Effect of acid infusion into various levels of the intestine on gastric and pancreatic secretion in the cat

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SUMMARY Intraduodenal infusion of increasing amounts of hydrochloric acid solution results in a stepwise increase in the volume of pancreatic secretion and output of bicarbonate, reaching about 90% of amounts attained with exogenous secretin infused intravenously in increasing doses.

Acid infusion into the different regions of the intestine stimulates pancreatic secretion only from the duodenum and upper jejunum, suggesting that the area of endogenous release of secretin by acid is confined to the upper part of the small bowel in the cat.

Gastric acid secretion induced by pentagastrin, but not by histamine, is inhibited by acid perfusion of the duodenum. The acidification of other parts of the small intestine does not result in any change in gastric acid secretion induced either by pentagastrin or by histamine.

Previous studies have shown that acidification of the duodenum in the cat inhibits gastric acid secretion and stimulates pancreatic secretion, due to the endogenous release of secretin (Konturek, Dubiel, and Gabryś, 1969; Konturek, Gabryś, and Dubiel, 1969). No study, however, has compared the relative effects on gastric and pancreatic secretion of acid infusions into various regions of the small intestine. This report is an attempt to localize the extent to which secretin is released by acid irrigation of different levels of the intestine in cats with chronic gastric and pancreatic fistulas.

METHOD

SURGICAL PROCEDURE The study was performed on five cats weighing 2-5 to 3-0 kg, prepared with gastric fistulas according to the method previously described (Konturek and Król, 1966), and pancreatic fistulas using a Thomas-type cannula placed in the duodenum opposite the common ampulla of Vater (Fig. 1). The common bile duct was transected within the duodenal wall, allowing for the flow of bile into the duodenum through the transected duct. The remaining part of the duct was ligated at the point where it joins the major pancreatic duct to form a single channel entering the duodenum through the common ampulla. The animals were also provided with three small Thomas-type cannulas (Fig. 1), of which one was placed in the upper jejunum about 25 cm distal to the ligament of Treitz, the second in the distal jejunum about 50 cm distal to the ligament of Treitz, and the third in the ileum about 25 cm proximal to the caecum.

SECRETORY PROCEDURE The secretory tests were started about two weeks after the cats had recovered from surgery.

FIG. 1. The different types of cannula used in the study: left, intestinal cannula; middle, duodenal cannula; and right, gastric cannula.
Gastric juice was collected into the graduated tubes by opening the gastric fistulas. Pancreatic juice was collected in the following manner. The duodenal fistula was opened and a polyethylene tube, 1 mm external diameter, was inserted through the ampulla about 6 cm into the major pancreatic duct and brought out through a small hole in the cok placed in the duodenal cannula.

At least two basal 15-minute collections of gastric and pancreatic juice were made each time to determine the fasting level of gastric or pancreatic secretion. If food was present in the stomach, or a high level of gastric acid secretion was found, the experiment was not carried out that day. The tests were made on the same animals no more than three times a week.

The acidity of gastric juice was determined by titration of 0.2 ml samples to pH 7.0 using 0.1 N NaOH with an autoburet titrator. Acid output was expressed in milliequivalents per 15 minutes.

The concentration of bicarbonate in pancreatic juice was estimated in 0.5 ml samples by adding 1.0 ml of 0.1 N HCl. The mixture was briefly boiled, cooled to room temperature, and the residual acid was titrated to pH 7.0 using 0.1 N NaOH (autoburet). The output of bicarbonate was expressed in m-equiv/15 minutes or per hour.

Test Procedure Gastric acid secretion was examined under basal conditions and after the intravenous infusion of a constant dose of either histamine dihydrochloride (80 μg/kg/hour) or pentagastrin (8 μg/kg/hour), using a peristaltic pump. These doses had been shown previously on the same animals to induce near maximal gastric acid secretion. Throughout each experiment one level of the intestine was perfused from a peristaltic pump at a constant rate of 20 to 40 ml per hour. Irrigation was performed with a plastic tube, 1.5 mm external diameter, which was passed into a given region of the intestine through the intestinal cannulas. The perfusion fluid was 0.15 M NaCl during the first seven 15-minute periods, then 0.1 N HCl for four 15-minute periods, and finally 0.15 M NaCl for the last four 15-minute periods. The amount of acid infused was adjusted to give about 1 m-equiv/kg/hour.

The percentage inhibition of acid output during acid perfusion of a given region of the intestine was calculated for each test. The mean output of acid during the three 15-minute periods immediately preceding the infusion of acid solution was taken as the control, and the mean output during the next 15-minute periods of acid infusion was expressed as a percentage change from this control rate.

Pancreatic secretion was examined under basal conditions and in response to graded doses of intravenously infused synthetic secretin or to hydrochloric acid solution infused into the duodenum in increasing amounts. Secretin, dissolved in 10 ml saline, was given intravenously during each day's tests in three doses ranging from 0.2 to 6.4 μg/kg/hour, through a polyethy-
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![Graphs of flow rate and bicarbonate output](https://via.placeholder.com/528x697)

**FIG. 2.** Pancreatic volume flow and bicarbonate output after intraduodenal infusion of increasing amounts of HCl or after infusion of synthetic secretin in increasing doses. Each curve is a mean of two experiments on each of five cats with gastric fistula opened.

**FIG. 3.** Pancreatic flow rate and bicarbonate output after the infusion of acid amounts of 1 m-equiv/kg/hour into different regions of the intestine. Mean of two experiments on each of five cats.

Bicarbonate output were attained by intraduodenal acid infusion in amounts of 1 m-equiv/kg/hour, reaching about 90% of the maximum achieved by intravenous administration by synthetic secretin. The stimulation of pancreatic secretion was also obtained during acid infusion into the upper jejunum. In this instance the peak volume was about 80% and peak bicarbonate output was about 70% of that obtained with intraduodenal acid infusion. No change in pancreatic secretion was seen during the acidification of the distal jejunum or ileum (Fig. 3).

**EFFECT OF ACID INFUSION INTO VARIOUS LEVELS OF THE INTESTINE ON PENTAGASTRIN- AND HISTAMINE-INDUCED GASTRIC ACID SECRETION** Pentagastrin-induced gastric acid secretion was depressed significantly only during intraduodenal acid infusion. The inhibition of acid secretion reached about 50% of the control level (Fig. 4). Acid infusion into the upper jejunum caused an initial small decrease in the gastric acid secretion stimulated by pentagastrin, which then showed a slight tendency to increase. Acid irrigation of the distal jejunum or ileum did not result in any change in pentagastrin-induced gastric acid secretion, which showed a tendency to decline during the experiment. Histamine-induced gastric acid secretion remained unchanged by acid perfusion of the duodenum or other parts of the intestine (Fig. 5).

**DISCUSSION**

These data indicate that endogenous release of secretin by acid is confined to the duodenum and upper jejunum and that pentagastrin-induced gastric acid secretion is inhibited in the cat only after the acidification of the duodenum.

The distribution of secretin in the intestine has...
been previously studied by Mellanby (1926), who found that in cats, unlike other species, secretin can be extracted only from the duodenal mucosa. To our knowledge no study has been undertaken to localize the endogenous release of secretin in the cat by acid infusion into different regions of the intestine. We have demonstrated that the area in which secretin can be released by acid irrigation in the cat extends to the upper jejunum. It was found that jejunal acidification resulted in a somewhat lesser pancreatic stimulation than that observed during the acidification of the duodenum.

It is of interest that acid infused into the upper jejunum did not inhibit the pentagastrin-induced gastric acid secretion seen during acid infusion into the duodenum. This might be attributed to a relatively smaller endogenous release of secretin by acid in the jejunum as compared with that in the duodenum. In contrast to the almost complete inhibition of gastrin-induced gastric secretion
in the dog (Johnson and Grossman, 1968) by acid irrigation of the duodenum, we observed only about 50% inhibition of pentagastrin-induced gastric secretion in the cat. This agrees with our previous report (Konturek, 1968), showing that in the cat gastric secretion stimulated by pentagastrin is more resistant to inhibition by intraduodenal acid or intravenous secretin.

Among several agents releasing secretin from the intestinal mucosa and stimulating pancreatic secretion, hydrochloric acid was recognized over a century ago (Leuret and Lassaigne, 1825; Dolinski, 1894) as the most effective. The efficiency of hydrochloric acid in stimulating pancreatic secretion was not properly evaluated before highly purified secretin preparations were available (Ondetti, Sheehan, and Bodanszky, 1967).

Our present study demonstrates that the maximal pancreatic secretion achieved by exogenous synthetic secretin was only slightly higher than that obtained with intraduodenal acid infusion. The difference in the stimulation of the pancreatic secretion induced by exogenous secretin, and secretin released endogenously by acid in the duodenum, might be attributed to the acid perfusion of the middle and distal parts of the duodenum, which were shown to contain a smaller amount of secretin than the upper part (Mellanby and Huggett, 1926).

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