

A STUDY OF THE PANCREATIC RESPONSE TO FOOD AFTER GASTRECTOMY IN MAN*

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The results of intubation tests on 50 patients before and after gastrectomy have been reviewed. Following gastrectomy, the pancreatic response to food is modified in the following manner.

- (1) There is an increase in the resting volume of secretion.
- (2) After a Billroth I operation, the output in one hour after a meal is some two-thirds of the pre-operative output.
- (3) After a Polya gastrectomy, the pancreas continues to secrete at its resting rate after meals.
- (4) Dissociation of enzymes occurs in the afferent loop after a Polya operation. Lipase is frequently absent from the intestinal contents, and trypsin occasionally so.
- (5) Vagal section appears to be an important factor in the production of the new pattern of response.

Experimental studies on dogs have shown that the pancreatic response to food is reduced after gastrectomy (Annis and Hallenbeck, 1952; Richman, Lester, Hollander, and Dreiling, 1954). The early investigations of the problem in man (Stein and Fried, 1923; Glaessner, 1927; Stern, 1929; Santy, Mallet-Guy, Chambon, and Folliet, 1939) do not afford any clear picture of the effect of the operation. The recent work of Lundh (1958), however, has shown that the concentration of pancreatic enzymes in the intestine is very much reduced after gastrectomy, and that a large part of any meal does not mix with the enzymes. Studies with isotopic fat (Shingleton, Isley, Sanders, Floyd, Baylin, Postlethwait, and Ruffin, 1957; Baylin, Isley, Sanders, Reeves, Ruffin, Hymans, and Shingleton, 1957; Ruffin, Keever, Cheers, Shingleton, Baylin, Isley, and Sanders, 1958) have indicated that the absorption defect that follows gastrectomy is similar to that occurring in patients with pancreatic deficiency. This may be due either to reduced pancreatic output after gastrectomy or to the meal and pancreatic enzymes mixing poorly.

Dragstedt (1952), Warren (1954) and MacLean, Perry, Kelly, Mosser, Mannick, and Wangenstein (1954) have stated that any modification of pancreatic response following gastrectomy is not important. Indeed, the view of the majority is that

inadequate mixing of food and enzymes is one of the features of the post-gastrectomy state (Warren, 1954; Wells, 1955; Polak and Pontes, 1956; Kiekens and Lundh, 1957).

PRESENT INVESTIGATION

The purpose of this paper is to summarize the results of a study of the pancreatic response to food after gastrectomy carried out in Bristol during the past nine years. Intubation tests with a meal were carried out on 50 patients before and after a Billroth I gastrectomy, each patient having four tests, two before the operation to give controls, and two after the operation. The aim of the investigation was to determine the effect of gastric resection on the pancreatic response to food entering the duodenum on the one hand, and entering the jejunum on the other. The tests were therefore grouped as follows:

Series A.—The pancreatic response to a meal entering the duodenum before operation

Series B.—The response to a meal entering the jejunum before operation

Series C.—The response to a meal entering the duodenum after gastrectomy

Series D.—The response to a meal entering the jejunum after gastrectomy.

In each series, 50 results were obtained for analysis, and it is submitted that those in Series C indicate the pancreatic response occurring after a Billroth I operation, and those in Series D afford an approximate index of the response after a Polya operation.

A four-lumen tube was used throughout the investigation, and it was passed under radiological control so as to occupy a position illustrated in Fig. 1. This

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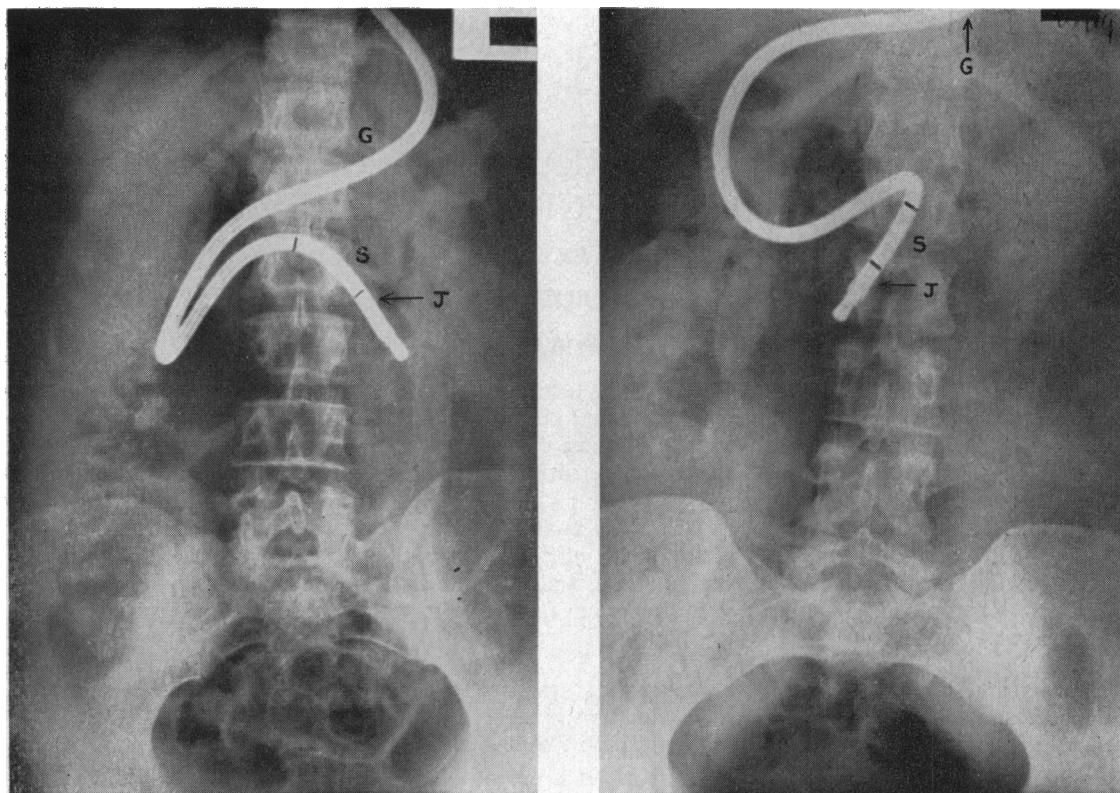


FIG. 1.—Radiograph of the position of the tube. G = site of holes for gastric suction. J = hole for introducing meal into the jejunum.

tube afforded access to the jejunum as well as permitting continuous gastric and duodenal aspiration. The general technique of intubation tests is well known, and it will be sufficient to say that the drill followed in these studies was similar to that of Lagerlof (1942) with reference to continuous suction and the treatment of the aspiration samples by ice-cooling and the addition of glycerine. In the tests in Series A and C, when two resting 10-minute samples of duodenal aspirate had been collected, 50 ml. of a meal (Table I) was introduced into the duodenum slowly over a period of four minutes. After two more minutes, the duodenum was emptied, and the aspirate was passed through the appropriate lumen in the tube into the jejunum. The duodenal contents were then collected for one hour in six 10-minute samples.

In Series B and D, resting samples were collected, but the 50 ml. meal was then given through the tube directly into the jejunum. After the lapse of the same time interval as in Series A and C, the duodenal contents were collected for an hour in six samples.

On all the samples, the following estimations were carried out: Volume, bicarbonate concentration and total bicarbonate output per sample, enzyme concentration and total enzyme output per sample. The bicarbonate content was determined by the indirect

TABLE I
COMPOSITION OF MEAL FOR INTUBATION TESTS

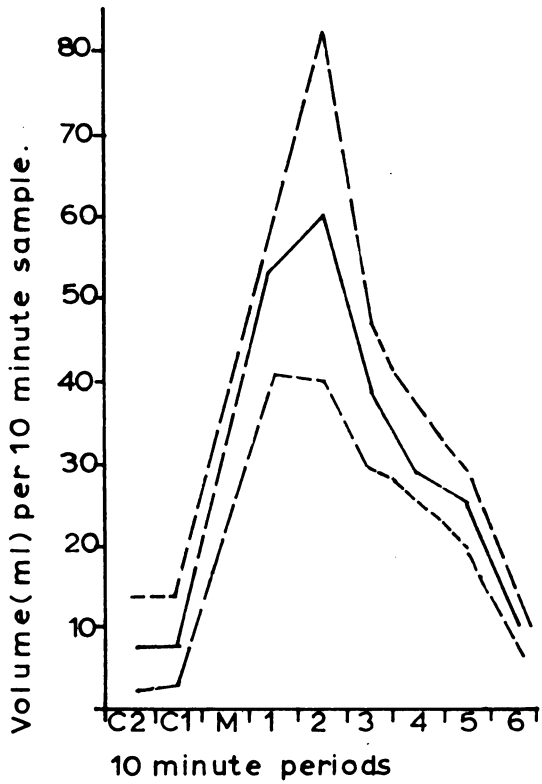
	Protein (g.)	Fat (g.)	Carbohydrate (g.)
Whole milk powder (per 100 g.)	27.5	27.0	37.5
Reconstituted 1 : 8 50 ml. contains	1.72	1.7	2.34
+ hepatovite	3.5	—	—
+ glucose	—	—	10.0
	5.2	1.7	12.34

titration technique of Lagerlof (1942), amylase by the Wohlgenuth method, trypsin by the Lagerlof (1942) method, and lipase by the technique of Cherry and Crandall. To avoid repetition, therefore, the various units referred to in the text are expressed as follows: Amylase in Wohlgenuth units, trypsin in ml. N/10 alcoholic KOH, and lipase in ml. N/20 NaOH.

RESULTS

COMPARISON OF SERIES A AND C.—This shows the effect of gastric resection on the pancreatic response to food entering the duodenum. The general pattern

Series A. Pre-operative Controls.



Series C. Post-operative.

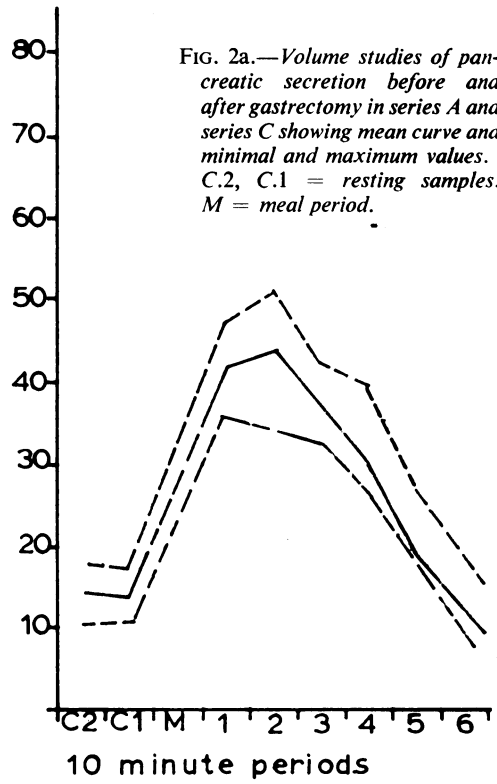


FIG. 2a.—Volume studies of pancreatic secretion before and after gastrectomy in series A and series C showing mean curve and minimal and maximum values. C.2, C.1 = resting samples. M = meal period.

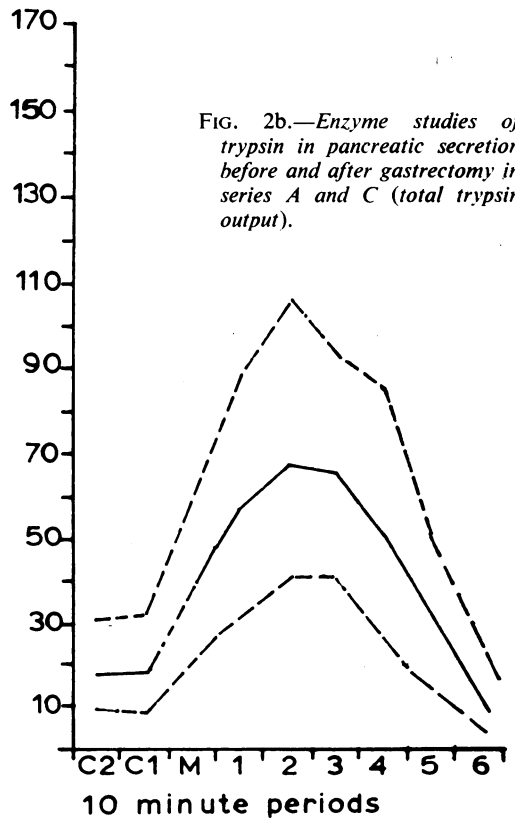
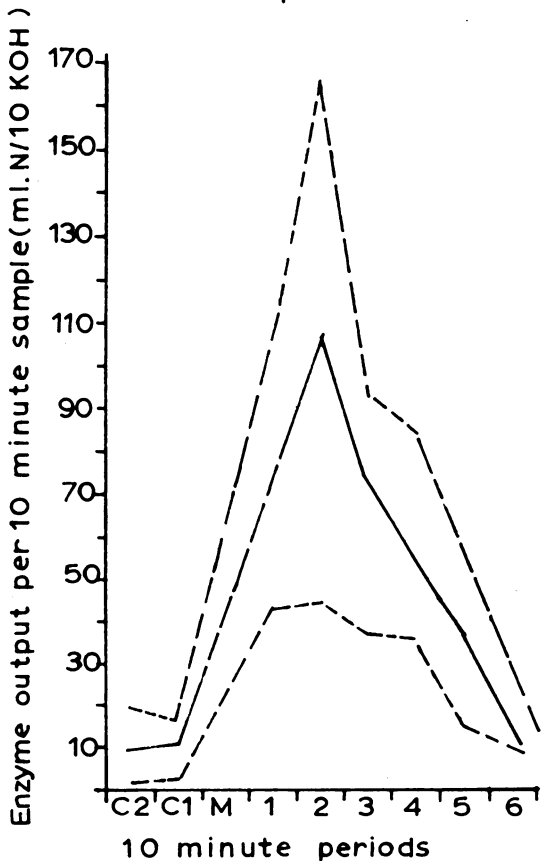


FIG. 2b.—Enzyme studies of trypsin in pancreatic secretion before and after gastrectomy in series A and C (total trypsin output).

before and after operation is illustrated in Fig. 2 (a) and (b), but the differences may be summarized thus:

(1) There was an increase in the resting volume per sample in the post-operative series compared with the pre-operative controls. In Series A, the mean 10-minute resting volume was 7.85 ml. (2.4-14.2 ml.), whereas in Series C it was 14.05 ml. (10.5-18.0 ml.). This increase was observed in 45 (90%) of the patients, and in 22 (44%) the post-operative volume was greater than the maximal levels recorded in Series A.

(2) The resting concentrations of bicarbonate and enzymes remained unchanged after operation, and are shown in Table II.

TABLE II
RESTING CONCENTRATIONS OF CONSTITUENTS OF PANCREATIC SECRETION BEFORE AND AFTER GASTRECTOMY

	Series A	Series C
Bicarbonate (mEq./litre)	18.82 (6.34)	19.15 (12.28)
Amylase (units/ml.)	2,580 (1000-5000)	2,761 (1000-4444)
Trypsin (units/ml.)	1.2 (0.4-1.7)	1.28 (0.6-1.9)
Lipase (units/ml.)	114 (91-162)	107 (81-156)

(3) After the meal, the variation in the total output in volume and in the various constituents of pancreatic secretion are shown in Table III.

TABLE III
COMPARISON OF PANCREATIC RESPONSE TO DUODENAL MEAL BEFORE AND AFTER GASTRECTOMY (OUTPUT PER 60 min. MEAN ± S.D.)

	Pre-operative Series A	Post-operative Series C
Volume (ml.)	219.8 ± 15.7	183.9 ± 14.5
Bicarbonate (mEq.)	12.27 ± 1.47	8.20 ± 1.01
Trypsin (units)	364 ± 38	275 ± 61
Lipase (units)	38,329 ± 3,534	27,364 ± 5,778
Amylase (units)	1,043,950 ± 690,299	651,664 ± 231,808

In the post-operative series, 46 (92%) of the patients had reduced volume, and in 18 (36%) the new volume was below the minimal values recorded in Series A. The mean reduction in volume for the one-hour period was 36.07 ml. (S.D. ± 20.4 ml.). The bicarbonate concentrations reached in the post-operative series were roughly two-thirds or three-quarters of the values reached in Series A. With reference to the total bicarbonate output for one hour, all the patients showed reduced output after operation, and in 45 (90%) the post-operative level was below the lowest values in the pre-operative controls. The mean reduction was 4.076 mEq. (S.D. ± 1.49 mEq.). The highest enzyme concentrations reached after operation were about half those recorded before operation. The total enzyme output

for one hour was also reduced after operation. In the case of amylase, 46 (92%) of the patients had a reduced output, the new level being below the pre-operative range in 20 (40%). In 45 patients (90%), trypsin output was reduced, and in 17 (34%) this was below the minimum pre-operative value. The output of lipase was reduced in 49 (98%) of the patients, being below the pre-operative range in 22 (44%). The mean reductions were as follows:

Amylase	392,292 units (S.D. ± 293,622 units)
Trypsin	89.30 units (S.D. ± 77.0 units)
Lipase	109.64 units (S.D. ± 68.0 units)

(4) The bile content of the samples differed in the two groups. In the pre-operative series, the maximum bile coloration was seen in the first samples in 39 (78%) of the patients, but in Series C, the bile content of the samples was greatest at the end of the hour in 36 (72%) of the patients.

COMPARISON OF SERIES B AND D.—This comparison indicates the effect of gastrectomy on the pancreatic response to food entering the jejunum directly. The general pattern of the response before and after operation is illustrated in Fig. 3 (a) and (b). The observed differences were as follows:

(1) Again, there was an increase in the resting output in the post-operative group, *i.e.*, a mean volume of 12.1 ml. (9.16-2 ml.) per 10-minute sample in Series D compared with 7.7 ml. (2.6-12.0 ml.) per sample in Series B. The increase was recorded in 37 (74%) of the patients, and in 19 (38%) the new value was greater than the maximum levels observed pre-operatively.

(2) The resting concentrations of bicarbonate and enzymes were unchanged and were similar to those shown in Table II.

(3) After the meal, the total output in the two groups is shown in Table IV.

TABLE IV
COMPARISON OF PANCREATIC RESPONSE TO JEJUNAL MEAL BEFORE AND AFTER GASTRECTOMY (OUTPUT PER 60 min. MEAN ± S.D.)

	Pre-operative Series B	Post-operative Series D
Volume (ml.)	102.4 ± 6.96	78.5 ± 10.6
Bicarbonate (mEq.)	2.768 ± 0.476	2.0344 ± 0.401
Trypsin (units)	121 ± 15	89 ± 19
Lipase (units)	12,800 ± 1,386	8,053 ± 1,204
Amylase (units)	330,782 ± 72,550	187,652 ± 40,652

With reference to the volume for the one-hour period, 48 (96%) showed a reduction in Series D compared with Series B, and in 39 (78%) the post-operative volume was less than the minimum observed in the pre-operative series. Indeed, the main feature of the volume response curve post-operatively is that it is virtually flat. Similarly, the

Series B. Pre-operative Controls.

Series D. Post-operative.

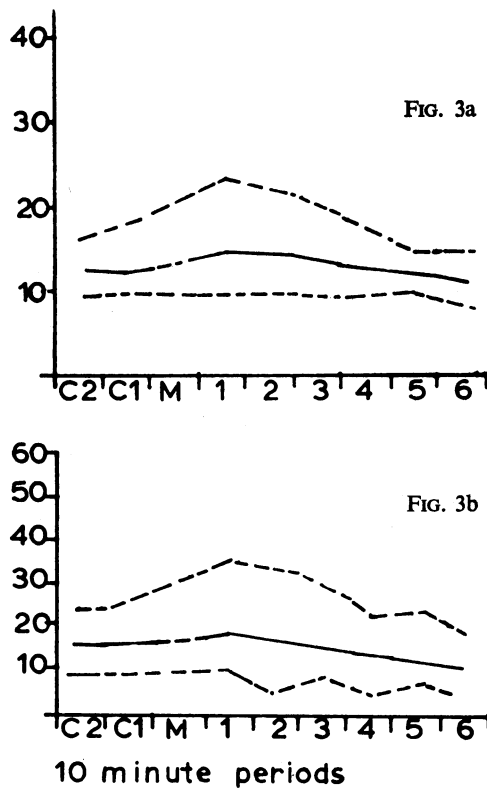
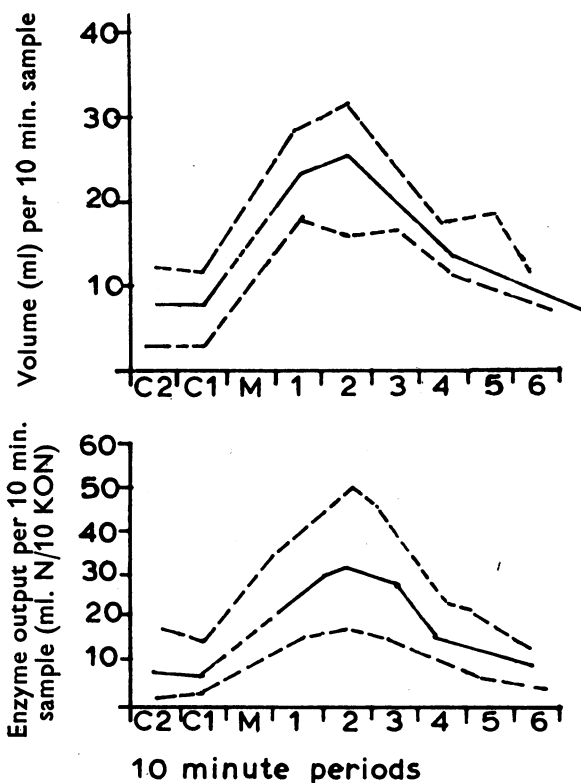


FIG. 3a.—Volume studies of pancreatic secretion before and after gastrectomy in series B and D.

FIG. 3b.—Total trypsin output in pancreatic secretion before and after gastrectomy in series B and D.

bicarbonate and enzyme concentrations observed in the post-operative series after the meal was given showed minimal variation. The total bicarbonate output for one hour was reduced in 46 (92%) of the patients following operation, being below the lowest values in Series B in 24 (48%). The total amylase output was decreased in 48 (96%) of the patients after operation, and was below the range observed in Series B in 41 (82%). A reduced output of trypsin was recorded post-operatively in 45 (90%) of the patients, and in 39 (78%) the value was below the pre-operative range. The lipase output was found to be reduced in all the patients in the tests in Series D, 48 (96%) having an output below the minimum pre-operative level. The mean reduction for each of the various components mentioned was as follows:

Volume	23.78 ml.	(S.D. ± 13.55 ml.)
Bicarbonate	0.734 mEq.	(S.D. ± 0.650 mEq.)
Amylase	143,125 units	(S.D. ± 90,168 units)
Trypsin	31.48 units	(S.D. ± 25.8 units)
Lipase	47.46 units	(S.D. ± 18.5 units)

(4) The maximum bile coloration of the samples was observed in the early samples in Series B, but towards the end of the hour period in Series D.

STATISTICAL ANALYSIS.—Since the same patients were subjected to tests in each series, it is permissible to apply statistical criteria to the mean reductions already given. Student's test was used, and it was found that the differences between Series A and C, and between Series B and D were significant ($P < 0.001$).

DISCUSSION AND CONCLUSIONS

It is evident that one effect of gastrectomy on pancreatic function is to increase the resting rate of secretion. This may account for the so-called compensatory hypersecretion observed by Stein and Fried (1923). A second effect of the operation is a delay in the appearance of bile in the duodenal contents following meals. In this respect, the

findings are in agreement with the observations of Lundh (1958).

With reference to the response to food entering the duodenum, *i.e.*, after a Billroth I operation, the pancreatic output in one hour following the meal is approximately two-thirds to three-quarters of the pre-operative output. Not only is the volume reduced, but the highest concentrations of bicarbonate and enzymes reached are less than those occurring before operation.

When the duodenum is bypassed, and food enters the jejunum directly, the pancreatic response is modified by gastrectomy in a different manner. The characteristic response observed after operation is one in which the pancreas continues to secrete at its new resting rate. By inference, this must resemble the pattern of response to be expected after the Polya operation.

In addition to this primary modification of the pancreatic response after Polya operations, there are other changes of a secondary nature which are related to the creation of the afferent loop. If the contents of this loop are collected as they escape after meals (Butler, 1959), a degree of dissociation of the pancreatic enzymes may be observed. Table V shows that the enzymes are occasionally

TABLE V
FREQUENCY OF ABSENCE OF ENZYMES IN AFFERENT LOOP CONTENTS

Ante-colic Polya	Controls (30)	Steatorrhoea Group (30)
Lipase (90 estimations)	7 (7.7%)	33 (36.6%)
Trypsin (90 estimations)	3 (3.3%)	16 (17.7%)
Amylase (90 estimations)	0	0
Retro-colic Polya	Controls (16)	Steatorrhoea Group (16)
Lipase (48 estimations)	0	14 (29.2%)
Trypsin (48 estimations)	0	0
Amylase (48 estimations)	0	0

absent or inactivated, lipase more frequently than trypsin, and in patients with long afferent loops more often than those with shorter loops. This change is related to the degree of stasis occurring in the afferent loop, due to its length, its possible denervation, or even to actual obstruction at the stoma. It is probable that this finding reflects the normal instability of the enzymes, for it is known that lipase is notoriously unstable, especially in the presence of trypsin. The latter displays instability also, not so markedly as lipase, but amylase appears to be very stable. Lundh (1958) observed that trypsin was sometimes absent from intestinal contents after gastrectomy but he did not estimate the other enzymes.

To return to the pancreatic responses observed

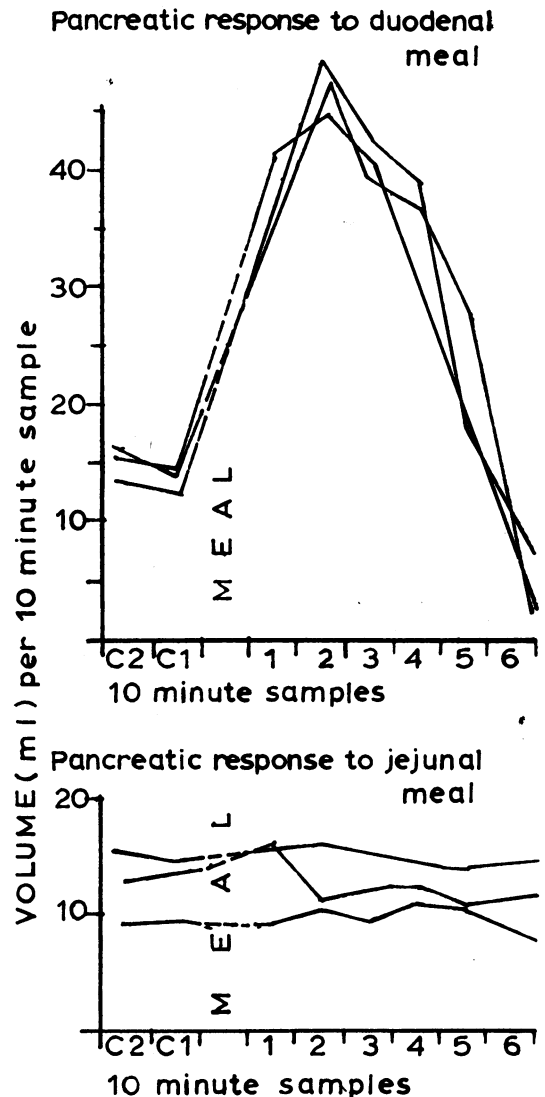


FIG. 4a.—Pancreatic response to a meal after vagotomy in three patients. Upper curves = duodenal meal. Lower curves = jejunal meal.

in the tests, especially in Series C and D, the chief problem concerns a possible explanation of the findings. According to the present concept of the control of pancreatic secretion, there is an unimportant psychic phase, no gastric phase, an all-important intestinal phase, involving the secretin-pancreozymin combination, and an uncertain degree of control by the vagus. It is unlikely that altered hormonal release is responsible for the changes observed in the post-operative experiments, since the same meal was given under the same conditions

before and after operation. In the early stages of the study, there were a few opportunities of investigating patients who had had a previous vagotomy. Figs 4 (a) and (b) show the pancreatic

response in such patients when a meal was introduced into the duodenum, and into the jejunum directly. The similarity of the responses to those recorded in Series C and D suggests that vagal section, coincident with gastrectomy, may be responsible for the modification of the pancreatic response.

It must be stressed that there are several other factors that may be important after gastrectomy. The normal stomach discharges its contents into the duodenum in small amounts, and this almost certainly results in a sustained output from the pancreas, which continues until the stomach is empty. Following gastrectomy, rapid emptying of the stomach remnant may lead to the production of pancreatic secretion over a shorter period of time. The duodenum following a Polya operation is bathed in alkaline secretion, and this factor may cause further reduction in pancreatic output. Finally, since some of the post-cibal syndromes occurring after operation are mediated by sympathetic nervous pathways, pancreatic secretion may be inhibited if the reflexes involve the pancreas.

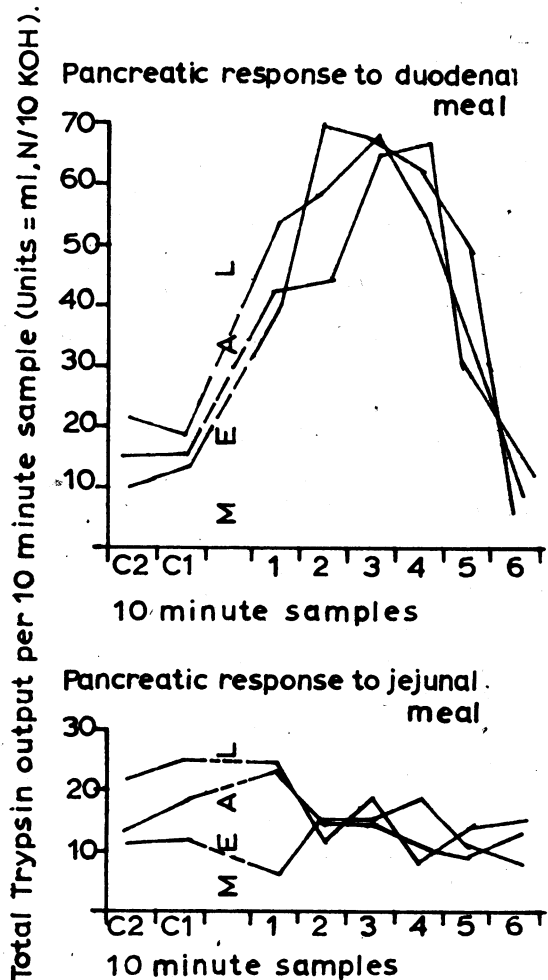


FIG. 4b.—Pancreatic response to a meal after showing total trypsin.

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