Pancreatic enzymes in human duodenal juice—a comparison of responses in secretin pancreozymin and Lundh Borgström tests

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SUMMARY We have compared the concentrations and total outputs of trypsin, amylase, and lipase secreted into the duodenum during secretin pancreozymin and Lundh Borgström tests in order to assess the relative intensity of pancreatic stimulation provided by these means. The mean concentration of trypsin, and the mean 10 minute total output of trypsin, amylase, and lipase after the meal (though less than the peak post-prandial responses) were equal to the respective peak enzyme responses after intravenous injection of 2 Crick Harper Raper units per kg of secretin Boots; and after intravenous injection of 2 Crick Harper Raper units per kg of pancreozymin Boots.

We are currently assessing the relative usefulness of the secretin pancreozymin test (Burton *et al.*, 1960) and the Lundh Borgström test (Lundh, 1962; Lundh and Borgström, 1962) in diagnosis and management of pancreatic disease. Preliminary results in normal subjects enabled us to compare the concentrations of pancreatic enzymes in duodenal juice after the physiological stimulus of a test meal, and after intravenously administered secretagogues. A formal study was then planned to measure total outputs of pancreatic enzymes secreted during the two tests.

Methods

INITIAL STUDY

The initial study was performed in 12 patients without pancreatic disease, and three normal volunteers. Each subject received a secretin pancreozymin test (SP test), and on a separate day a Lundh Borgström test; the order of tests was randomised. Both tests were performed as designed by the originators. In the SP test pancreatic secretion was stimulated by intravenous injection of 2 Crick Harper Raper (CHR) units per kg of secretin Boots (batch numbers 5360, 5664) followed 30 minutes later by intravenous injection of 2 Crick

Harper Raper (CHR) units per kg of pancreozymin Boots (batch numbers 5476, 5833) and duodenal juice was aspirated in 10 minute fractions for 30 minutes after each injection. In the Lundh Borgström test 500 ml of a standard meal (Borgström *et al.*, 1957) was ingested over 10 minutes, and duodenal juice was collected for four successive 30 minute periods.

SUBSEQUENT STUDY

In the subsequent study a quantitative secretin pancreozymin test was performed in three informed volunteers using the double marker technique of Go *et al.* (1970) which involves, after simultaneous intubation of stomach and duodenum, constant perfusion of the stomach at 1.5-2 ml per minute with isotonic saline containing a non-absorbable marker, ^{14}C labelled polyethylene glycol (New England Nuclear Co), and constant perfusion of the duodenum at 1.5-2 ml per minute with isotonic saline (pH 6) containing another non-absorbable marker, polyethylene glycol (molecular weight 4000 BDH Chemicals Ltd.). After an initial 40 minute equilibration period duodenal contents, recovered by means of an intermittent suction pump, were pooled into 10 minute fractions. Each volunteer was also given a quantitative Lundh Borgström test using a technique designed by Malagelada *et al.* (1976). The test meal which contained 2.5 μC

^{14}C labelled PEG was ingested over 10 minutes and subsequently at 10 minute intervals 50 ml of gastric contents were aspirated by syringe, mixed thoroughly, a 10 ml aliquot retained for analysis, and the remaining 50 ml returned to the stomach. At the end of 120 minutes the stomach was emptied and the volume of gastric contents recorded. Throughout the test the duodenum was perfused at 1.5-2 ml per minute with isotonic saline containing PEG (5 g/l) and duodenal contents were aspirated in 10 minute fractions.

Chemical methods

The pH of all gastric and duodenal samples was measured; concentration of trypsin was estimated by the pH stat method of Haverback *et al.* (1960) with p-toluene sulphonyl-L-argininemethyl ester (TAME) as substrate, amylase by Lagerlof's modification of the saccharogenic method of Norby (Lagerlof, 1942), lipase by a pH stat method with an olive oil emulsion as substrate (Marchis-Mouren *et al.*, 1959), and bilirubin by the method of Powell (1944). Concentrations of PEG 4000 in gastric and duodenal samples were determined by the method of Hyden (1955) and concentrations of ^{14}C by liquid scintillation counting.

Ten duodenal samples obtained during SP and Lundh Borgström tests were analysed in duplicate. The coefficients of variation in the determination of PEG, ^{14}C counts, amylase, lipase and trypsin were 1.0, 3.0, 2.0, 2.9, and 5.8 respectively. In *in vitro* experiments 5 mg PEG 4000 per ml of duodenal juice was found not to inhibit amylolytic proteolytic or lipolytic activity.

Analytical methods

The volume flowing past the sampling site in the distal duodenum was calculated from the rate of infusion of PEG saline into the proximal duodenum and the ratio of PEG concentration in the infusate and in aspirated samples (Go *et al.*, 1970).

Details of calculations to determine the total outputs of secreted pancreatic enzymes in studies employing gastric and duodenal markers have been provided by Go *et al.* (1970), and Malagelada *et al.* (1976). If it is assumed that complete mixing of duodenal marker and secreted pancreatic enzymes occurs, the volumes of duodenal juice regurgitating into the stomach in each 10 minute period of the SP test can be calculated by dividing the PEG 4000 content in successive gastric aspirates by the concentration of PEG 4000 in respective duodenal aspirates. We have not applied any systematic correction for reflux during the course of the Lundh Borgström test. Instead the volume of duodenal juice present in gastric contents aspirated

at the end of the test was calculated, and multiplied by the mean 10 minute concentration of each pancreatic enzyme in duodenal aspirates. This product was added to the cumulative two hour output of each enzyme in duodenal samples and the mean 10 minute total enzyme output was determined (Table 5).

We have used the log values of enzyme concentrations and outputs in this study, as the distribution of pancreatic enzyme output, which in a normal population is skew (Sarles *et al.*, 1963; Ammann *et al.*, 1968; Goldberg and Wormsley, 1970), can be normalised by logarithmic transformation (Sarles *et al.*, 1963; Sun, 1963, Ammann *et al.*, 1968). The concentrations and outputs of enzymes in response to meal and hormonal stimulation have been compared by paired *t* tests.

Results

COMPARISON OF CONCENTRATIONS OF PANCREATIC ENZYMES IN SP AND LUNDH BORGSTROM TESTS

As the effect of bolus intravenous injections of secretin and pancreozymin on enzymes is short lived (Fig. 1) peak enzyme concentrations, which invariably occurred within the first 10 minutes, were taken to represent enzyme responses to hormonal stimulation. In the Lundh Borgström test the peak concentration of each enzyme, which in an individual subject could occur 30, 60, 90, or 120 minutes after the meal (Table 1), was significantly higher than the mean concentration of the respective enzyme in pooled two hour collections of duodenal juice (Figs 2, 3, 4). Individual values for mean and

Fig. 1 Mean concentrations of trypsin (×—×), amylase (○---○), and lipase (Δ—Δ) in successive 10 minute collections of duodenal juice during SP tests in 15 patients.

Table 1 Concentrations of trypsin, amylase, and lipase in four successive 30 minute collections of duodenal juice during Lundh Borgström test in 15 subjects

N = 15	Trypsin (IU/ml)				Amylase (IU/ml)				Lipase (IU/ml)			
	30'	60'	90'	120'	30'	60'	90'	120'	30'	60'	90'	120'
M.P.	41.5	43.0	54.0	122.2	140.8	135.7	235.5	245.7	219	219	395	515
P.M.	54.7	166.2	89.5	99.2	143.4	839.6	580.6	552.9	389	1674	944	664
C.P.	36.0	34.5	110.5	84.7	112.6	61.4	271.4	138.2	189	184	794	442
J.R.	31.2	22.2	40.2	31.2	99.8	69.1	30.7	30.7	179	173	148	99
H.W.	102.5	88.0	81.5	100.0	143.3	151.0	194.5	225.3	589	405	440	347
I.S.	33.0	54.5	52.5	44.5	122.8	135.6	171.5	307.2	242	297	324	262
M.W.	28.2	44.7	51.0	29.7	76.8	230.4	220.1	199.6	138	263	235	143
W.B.	58.7	70.2	137.7	83.0	245.7	204.8	110.0	174.0	273	323	263	303
M.M.	104.0	81.7	51.2	81.7	194.5	184.3	240.6	286.7	417	224	162	245
A.B.	13.0	54.7	18.5	41.5	84.5	220.1	716.8	665.6	74	376	157	442
E.C.	28.5	37.5	52.5	68.5	58.8	112.6	168.9	199.6	134	204	414	300
T.M.	119.5	116.5	98.5	99.7	148.4	148.4	117.7	117.7	447	447	262	382
G.S.	44.0	22.0	56.5	51.5	76.8	122.8	99.8	92.1	362	180	445	440
R.K.	29.0	77.5	37.5	16.0	194.5	645.1	512.0	450.5	278	725	570	523
J.H.	31.5	31.5	27.5	41.5	184.3	153.6	122.8	174.0	243	234	193	266

Peak values are in *italics*.

peak concentrations of enzymes after the meal, and peak concentrations after secretin, and after pancreozymin are given in Table 2. Groups were compared by paired *t* tests after logarithmic transformation of data and the results are shown in Figs 2, 3, 4. For trypsin mean concentration after meal equalled peak concentration after secretin, and after pancreozymin, but peak response after meal significantly exceeded the response to either hormone (Fig. 2, Table 2); for amylase meal mean and peak responses were not significantly different from responses to hormones (Fig. 3, Table 2), while for lipase both meal mean and peak responses were significantly less than the values after secretin or pancreozymin (Fig. 4, Table 2).

Fig. 2 Mean and peak concentrations of trypsin after meal compared with peak concentration of trypsin after secretin, and after pancreozymin in 12 patients (●) and three volunteers (△).

Fig. 3 Mean and peak concentrations of amylase after meal compared with peak concentrations of amylase after secretin, and after pancreozymin in 12 patients (●) and three volunteers (△).

COMPARISON OF TOTAL OUTPUTS OF PANCREATIC ENZYMES IN QUANTITATIVE SP AND LUNDH BORGSTRÖM TESTS

During the quantitative SP test in three normal volunteers recovery of gastric marker exceeded 95% in all collections, while negligible amounts appeared in duodenal juice. The volumes of fluid recovered from the distal duodenum each 10 minutes are given in Table 3, which also indicates the calculated volume of regurgitated duodenal juice. Mean total outputs of trypsin, amylase, lipase, and bilirubin in each subject are detailed in Table 4. After secretin, the volume of fluid recovered from the duodenum

Fig. 4 Mean and peak concentrations of lipase after meal compared with peak concentration of lipase after secretin, and after pancreozymin in 12 patients (●) and three volunteers (△).

increased steadily and was highest in the 20-30 minute period after stimulation in each subject (Table 3). Total output of amylase and lipase increased with increase in volume, whereas the output of trypsin fell disproportionately after the first 10 minutes (Fig. 5). There was no consistent positive or negative correlation between the total 10

minute enzyme outputs and the extent of reflux in each 10 minute interval. Injection of secretin resulted in a modest increase in bilirubin content of duodenal juice soon after the injection and a rapid decline thereafter so that little or no bilirubin was present in the 20-30 minute collection (Table 4). Administration of pancreozymin resulted in an immediate marked increase in bilirubin in duodenal juice and a sharp increase in total trypsin output (Fig. 5, Table 4). However, the peak 10 minute outputs and total 30 minute outputs of trypsin, amylase, and lipase after pancreozymin were not significantly different from the respective values after secretin.

During the quantitative Lundh Borgström tests in the three volunteers total recovery of ^{14}C PEG (the amount from the stomach plus that recovered from the duodenum) was $99.1 \pm 1.2\%$ of the amount in the meal. The patterns of gastric emptying (calculated by the technique of Meeroff *et al.*, 1973) are shown in Fig. 6, while total outputs of pancreatic enzymes and bilirubin in successive 10 minute collections of duodenal juice are given in Table 5, and the overall pattern of enzyme response to the test meal is shown in Figure 7. The main determinant of the pancreatic enzyme response to the meal was clearly the load of acid and digestion products delivered into the duodenum at a given time. Thus, in subjects A and B peak concentrations of enzymes at 30 minutes after the meal (Table 5) corresponded closely to the peak phase of gastric emptying

Table 2 Actual concentrations of trypsin, amylase, and lipase in SP and meal tests in 15 patients*

Diagnosis (n = 15)	Trypsin (IU/ml)				Amylase (IU/ml)				Lipase (IU/ml)			
	Meal				Meal				Meal			
	Mean	Peak	S Peak	P Peak	Mean	Peak	S Peak	P Peak	Mean	Peak	S Peak	P Peak
	Mean	Peak	S Peak	P Peak	Mean	Peak	S Peak	P Peak	Mean	Peak	S Peak	P Peak
Irritable bowel												
M.P.	65	122	42	44	189	245	133	133	337	515	443	443
P.M.	102	166	54	107	522	839	424	655	917	1674	1174	1827
Duodenal ulcer												
C.P.	66	110	42	69	143	271	153	271	402	794	593	993
J.R.	31	40	33	75	56	99	225	373	149	179	561	863
Post vagotomy												
H.W.	93	102	94	67	179	225	199	138	445	589	1310	990
I.S.	46	54	32	36	184	307	133	174	281	324	290	334
G.B dysfunction												
M.W.	38	51	66	61	184	230	430	583	194	263	744	1024
W.B.	87	137	59	45	184	245	276	184	290	323	545	500
M.M.	79	104	77	77	225	286	184	204	262	417	923	1185
A.B.	32	54	88	72	419	716	537	296	262	442	861	698
E.C.	46	68	32	28	133	199	138	92	263	414	522	377
T.M.	108	119	60	63	133	148	189	153	384	447	474	722
Normal volunteer												
G.S.	54	56	35	59	97	122	148	122	442	445	750	428
R.K.	40	77	33	54	450	645	286	399	524	725	424	564
J.H.	33	41	26	40	158	184	194	266	234	266	355	598
Mean	56	78	47	57	184	261	220	230	326	444	611	680

*Mean values were calculated after logarithmic transformation.

Table 3 Calculated volumes of duodenal juice during quantitative secretin-pancreozymin test in three normal volunteers (A, B, C)

	A				B				C				Volume of duodenal juice (ml) mean $\pm$ SE
	Flow past duodenum (ml)	Reflux into stomach (ml)	Total (ml)	Net secretion (1.9 ml/min infused) (ml)	Flow past duodenum (ml)	Reflux into stomach (ml)	Total (ml)	Net secretion (1.5 ml/min infused) (ml)	Flow past duodenum (ml)	Reflux into stomach (ml)	Total (ml)	Net secretion (1.5 ml/min infused) (ml)	
Control 10 min	14.5	4.8	19.3	0.3	16.4	8.2	24.6	9.6	17.9	1.2	19.1	4.1	4.7 $\pm$ 2.6
Secretin (min)													
0-10	20.8	6.3	27.1	8.1	51.8	2.1	53.9	38.9	59.4	0	59.4	44.4	30.5 $\pm$ 11.2
10-20	48.4	13.5	61.9	42.9	61.1	2.6	63.7	48.7	75.0	9.1	84.1	69.1	53.5 $\pm$ 7.9
20-30	74.5	37.4	111.9	92.9	71.2	9.8	81.0	66.0	81.6	7.1	88.7	73.7	77.5 $\pm$ 7.9
D1-3 (ml)				143.9				153.6				187.2	161.6 $\pm$ 13.1
Pancreozymin (min)													
30-40	54.0	12.8	66.8	47.8	81.4	3.8	85.2	70.2	95.2	0	95.2	80.2	66.1 $\pm$ 9.6
40-50	39.5	7.2	46.7	27.7	131.6	6.5	138.1	123.1	78.3	0	78.3	63.3	71.4 $\pm$ 27.8
50-60	31.7	6.0	37.7	18.7	90.0	8.4	98.4	83.5	61.6	0	61.6	46.6	49.6 $\pm$ 18.8
D4-6 (ml)				94.2				276.8				190.1	187.1 $\pm$ 52.1
D1-6 (ml)				238.1				430.4				377.3	348.7 $\pm$ 57.4

Table 4 Total outputs of trypsin, amylase, lipase, and bilirubin in quantitative secretin-pancreozymin test in each of three normal volunteers (A, B, C)

	Total outputs											
	Trypsin (IU/10 min)			Amylase (IU/10 min)			Lipase (IU/10 min)			Bilirubin (mg/10 min)		
	A	B	C	A	B	C	A	B	C	A	B	C
Control 10 min	48	2714	732	1280	13772	7014	2903	1850	2214	0.52	3.06	1.87
Secretin (min)												
0-10	1074	2102	1903	3020	8396	15206	5275	7492	14986	2.64	4.85	2.91
10-20	836	1369	966	6656	5222	15923	16774	14455	16464	1.79	2.23	0.34
20-30	615	892	931	6502	9113	18124	26068	17838	19151	0.45	0.41	0.18
Pancreozymin (min)												
30-40	2076	6264	2251	6707	14848	13260	23199	40655	18007	12.68	46.50	37.35
40-50	1005	4282	2037	2764	11673	13260	12662	41988	15123	7.48	22.90	27.27
50-60	510	1182	1541	1331	4044	12288	7338	16743	10231	0.38	2.26	10.11

(Fig. 6), while in subject C delay in gastric emptying was associated with a delayed peak enzyme response (Fig. 6, Table 5). In two subjects, B and C, peak bilirubin output coincided with peak enzyme; in subject A peak bilirubin occurred 20 minutes earlier than peak enzyme (Table 5).

The mean 10 minute total outputs of trypsin, amylase, and lipase after the meal were two to three times less than the peak responses (Table 6), but similar to the peak 10 minute total enzyme outputs after secretin, and after pancreozymin (paired *t* tests, Table 6). Peak postprandial output of trypsin significantly exceeded the response to either hormone. Peak postprandial outputs of amylase and lipase were significantly higher than the responses to pancreozymin; although these values were clearly higher than the responses to secretin also, the differences were not judged to be significant in

paired *t* tests (Table 6). Peak postprandial outputs of bilirubin were twice the peak response to intravenous pancreozymin in subjects A and B, but the peak responses of bilirubin to endogenous and exogenous stimulation were equal in subject C (Tables 4 and 5).

Discussion

We are aware of three studies in which the responses of pancreatic enzymes to a test meal, and to exogenous hormones were compared in order to assess the relative intensity of pancreatic stimulation provided by these means; other investigators (Moeller *et al.*, 1972; Gyr *et al.*, 1975; Waller, 1975; Fiore *et al.*, 1976) concentrated specifically on the relative usefulness of the two tests in diagnosis. Zieve *et al.* (1966) gave subjects 250 ml of test

Fig. 5 Mean total outputs of trypsin, amylase, and lipase in successive 10 minute collections of duodenal juice during quantitative SP tests in three volunteers.

meal, followed two hours later by a combined intravenous injection of 100 CHR units secretin

and 100 CHR units pancreozymin and found the meal by far the more potent stimulus of pancreatic secretion, while Lurie *et al.* (1973) observed that the concentrations of pancreatic enzymes in duodenal juice collected for 20 minutes after intravenous injection of 2 CHR units per kg secretin and for 20 minutes after intravenous injection of 1.5 CHR units per kg pancreozymin were similar to the mean concentrations of pancreatic enzymes in duodenal juice collected for two hours after 300 ml of test meal. In the study of Hartley *et al.* (1966) the concentration of duodenal juice trypsin after an augmented dose of 3 clinical units per kg cholecystokinin pancreozymin (CCK.PZ Vitrum cecekin) was twice as high as the concentration of trypsin after 300 ml of a test meal given 60 minutes after CCK.PZ.

We have analysed both concentrations and total outputs of pancreatic enzymes, as values of enzyme concentration depend not only on the functional state of the pancreas but also on dilution by intestinal and biliary secretions, gastric emptying, and escape of duodenal contents into the jejunum.

Our initial study shows that the peak post-prandial concentration of each pancreatic enzyme significantly exceeds its mean concentration (Figs 2, 3, 4), but that the relationship between the responses to meal and to hormonal stimulation are considerably different for trypsin (Fig. 2), amylase (Fig. 3), and lipase (Fig. 4). As the three enzymes were secreted in parallel during the SP test (Fig. 1) and as parallel secretion of these enzymes after a test meal has been reported in normal subjects (Lundh, 1962; Lundh and Borgström, 1962), our results in patients with a

Table 5 Total 10 minute outputs of trypsin, amylase, lipase, and bilirubin in quantitative Lundh Borgström test in each of three volunteers (A, B, C)

Collection period (min)	Total outputs											
	Trypsin (IU/10 min)			Amylase (IU/10 min)			Lipase (IU/10 min)			Bilirubin (mg/ 10 min)		
	A	B	C	A	B	C	A	B	C	A	B	C
0- 10	2680	1492	1704	4782	3190	12344	29399	13442	27036	23.17	3.19	11.70
10- 20	3208	5795	3108	9539	14664	14377	41392	45271	15985	13.66	10.90	26.40
20- 30	3829	14021	1973	11443	36731	10522	43461	135005	25594	7.45	93.90	9.60
30- 40	2359	7826	1054	9467	25047	4941	23466	70116	8121	8.79	24.46	2.06
40- 50	2259	7050	2042	6820	18836	13138	21660	44975	21583	4.70	17.79	6.20
50- 60	1902	3750	2042	7450	11873	13138	15377	24688	21583	3.90	9.41	6.20
60- 70	2711	9054	2158	6835	19732	14039	18371	58867	24732	4.45	15.18	5.59
70- 80	1889	6795	6798	4777	15176	35496	13629	33317	67175	3.16	7.36	32.58
80- 90	1783	4496	1578	4685	10988	9211	15252	20542	20879	4.41	5.11	9.12
90-100	2241	8072	549	4844	16742	5448	16818	43128	9589	2.26	4.09	0
100-110	1928	4261	549	4490	6287	5448	19686	27553	9589	2.11	1.36	0
110-120	2317	—	217	3343	—	3031	15695	—	6535	2.41	—	0
Enzymes in duodenal juice in stomach at end of test	582	562	844	1413	1300	2703	4998	7716	5602	1.57	1.09	2.15

Peak values are in *italics*.

Fig. 6 Simultaneous measurement of postprandial volume of gastric contents (top), and its fraction being emptied into duodenum (bottom)—that is, gastric emptying rate for each of three subjects A, B, C.

Fig. 7 Mean total outputs of trypsin, amylase, and lipase in successive 10 minute collections of duodenal juice during quantitative Lundh Borgström tests in three volunteers.

wide variety of non-pancreatic abdominal disorders (Table 2) suggest that a reduction in amylase and particularly lipase after meal stimulation is due to secondary inhibition or inactivation of these enzymes. A selective decrease in lipase, especially seen in the subgroup with poor gall bladder function (Table 2), has previously been reported by Worning *et al.* (1967) in patients with anicteric biliary disease and cirrhosis of the liver and may be due to qualitative and quantitative changes in bile salt composition

Table 6 Comparison of total outputs of three enzymes in quantitative SP and meal tests in three normal volunteers (A, B, C)

IU/10 min	Meal mean	Meal peak	S Peak	P Peak	Significance of difference in outputs			
					Meal S	Mean P	Meal S	Peak P
Trypsin								
A	2474	3829	1074	2076	NS	NS	*	*
B	6652	14021	2102	6264				
C	2051	6798	1903	2251				
Amylase								
A	6656	11418	6656	6707	NS	NS	NS	*
B	16333	36710	9114	14848				
C	11776	35482	18125	18637				
Lipase								
A	23267	43461	26068	23199	NS	NS	NS	*
B	47692	135005	17838	41988				
C	22000	67175	19151	18007				

Significance of differences in outputs was calculated by paired *t* tests after logarithmic transformation of data. NS = not significant. * *P* < 0.05.

in these patients. In addition, low lipase and amylase concentrations in two subjects with active duodenal ulceration (Table 2) were probably related to irreversible inactivation of these enzymes by unusually low duodenal pH, while trypsin, which is more stable, remained unaffected.

The use of nonabsorbable markers to measure pancreatic enzyme secretion fell into disrepute after Worning's experimental (Worning and Amdrup, 1965) and clinical (Worning, 1967) studies from which he concluded that uneven mixing of marker in intestinal contents leads to over-estimation of intestinal volume—an interpretation that has been criticised by Jacobson (1966) and Fordtran (1966). Uniform mixing of marker and secretions is indeed an essential prerequisite—thus the powerful stimulant effect of CCK.PZ on duodenal peristalsis (Dahlgren, 1966; 1967) should ensure that marker dilution truly reflects secretory events after intravenous pancreozymin and endogenous CCK.PZ released by the meal. Certainly the pattern of post pancreozymin enzyme response in the quantitative SP test (Fig. 5) is similar to results of our initial study (Fig. 1) and to results published by Burton *et al.* (1960), while the response to meal stimulation (Fig. 7) closely resembles the results in Lundh's (1962) report. In each subject, however, intravenous injection of secretin resulted in a delayed response, the peak flow rate occurred 20–30 minutes after stimulation, with concomitant increase in amylase and lipase. As numerous clinical investigations have demonstrated secretin-induced secretion to be most intense within the first 10 or 20 minutes of injection as obtains in the first part of our study (Fig. 1), the delayed volume response to secretin in the quantitative study (Table 3, Fig. 5), as previously encountered by Worning (1967), must be considered to be anomalous. Both pure secretin and Boots secretin have been shown to inhibit duodenal motility (Dinosa *et al.*, 1966; Chey *et al.*, 1967; Osnes, 1975) and it is likely that this effect, like the effect on flow rate of pancreatic juice, is greatest soon after intravenous injection. Duodenal ileus would mitigate against adequate mixing of marker and secretions which could lead to under-estimation of the actual volume within the duodenum in the early periods after injection. In contrast to Worning's report, in our study the calculated total volume of duodenal juice recovered in 30 minutes after secretin 161.6 ± 13.1 ml (mean $\pm$ standard error of the mean in three subjects, Table 3) was not unduly excessive ($0.8 < P < 0.9$) when compared to 135 ± 4.2 ml (mean $\pm$ standard error of mean in 21 subjects) aspirated in 30 minutes after intravenous injection of 1.7 CHR units per kg of secretin Boots in the study of Burton *et al.* (1960).

The similarity in magnitude of peak enzyme responses to secretin and to pancreozymin (Figs 1, 2, 3, 4, 5) is puzzling if one accepts the traditional viewpoint that pancreozymin specifically stimulates synthesis (Rothman and Wells, 1967) and secretion (Harper *et al.*, 1962) of enzymes, while secretin specifically stimulates the secretion of water and electrolytes which wash-out preformed enzyme from the pancreatic ducts (Lagerlof, 1942; Burton *et al.*, 1960). We have not tested this hypothesis by reversing the order of stimulants, but, when Burton *et al.* (1960) substituted a second injection of secretin instead of an injection of pancreozymin, they noted a second rise in volume without a second rise in enzyme, lending support to the wash-out theory. Another explanation for the large enzyme response to secretin may, however, be the sizeable amount of CCK.PZ in secretin Boots (Henriksen and Worning, 1967; Harper, 1972; Edmondson personal communication, 1974). The final possibility, that secretin may itself act on acinar cells, seems unlikely, as there is no convincing evidence that secretin in physiological doses either stimulates enzyme secretion or enhances the action of pancreozymin on enzyme secretion (Harper, 1972; Dembinski *et al.*, 1974; Harper, 1975) although Wormsley (1968) has shown that very large doses of secretin Boots given by infusion increase trypsin secretion in man.

It is difficult to extrapolate a value for postprandial endogenous CCK.PZ release on the basis of our comparative study, as responses of target organs to the sustained stimulus of a meal often differ greatly from their responses to bolus intravenous injections, as was clearly shown by Torsoli *et al.* (1961) when they assessed gall bladder responses to exogenous and endogenous CCK.PZ. Nevertheless, our results indicate that in man intravenous injection of 2 CHR units per kg of pancreozymin Boots elicits a submaximal response of pancreatic enzymes which equals the mean enzyme response following the physiological stimulus of a meal.

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