

antihypertensive effect. Moreover, a preliminary experiment with the dog lung extract in rats likewise indicated no prophylaxis against experimental renal hypertension.¹⁰ However, antihypertensive substances not obtained by this method of extraction may be present in lung.

A reduction in the amount of functioning lung tissue was shown to be without effect on the systemic blood pressure of moderately hypertensive animals. No regeneration of lung tissue was found in these dogs on sacrifice, and it seems likely that sufficient tissue was removed to demonstrate some effect if the lung plays an active antipressor role in experimental renal hypertension.

Summary. 1. Daily intramuscular injections of lung extract for two months preceding and following clamping of the renal artery and

¹⁰ Klatch, B. Z., unpublished data.

contralateral nephrectomy failed to prevent the development of hypertension in two dogs. 2. Pneumectomy performed on 2 renal hypertensive dogs and pneumectomy plus contralateral lobectomy on 2 other hypertensive animals did not alter their pressure levels. 3. The pressures of 2 normotensive dogs were not influenced by pneumectomy, nor were the hypertensions subsequently produced by renal artery constriction and contralateral nephrectomy. 4. The results of these experiments suggest, but do not prove, that the lungs do not elaborate an antihypertensive substance and do not inactivate the pressor agent of experimental renal hypertension. 5. Further work is necessary to explain the pulmonary normotension of renal hypertensive dogs.

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16352

Relationship Between the pH of the Duodenal Content and Pancreatic Secretion.*

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Bayliss and Starling¹ demonstrated the mechanism whereby acid introduced into the intestine provoked a flow of pancreatic secretion. With increasing interest in the role of the endocrine glands in the regulation of bodily function it has been widely assumed that the secretin mechanism largely determined the volume of pancreatic secretion.² Farrell and Ivy,³ who feel the secretin mech-

anism is the most important, found that a denervated pancreas failed to secrete as much as expected. McClure,⁴ on the basis of his determination of enzyme in the duodenal content, stated that "stimulation of the external enzymic function of the pancreas is dependent on some factor or factors unrelated to acidity of intestinal contents." Thomas

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¹ Bayliss, W. M., and Starling, E. H., *Am. J. Physiol.*, 1902, **28**, 325.

² *Howell's Text Book of Physiology*, 15th Edition, 1946, p. 1064, W. B. Saunders Co., Philadelphia; *Physiology in Health and Disease*, C. S. Wiggers, 4th Edition, 1947, p. 809, Lea and Febiger, Philadelphia.

³ Farrell and Ivy, *Am. J. Physiol.*, 1926, **78**, 325.

⁴ McClure, C. W., *Functional Activities of the Pancreas and Liver*, Medical Authors Publishing Co., 1937.

⁵ Thomas, J. E., and Crider, J. O., *Am. J. Physiol.*, 1940, **131**, 349.

and Crider⁵ found that acid, as a stimulant for pancreatic secretion was effective when the pH was about 4; however, a copious flow of pancreatic juice was produced only when the pH was reduced to 3 or less. The latter investigators also⁶ found that, in the dog, after a meat meal, the pH of the duodenal content generally hovered around 4, at which level, a threshold response only would be expected.

Since pancreatic juice with a pH of about 8 is secreted into a vulnerable part of the duodenum, and is an excellent buffer, it is generally believed that this secretion plays a decisive role in the neutralization of acid chyme.⁷ Hoerner⁸ showed that even when the pancreatic juice was excluded from the duodenum, a significant degree of neutralization of the acid gastric contents occurred. On the other hand, DeBakey⁹ felt that the pancreatic juice played a lesser role than did bile in the prevention of ulcer in the intestinal tract.

In the course of study undertaken to determine the normal secretion of the pancreas after the ingestion of various foodstuffs, observations were made which yielded information pertaining to both of these problems.

Methods. Healthy adult dogs were provided with gastric and duodenal tubulated fistulae as has been described elsewhere.¹⁰ The accessory pancreatic duct was doubly ligated and severed; the duodenal fistula was placed opposite the ostium of the main pancreatic duct. (Fig. 1). After complete recovery from the above operation, the animal was placed in a standing position on a table by means of a comfortable muslin harness. A glass cannula was introduced into the main pancreatic duct; two tubes were placed into

the stomach and then through the pylorus into the duodenum, the shorter tube being so placed that its end was in the region of the orifice of the main pancreatic duct while the end of the longer tube was placed 3 inches beyond this point. The gastric fistula was stoppered and the duodenal fistula was covered with a rubber dam which was pierced to permit the small pancreatic cannula to protrude to the outside.

Observations were made on 3 dogs so prepared. The pancreatic juice was collected and the volume measured every 10 minutes. In one series of experiments, each 10-minute specimen was introduced into the duodenum through the proximal tube; in a second group the pancreatic juice was excluded from the intestine during the period of observation. Samples of duodenal content were withdrawn from the longer tube at intervals and the pH determined electrometrically, using a glass electrode. These samples were then promptly returned to the duodenum. Preliminary observations were made in the fasting state for one hour, after which the animal was fed small amounts of different foodstuffs and observations were continued for five hours. In a few experiments large meals were fed, and observations continued for a longer period of time.

Results. A comparison of the pH determinations of the duodenal contents made when the pancreatic juice was excluded from the intestine with the observations made when it was reintroduced, reveals that although, in general, the pH is lower when the juice is not present, the acidity did not exceed that observed when the juice was replaced into the duodenum. The difference between the 2 groups of experiments is evident when individual foodstuffs are considered separately. There is a tendency for the pH to be higher when the pancreatic juice is present.

Fig. 2 presents this data *in toto*. The ordinates represent the pH determined after the ingestion of food, the abscissae denote the volume of pancreatic juice secreted in the ensuing 10-minute period. Entirely similar results were obtained when the volume of pancreatic juice secreted during the same ten-

⁶ Thomas, J. E., *Am. J. Dig. Dis.*, 1940, **7**, 195.

⁷ Mann, F. C., and Bollman, J. L., *Am. J. Dig. Dis.*, 1935, **2**, 284; Hoerner, M. T., *Am. J. Dig. Dis.*, 1935, **2**, 300.

⁸ Hoerner, M. T., *Am. J. Dig. Dis.*, 1935, **2**, 288.

⁹ DeBakey, M. E., *Arch. Surg.*, 1937, **34**, 230.

¹⁰ Scott, V. Brown, Collingnon, W. J., Bugel, H. J., and Johnson, G. C., *Am. J. Physiol.*, 1941, **134**, 248; Hart, Wm. M., and Thomas, J. E., *Gastro-enterology*, 1945, **4**, 409.

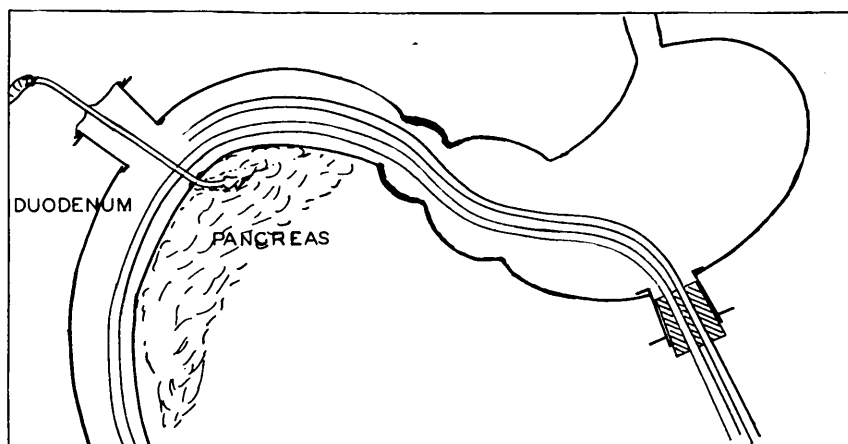


Fig. 1.

Diagram showing relationships of the gastric and duodenal fistulas and the pancreatic cannula; also, the position of the two tubes introduced into the duodenum.

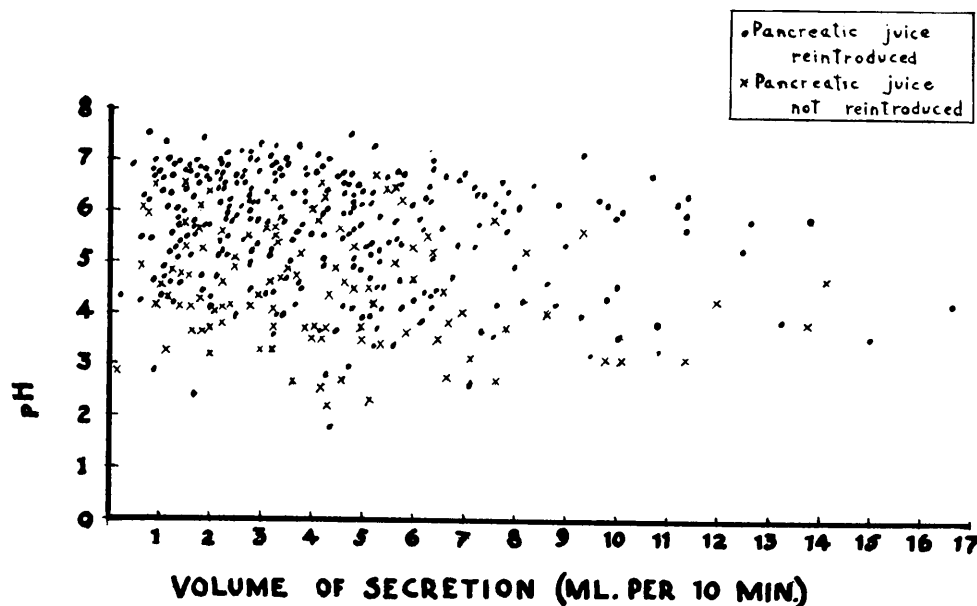


Fig. 2.

Scattergram showing the relationship between the pH of the duodenal content and the volume of pancreatic juice secreted during the ensuing 10-minute period.

minute period was plotted against the pH. Dots represent determinations made when the pancreatic juice was returned to the duodenum, crosses represent similar determinations made when the juice was withheld for the entire period of observation. The range of the pH was lower, but did not exceed the limits observed when the pancreatic juice was present in the duodenum. It is evident that the pancreatic juice exerts only a mod-

erate effect on the pH of the intestinal content.

The same data may be used to study the effect of acid in the intestine on the volume of pancreatic secretions. It is evident from a glance at this graph that no clear correlations between the volume of pancreatic secretion and the pH of the duodenal content existed in these experiments. This is rather strikingly illustrated by individual experi-

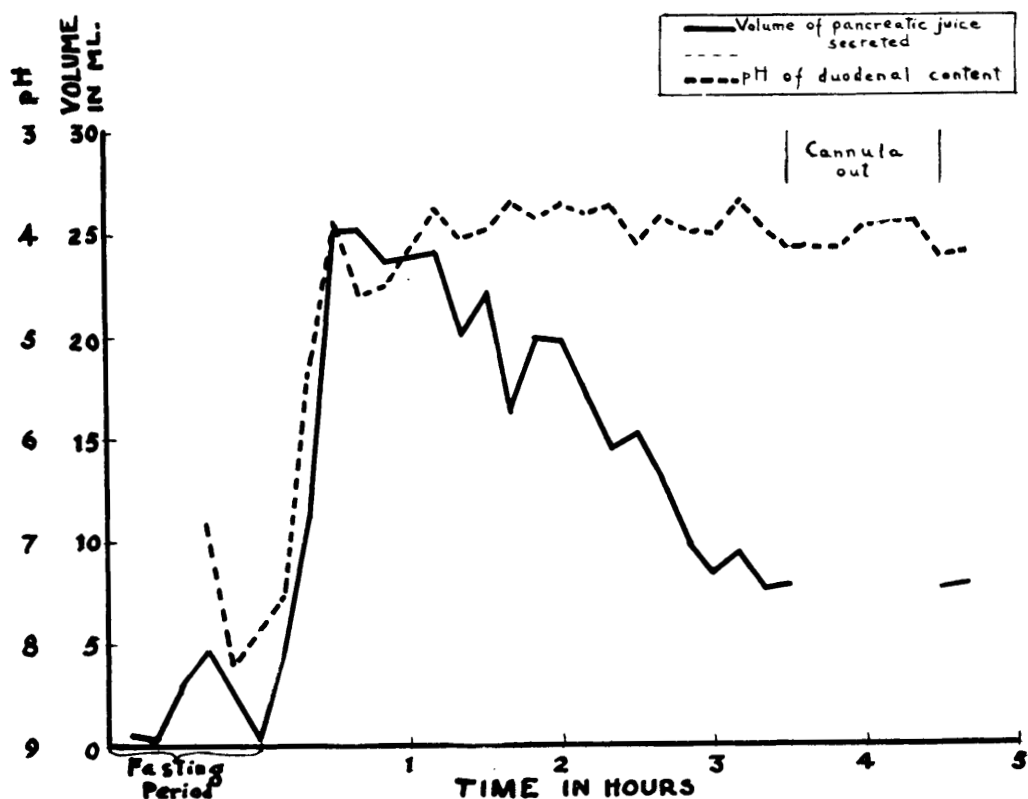


FIG. 3.

Curves of a typical experiment after the feeding of a large meal of meat, showing the relatively constant pH of the duodenal content in relation to the marked variation in the secretion of pancreatic juice at 10-minute intervals.

ments. Fig. 3 illustrates the results obtained when a large meal of meat was fed. It will be noted the pH of the duodenal content throughout the period of observation hovered about 4, whereas, the volume of pancreatic juice varied considerably. Fig. 4 represents data obtained after a small feeding of bread. It does not seem likely that the fluctuations in the volume of the pancreatic juice were related to the differences in pH observed.

Comment. Our observations are in conformity with those of Hoerner; namely, that some neutralization of the acid chyme is attained by the action of bile, succus entericus and other secretions of the small intestine and its appendages, but that generally more complete neutralization results when pancreatic juice is present in the intestine.

In addition, our findings would suggest that during digestion, the volume of pancreatic

juice secreted is determined by other factors than the acidity of the duodenal content alone. It would seem plausible that the secretin mechanism may "prime the pancreatic pump," since the duodenal acidity is at, or may exceed, the threshold value. However, other factors must play a determining role. Thus Crider and Thomas¹¹ found that, after section of the vagus nerves, the introduction of acid into the intestine was less effective in promoting pancreatic secretion than previously. Possibly two or more different stimuli must be active at any one time to evoke a copious pancreatic secretion, as does occur during the digestive period. However, it would seem that when the duodenal acidity exceeds a given threshold value, as does oc-

¹¹ Crider and Thomas, *Am. J. Physiol.*, 1944, **141**, 730.

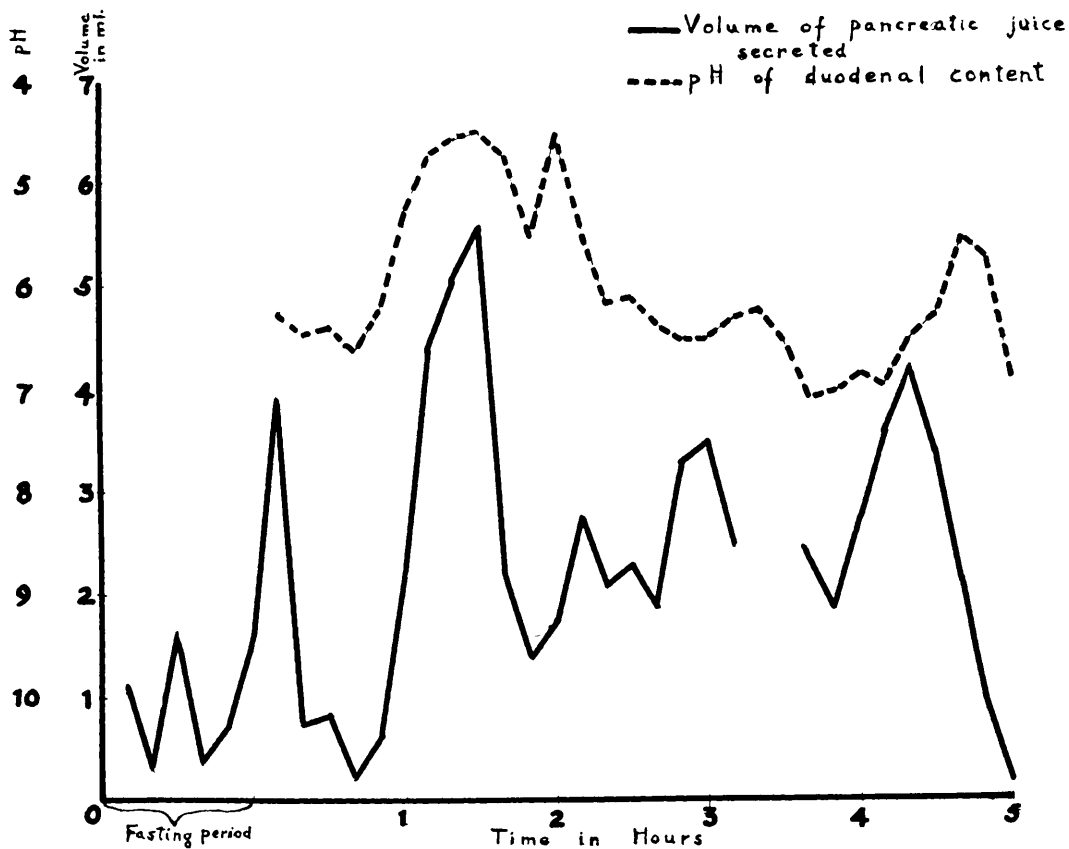


FIG. 4.

Curve showing a typical experiment after small feeding of bread, demonstrating the lack of relationship between the pH of the duodenal content and the secretion of pancreatic juice at any given time. Determinations were made at 10-minute intervals.

casionaly occur, the secretin mechanism may call forth a larger volume of neutralizing pancreatic juice.

Conclusions. 1. Pancreatic juice provides buffering material which serves to neutralize gastric content more effectively, but some

degree of neutralization is attained from other secretions of the small intestine and its appendages.

2. No correlation is evident between the acidity of the duodenal content and the volume of pancreatic secretion.