerful depressor action (dog O-40, strong female pup; weight 21 pounds).

Feb. 13, 4 P.M. Kymograph. The blood pressure curve returned rapidly to normal and there was no slowing of the pulse. There was remarkable and forcible dyspnea. 6 P.M. Dog appears to be recovering normally from ether. No diarrhea.


The liver residue obtained after centrifugization and removal of fluid tested above (dog O-40) was carefully saved and digested at 38° C. together with normal pancreas for a period of three weeks. This gave a clear, deep brown
fluid, strongly acid in reaction. It is made faintly alkaline by sodium hydroxide. The fluid was given rapidly intravenously to dog O-45, a small male fox-terrier, weighing 13½ pounds.

Mar. 6, 10 A. M. Ether anesthesia and kymograph. Intravenous injection of total fluid obtained, 270 c.c. This caused a rapid drop in blood pressure with return to normal at the end of thirty minutes. 12 M. No vomiting or diarrhea. Dog is recovering rapidly. There was no abnormality except prolonged oozing from the neck wound, probably associated with antithrombin excess in the blood.

Mar. 7. Dog is normal.

LIVER EXTRACT FILTRATE OF IMMUNE DOG DESTROYS DUODENAL LOOP POISON.

Dog O-55.—Mongrel pup, male; weight 20½ pounds.

Mar. 20, 4 p. m. Intravenous injection of extract made from the mucosa of the drained duodenal loops of dogs O-21 and O-24. The total amount, 125 c.c., caused no immediate change in blood pressure. 8 p. m. Much vomiting and bloody diarrhea. Pulse fair, but animal appears considerably shocked.

Mar. 21. Dog is still quite sick.

Mar. 24. Dog appears well. 12 M. Intravenous injection of 20 c.c. of duodenal loop fluid (dogs O-33 and O-34). This fluid had been standardized on normal dogs. 3 p. m. Dog is quite sick. There is marked salivation and vomiting with profuse diarrhea and severe shock. 5 p. m. Mucous diarrhea and severe intoxication.

Mar. 25. Dog is improving, but still weak.

Mar. 29. Dog in fairly good condition except for infected neck. Ether anesthesia, bleeding from carotid, and washing of organs free from blood with large amounts of normal saline given intravenously during bleeding.

Liver quite bloodless, weight 294 gm., minced and ground up with sand to a thick paste, which was placed in a Buchner press. About 50 c.c. of thick, viscid juice was expressed, and this was diluted to about 130 c.c. This thin, soupy material was allowed to undergo autolysis at 38 ° C. for sixteen days, giving a clear, deep brown fluid which filtered with ease.

30 c.c. of this clear filtrate were added to 20 c.c. of duodenal fluid (X), a known lethal dose. Autolysis of the mixture for three days gave a very slight turbidity. The material was centrifuged but not heated, filtered, and injected intravenously, 50 c.c. in amount, into dog O-72, a strong male fox-terrier, weighing about 12 pounds. Kymograph record and ether anesthesia during the period of injection. The filtrate caused a drop in blood pressure followed by rapid recovery. There was no evidence of intoxication, no vomiting, and no diarrhea. The following day the dog was normal in all respects.

The same liver extract (dog O-55), 90 c.c. in amount, was kept in the incubator (38° C.) with chloroform and toluol for a period of sixteen weeks. At the end of this time filtration gave the same clear, whiskey-colored, odorless fluid. This was combined with fresh duodenal fluid, 50 c.c. (dog O-86). This mixture of immune liver juice and duodenal fluid was allowed to remain in the incubator with chloroform and toluol for ten days. At the end of this time the solution filtered with great rapidity. There was only the slightest turbidity, and no odor.
Intestinal Obstruction.

July 31, 12 M. Unheated fluid, 135 c.c., given intravenously to dog O-116, a young female mongrel, weighing 17½ pounds. 3 P. M. Dog greatly shocked. 4 P. M. Death, preceded by vomiting and diarrhea.

Autopsy.—Aug. 1. The usual picture following acute intoxication is present. This shows that the ferment capable of destroying the duodenal poison is an unstable body and may disappear from the immune organ extracts after a period of many weeks.

The preceding experiment (dog O-55) adds another important point. The immune liver juice kept in an incubator undergoes autolysis rapidly yielding a clear, whiskey-colored filtrate, which at the end of two weeks contains a ferment capable of rapidly destroying in vitro the duodenal loop poison. However, after a period of incubation at 38° C. for sixteen weeks the active body disappeared and the liver extract was inert towards duodenal fluid. This fact should be compared with the observations above (dog O-43), where it is noted that the immunity of an animal will vanish or drop nearly to a normal level during a period of four months.

DISCUSSION.

The series of experiments here reported provide, we believe, conclusive evidence that a definite intoxication occurs in animals with closed loops, and that the intoxication is due to absorption of the loop poison. There are good reasons for believing that the intoxication seen in cats and dogs with intestinal loops and in human intestinal obstruction is due to the same poison or a similar one. It is noteworthy that a dog recovering from simple obstruction showed little evidence of intoxication when a closed duodenal loop was established. Other evidence will be brought forward later to show that dogs with simple intestinal obstruction begin to acquire a certain immunity to the intoxication which will protect them against a closed-loop intoxication or the intravenous injection of duodenal loop fluid.

In a recent paper Hartwell (5) criticizes our conclusions and endeavors to minimize the factor of intoxication while emphasizing the loss of fluid as the essential and primary condition. In the conclusions of their first paper Hartwell and Hoguet (6) state: "The above findings indicate that death from intestinal obstruction in dogs results from the presence of toxic substances in the circulating
blood which produce fatal lesions in the kidney, liver and other tissues."
In their second paper (7) they say: "The important element, therefore, in the development of the symptoms seen in intestinal obstruction in dogs is the loss of water due to vomiting. The symptoms of intoxication are those resulting from tissue disintegration following this loss."

We have claimed that intoxication is the primary feature and that loss of fluid is secondary to the intoxication, instead of the reverse, as claimed by Hartwell. In his last paper Hartwell (5) admits that there may be intoxication, and so reverts in part to the theory supported by his first paper. He states that intoxication can only appear when there is obvious injury to the intestinal mucosa, and in this we believe he is mistaken, although we admit that given an obvious mucosal injury with ulceration, the intoxication may be more profound. If the theory of injury to the mucosa is the essential factor, why do not all cases of gastro-enterostomy show signs of acute intoxication? Why do not dogs with drained loops where the gut is cut across and drawn into the abdominal wound die sooner than dogs with simple closed loops? Dogs with closed loops may show evidences of grave intoxication at the end of twenty-four hours and yet autopsy may show a collapsed loop with intact mucosa, containing a little pasty material. The entire intestinal mucosa shows very slight congestion, and it has been shown clearly that the poison concerned causes splanchnic dilatation and even paralysis. The mucosa of the loop is often slightly injected and Hartwell states that this indicates injury to the mucosa; however, the microscope shows a normal mucosa except for a slight widening of the capillaries in the villi.

We have held that the poison is elaborated by the mucosa, for when the mucosa is destroyed no poison is formed. It is conceivable that the mucosa can be disturbed so as to functionate abnormally, without any gross evidence of disturbance, and we may assume a perturbed physiological balance of the mucosa by which abnormal products are formed and secreted into the bloodstream. We feel that the experiments here published give adequate basis for the belief that intoxication is the essential factor in intestinal obstruction or in the closed duodenal loop complex, and that the intoxica-
tion in the two conditions is similar if not identical, and the perverted activity of the mucosa, not an anatomical injury, is responsible for the formation of the poison.

It is clear that the cells and organ extracts of immunized animals can destroy the duodenal loop poison which is so resistant to simple digestion. The destruction \textit{in vitro} during autolysis is quite rapid and the resultant material is non-toxic. The possibility that this immune tissue juice might be potent when given intravenously at once suggests itself. It is of course possible that the immune organ extract may destroy the poison \textit{in vivo} and help to tide the animal over a period of acute intoxication. This point is being investigated at present.

**CONCLUSIONS.**

Dogs may be immunized against lethal doses of the duodenal loop poison by means of small doses of the loop fluid from dog or cat and by material obtained from human cases of intestinal obstruction. The immunity is transient and may disappear within a few weeks.

Dogs immunized by repeated doses of loop fluid show a definite resistance against the intoxication of a closed duodenal loop and may survive twice the usual period.

A dog that recovers from simple intestinal obstruction may possess a strong resistance to the intoxication of a closed duodenal loop, thus indicating a similar type of intoxication in the two conditions.

The sera of immune dogs are inactive when incubated with duodenal loop fluid.

The organ extracts and emulsions (liver, spleen, lung) of immune dogs rapidly destroy the loop poison during incubation \textit{in vitro}.

This destructive property is possessed by a clear filtrate of the digested immune organs, excluding adsorption, and is lost after long periods of incubation (twelve weeks).

We are investigating the action of this immune organ extract to determine whether it can destroy the closed-loop poison \textit{in vivo} and perhaps be of value in treatment.
BIBLIOGRAPHY.
3. Whipple, Stone, and Bernheim, idem, p. 307.