

Effect of Duodenal Freezing on the Secretin Mechanism.* (28156)

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Local gastric cooling (5 to 10°C) results in temporary cessation of HCl and peptic secretion(1,2) and such cooling of an isolated canine antral pouch markedly inhibits its ability to liberate gastrin(3) in response to peptone stimulation, during the period of cooling. Gastric freezing, with temperatures in the range of -10°C for 60 minutes, produces a more profound and prolonged secretory depression, which has also been demonstrated following freezing of isolated canine Heidenhain, Pavlov and antral pouches. These depressions commonly last for several months, and in some instances up to one year(4). The purpose of the present experiment is to determine whether freezing the duodenum will abrogate the secretin effect described by Bayliss and Starling(5).

Procedure. Mongrel dogs were anesthetized with sodium pentobarbital, and the duodenum was mobilized through a short upper midline abdominal incision. A 25 cm long duodenal balloon was fashioned out of an inch wide piece of Penrose rubber drain tied at the distal end. The proximal end was attached to the Mayon 5/16" outflow tube of a gastric hypothermia machine.[†] The inflow tube was #320 polyethylene. In most experiments this was a multiperforated tube extending almost the entire length of the duodenal balloon, thus achieving a fairly uniformly dispersed inflow and freezing. The duodenal balloon was introduced into the duodenum through a short pre-pyloric gastric incision and positioned within the abdomen under direct vision to fit the entire duodenal loop, distending it slightly. Cold absolute alcohol was pumped into and circulated through the balloon at inflow temperatures of -17° to -20°C. In 23 dogs, prepared in this manner, the duo-

denal loop was frozen for 10 minutes, in 21 dogs it was frozen for 20 minutes, in 4 for 30 minutes and in 2 for 60 minutes. At the end of the perfusion period the balloon was emptied and withdrawn. The gastrotomy incision was closed transversely with a few stitches of chromic catgut, and the abdomen was closed.

The animals were reoperated upon from 4 to 90 days later. The duodenum was exposed and the duodenal loop, previously frozen, was isolated with its blood supply intact, by means of ligatures about the pylorus and distal duodenum, just proximal to the ligament of Treitz. The common bile duct was ligated to preclude the influx of bile into the isolated duodenal segment. The main pancreatic duct was isolated and cannulated with a No. 90 polyethylene tube. Over a period of 15 minutes, the basal pancreatic flow rate was established by counting the number of drops of pancreatic juice secreted during 3 successive intervals of 5 minutes (Fig. 1). After the third such period, 15 to 25 cc of 0.1N HCl was introduced into the isolated duodenal loop. The secretory response of the pancreas upon placement of the HCl in a normal and a previously frozen duodenal loop is shown in Fig. 2 and 3.

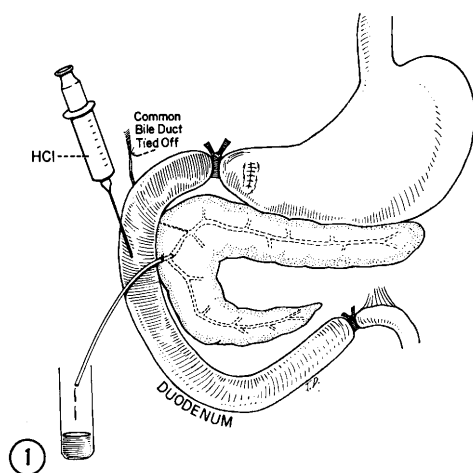
The duodenal response to intraluminal HCl was usually complete in 30 minutes—after which the pancreas again secretes at its basal rate of 1 or 2 drops per 5 minutes. The HCl was then withdrawn from the duodenum.

To investigate the possibility of pancreatic failure, the pancreas was then tested by a standard dose of 10 Ivy units of purified secretin (Lilly) given intravenously in a single injection. The secretion was measured as drops per 5 minutes, and total secretory response was usually completed within 30 minutes. In 13 control dogs the isolated duodenal loop was prepared in the same manner, and the response to HCl and secretin quantitated in the same way.

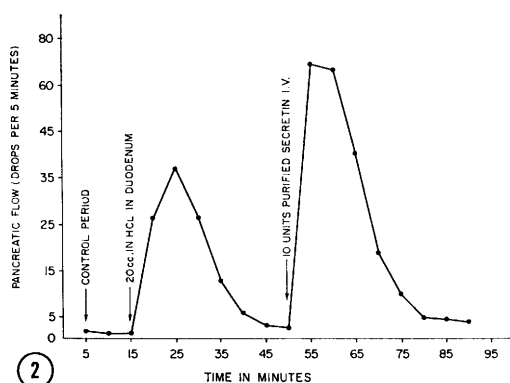
Results and discussion. Twenty-three dogs

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THE MEAN RESPONSE TO HYDROCHLORIC ACID INFUSION AND SECRETIN INJECTION IN 13 CONTROL DOGS



A TYPICAL RESPONSE TO HYDROCHLORIC ACID INFUSION AND SECRETIN INJECTION ONE WEEK AFTER DUODENAL FREEZING FOR TEN MINUTES

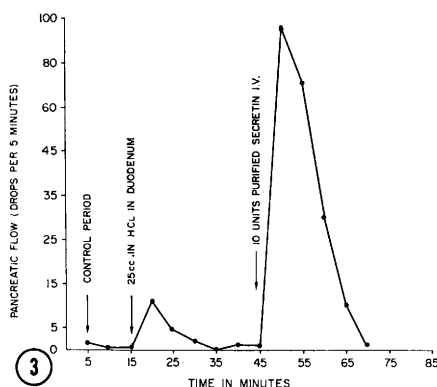


FIG. 1. Secretin test preparation employed in control and post-duodenal freezing animals. Note ligatures about pylorus, distal duodenum and common bile duct.

were subjected to duodenal freezing for 10 minutes at inflow temperatures ranging from -17°C to -20°C . At the end of the freezing period, the duodenum was felt to be firm and cold, but not stone hard, as is the stomach when perfused for one hour at this temperature. The duodenal wall immediately post-freezing becomes slightly edematous and aperistaltic. If, however, the duodenum is first extraperitonealized on sterile towels, and then frozen, a white frost soon appears on the serosa and the entire wall becomes solid. It soon became apparent that the duodenum does not tolerate exposure during freezing, nor long periods of freezing (1 hour) as well as the stomach. No mortality from necrosis of the duodenum was encountered when the duodenum was frozen for 10 minutes within the abdomen (17 dogs). When the freeze period was increased to 20 minutes with the duodenal loop within the abdomen, the mortality from duodenal necrosis rose to 42.9%. The 17 dogs surviving 10 minutes of duodenal freezing to undergo subsequent secretin testing exhibited no significant intraperitoneal pathological findings. Adhesions between the liver and the duodenum were present in 7 dogs. The duodenal mucosa looked normal grossly in most instances, and was not friable. A few times, areas of mucosal brown discoloration with thinning were noted.

The pancreatic secretory data show essentially the same basal secretory rates in control and test groups. When the control group was stimulated with 0.1N HCl infusion into the duodenum, the average total pancreatic response to the secretin released was 120 drops (Table I). This response was significantly reduced in the test group, to 33.8 drops average which is 28.2% of the control response. The *p* value is less than .01; thus, the difference between these groups is statistically significant. In sum, duodenal freezing significantly reduces the secretin response of the duodenum to acid stimulation.

In animals in which the duodenal loop was

FIG. 2. Pancreatic secretory response to secretin and HCl in 13 control dogs, tested as in Fig. 1.

FIG. 3. A typical response in an animal with prior duodenal freezing, indicating marked depression of secretin release.

TABLE I. Secretin Response in Control Dogs.

No.	Total response to HCl	Total response to secretin (10 Ivy U)
1	291	328
2	93	257
3	81	99
4	33	112
5	160	280
6	185	217
7	172	227
8	61	72
9	23	273
10	122	277
11	173	401
12	26	55
13	134	107
Avg response	120	208
Standard deviation	± 77.8	± 109

for at least 3 months. Average total response to HCl instillation in the post-freeze duodenum is 28.2% of control mean response. More prolonged periods of freezing do not result in greater depression. 2. No evidence of significant pancreatic derangement has been found to result from duodenal freezing. 3. If the duodenum is exposed to air during the freezing process, there is a significant incidence of duodenal necrosis, which was not observed with intraperitoneal freezing for 10 minutes.

1. Wangensteen, O. H., Root, H. D., Jenson, C. B., Imamoglu, K., Salmon, P. A., *Surgery*, 1958, v44, 265.

TABLE II. Secretin Response to Duodenal Freezing of Various Durations.

No.	Duration of freezing (min)	Total response to HCl	Total response to secretin	Test interval (days)
1	10	13	118	4
2, 3	10	19, 41	206, 31	7
4, 5, 6	10	66, 72, 126	198, 86, 89	14
7, 8, 9, 10	10	2, 3, 39, 58	130, 173, 200, 97	28
11, 12, 13	10	29, 52, 12	116, 59, 168	56
14	10	2	243	67
15, 16, 17	10	12, 26, 2	120, 182, 96	90
Avg response		33.8	136	
Standard deviation		± 33.2	± 52.5	
18	20	6	162	3
19, 20, 21	20	29, 53, 93	135, 324, 485	4
22	20	6	75	18
Avg response		37.4	236	
23	30	11	62	4
24	30	45	204	5
25	60	6	266	32
Avg response		20.6	177	

frozen 20, 30, and 60 minutes, the secretin response to intra-duodenal HCl was also markedly depressed (Table II), but no more so than the depression following a 10 minute freeze. The response to purified secretin showed no significant difference in control and test groups.

Conclusions. 1. Experience with 17 dogs subjected to duodenal freezing for 10 minutes suggests that secretin release to acid stimulation of the duodenum is significantly impaired

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