Comparative Study of Secretin and Lundh Tests

Klaus Gyr, MD, MPH, TM, Naurang M. Agrawal, MD, Oscar Felsenfeld, MD, MS, and Robert G. Font, MD

Exocrine pancreatic function in 19 patients with pancreatic disease and in 14 of 16 controls was measured by secretin stimulation and by the Lundh test on two different occasions. Peak bicarbonate concentration in the secretin test and mean trypsin concentration in the Lundh test emerged as the most reliable parameters. No additional diagnostic value was obtained by measuring enzymes after secretin injection. In 6 patients with chronic and in 8 of 13 patients with acute pancreatitis, both tests gave results that agreed with each other. The remaining 5 patients showed either an abnormal secretin value or an abnormal Lundh test. This is consistent with the wide variation seen in acute pancreatitis. It is concluded that the Lundh test as well as the secretin test were of value in the assessment of chronic pancreatic disease. The secretin test may be slightly more sensitive to mild and acute pancreatic damage than is the Lundh test. However stimulation of the pancreas by a test meal is easier to perform and more economic.

Several procedures are available for assessing exocrine pancreatic function (1). The secretin test has been well established by the extensive studies of Lagerlof (2), Dreiling and Janowitz (3). Stimulation of the pancreas by the combination of pancreozymin and secretin (3–5) added some new information, but no significant increase in the diagnostic value of these tests has been generally recognized (6). Pancreatic stimulation by a test meal was introduced as a diagnostic procedure by Lundh (7), and this test is widely used in Europe (7–9) but is infrequently applied in the Americas (10–11). Moreover, only few studies have been performed comparing the various procedures (11–17). The present study was undertaken to compare the diagnostic value of the Lundh test with that of the simplest of the hormonal stimulation tests, ie, the secretin test, in patients with and without pancreatic disease.

From the Gastroenterology Section, Veternas Administration Hospital, New Orleans, Louisiana, and the Tulane University Delta Primate Research Center, Covington, Louisiana.

Partly presented at the Annual Meeting of the American College of Gastroenterology in Hawaii, October, 1973.

Address for reprint requests: Dr. R. G. Font, Chief, Gastroenterology Section, Veterans Administration Hospital, New Orleans, Louisiana 70146.

MATERIALS AND METHODS

Clinical Material

A total of 35 males were evaluated. These included 13 cases of acute pancreatitis with characteristic clinical symptoms and repeatedly proven elevations of amylase in serum and urine. The time interval between the attack and the first pancreatic function test ranged from 1 to 10 weeks, with a mean of 4.1 weeks. In 6 patients evidence of chronic pancreatitis was found; 3 had diabetes, 2 had intra-abdominal pancreatic calcifications, and 3 had obvious steatorrhea. Chronic pancreatitis was verified histologically in 3 of these 6 patients. All 19 patients with pancreatic disease indulged in heavy alcohol intake for a prolonged period of time. All persons studied had a thorough examination consisting of history, physical examination, gastrointestinal x-ray series, routine laboratory tests, including at least two amylase determinations in serum and urine. If indicated, hypotonic duodenography, pancreatic scan, celiac angiogram, and gastroduodenoscopy were performed. The control group consisted of 16 persons without clinical or laboratory evidence of pancreatic disease, past or present. Except for one of them, none had a history of alcoholism.

Table 1. Subjects Examined

Classification	Patients (*N*)	Diagnosis	Number	Age (yr) Mean	Age (yr) Range	Interval in days between Lundh and secretin tests Mean	Interval in days between Lundh and secretin tests Range
Pancreatic disease group	19	Acute pancreatitis	13	39.9	23-62	3.4	1-15
		Chronic pancreatitis	6	49.8	37-56	6.2	1-27
Control group	16	Functional disorders	5	40.9	21-65	5.7	1-23
		Healed peptic ulcer	4				
		Erosive gastritis	1				
		Esophagitis	1				
		Paget's disease	1				
		Cholelithiasis	1				
		Photodermatitis	1				
		Psychic disorders	2				

Methods

In each patient with pancreatic disease and in 14 controls the secretin and Lundh tests were performed at least one day apart (Table 1). Only one of the two tests was carried out in 2 of the controls. The sequence of procedures was chosen randomly. After overnight fasting a Dreiling double-lumen tube was advanced to the duodenojejunal junction. Its position was ascertained by fluoroscopy. In the Lundh test the duodenal juice was allowed to drain by simple siphonage and collected into an ice-cooled container.

After a fasting sample was obtained over a period of 20 minutes, a standard meal containing 18 g corn oil, 15 g skimmed milk powder, 40 g glucose, 15 g vanilla syrup, and water to 300 ml (7) was given.

The duodenal contents were then collected for four consecutive 30-minute periods. Color, volume, and pH were immediately recorded. An aliquot of the samples was frozen and stored at -20° C until the respective enzymes could be determined. With one exception, enzymes were estimated within 1 week after the sample was collected.

In the secretin test the gastric tube was connected to continuous suction at -30 to -40 mm Hg. The duodenal contents were aspirated with a syringe. After a 20-minute control sample was collected, one clinical unit of secretin (Boots) per kilogram of body weight was injected intravenously after a negative skin test. Four samples, each of 20 minutes duration, were then collected on ice. Appearance, volume, pH, and bicarbonate concentration were determined immediately. Aliquots frozen at -20° C were later tested for enzymatic activity as in the Lundh test.

Chemical Analysis. pH was determined with a Beckman pH-Meter (Zeromatic II). The *bicarbonate concentration* was measured by titration, as described by Lagerlof (2). *Lipase* activity was estimated according to the method of Cherry and Crandall (18) modified by Johnson and Bockus (19). The olive oil emulsion of Sigma Chemical Co was used as substrate. Specimens were diluted 1:10 with normal saline for the assay. *Trypsin* was measured using *N*-benzoyl-L-arginine ethyl ester as specific substrate by Wiggins' (20) method. The time necessary to release from the substrate a known amount of H^+ ions was measured. *Amylase* activity was determined with a dyed starch amylase substrate. The method described by Sigma Chemical Co was followed (21). The specimens was diluted 1:150 with normal saline. The amyloclastic method developed by Somogyi (22) had to be abandoned because of erroneous results caused by the presence of bile and protein in the intestinal contents. *Statistical calculations* were performed according to Remington and Schork (23).

RESULTS

Controls

Amylase determinations were performed in 10 controls. The mean concentration showed a variation coefficient of 26.1% after the injection of secretin. The results in the Lundh test were erroneous in the 5 patients whose intestinal samples had a pH below 5.5. The mean concentration of samples from the remaining 5

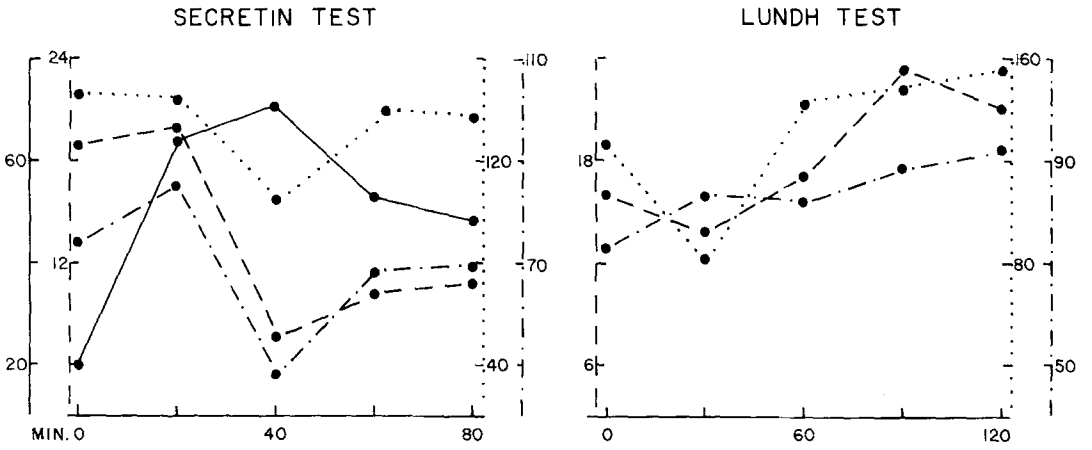

Fig 1. Pancreatic response after stimulation by secretin and test meal in controls. The dots represent mean values at the various collection periods. The ordinates were drawn using the same pattern of line as for the respective tests. Unbroken line represents bicarbonate in mEq/liter; broken line represents trypsin in IU/ml (μEq H^+ released/min-ml); dotted line represents amylase in Somogyi U/100 ml X 10^3; dot-dash line represents lipase in U/ml (ml N/20 NaOH).

patients was 132,906 + 26,590 Somogyi Units/100 ml. Because the Lundh test was not reliable, the amylase determination was discontinued despite good results in the secretin and some of the Lundh tests. Figure 1 presents the pattern of secretion for amylase, trypsin, and lipase after secretin and test meal in the 10 controls.

After secretin stimulation, bicarbonate peak concentration (BPC) emerged as the most valuable criterion. It was used in this study for the distinction between normal or abnormal outcome of the secretin test. Because 2 persons were hypersecretors, the volume did not appear to be a reliable parameter in the control group. Whether expressed as mean and peak concentration or as total output and output/kg body weight trypsin and lipase values had no diagnostic value. Mean concentrations generally had the lowest coefficient of variation, which still exceeded 30%. There was significant correlation between trypsin mean concentration (TMC and lipase mean concentration (LMC; $r = 0.63$, $P < 0.02$).

The Lundh test revealed that mean concentrations of trypsin and lipase were the most reliable criteria. The TMC was used to determine normal or abnormal outcome of the test in this study. Total output and output/kg body weight did not contribute to the discriminatory value of the test. There was no significant correlation found between LMC and TMC in the controls. However, if controls and patients with pancreatic disease were considered together, the correlation was significant ($r = 0.66$, $P < 0.001$).

Chronic Pancreatitis

Results are presented in Table 2 to 4. Secretin and Lundh tests were abnormal in all 6 patients, using the above criteria. The TMC was abnormally low in 4 of the 6 patients after secretin stimulation. In the Lundh test LMC was abnormal only in those 3 patients who also had the lowest TMC. All measurements except mean pH of both tests and volume of the Lundh test were significantly different from the control group ($P < 0.05$–0.001).

Acute Pancreatitis

There was a significant increase in the mean pH of both tests and a significant decrease in the BPC. Otherwise, no statistical difference

Table 2. Results of the Secretin Test*

Criteria	Controls ($N=15$)			Acute pancreatitis ($N=13$)		Chronic pancreatitis ($N=6$)	
	$\bar{X}\pm$ SD	VC	LLN	$\bar{X}\pm$ SD	P	$\bar{X}\pm$ SD	P
Mean pH/80 min	7.7± 0.31	4	—	8.0± 0.2	<0.02	7.9 ± 0.3	NS
Total volume/80 min (ml)	246.5±98.8	40.1	48.9	218 ±116.8	NS	105 ±36.6	<0.01
Volume/80 min/kg body weight	3.4± 1.4	41.0	0.6	3.5± 1.4	NS	2.06± 1.0	<0.05
HCO_3 mean concentration/80 min (mEg/liter)	59.7± 9.9	16.6	39.9	52.5± 11.0	NS	33.3 ± 7.3	<0.001
HCO_3 peak concentration/20 min (mEq/liter)	72.7± 6.9	9.5	58.9	60.3± 12.5	<0.01	41.3 ±11.0	<0.001
HCO_3 output/80 min (mEq)	14.5± 5.9	41.0	2.6	11.9± 7.5	NS	3.6 ± 1.3	<0.001
Trypsin mean concentration (IU/ml)	13.8± 4.6	33.8	4.6	13.1± 3.8	NS	3.9 ± 2.1	<0.001
Lipase mean concentration (U/ml)	74.5±28.6	38.3	17.3	77.0± 32.4	NS	32.0 ±23.2	<0.01
Amylase mean concentration (Somogyi U/100 ml)†	128,352±33,437	26.1	61,478	—	—	—	—

*$\bar{X}\pm$ SD represents mean and standard deviation; VC, variation coefficient in percent; LLN, lower limit of normal (mean - 2 SD); P, level of significance; NS, not significant.
†Determined in 10 controls.

was found between values for controls and patients with acute pancreatitis. The data varied widely. The Lundh and secretin tests of 6 patients fell within normal limits using our criteria. 2 patients (Table 4, patients 8 and 9) showed an abnormal secretin test and TMC and LMC above the upper limit of normal after the test meal, which was interpreted as an abnormal Lundh test. In 3 patients only the secretin and in 2 only the Lundh test were abnormal. 4 of the 5 patients with an abnormal secretin test had a LMC above the upper limit of normal. The same was noted in the patient with a borderline BPC of 59 mEq/liter after secretin (Table 4, patient 1). No correlation was found between the outcome of the tests and the time elapsed between test and attack of pancreatitis.

Side Effects

One control patient developed abdominal pain, headache, and fainting after the administration of secretin. In another the secretin test could not be performed because of a positive skin test.

DISCUSSION

The results of this study reveal the usefulness of the Lundh test as a valuable alternative to the secretin test in the diagnosis of pancreatitis. Both tests were performed after the original procedures (2, 3, 7) with only insignificant modifications. 30-minute instead of 10-minute samples were collected during the first hour of the Lundh test (9). After secretin stimulation, the bicarbonate concentration was determined in 20- instead of 10-minute samples, which partly explains the lower mean value of the BPC compared to other reports (3, 11). However the lower limit of normal for BPC was close to the one described by other authors (5, 11, 24).

The volume has no diagnostic meaning in the test meal, as no attempt was made to collect the total intestinal contents. Nevertheless the great variation in volume observed in the secretin test

Table 3. Results of the Lundh Test*

Criteria	Controls ($N=15$) $\bar{X}\pm$SD	VC	LLN	Acute pancreatitis ($N=13$) $\bar{X}\pm$SD	P	Chronic pancreatitis ($N=6$) $\bar{X}\pm$SD	P
Mean pH/120 min	5.9± 0.7	11.6	—	6.6± 0.6	0.02	6.6± 0.7	NS
Total volume/120 min (ml)	407.1±169.2	41.6	68.7	361.5±144.8	NS	267.5±126.9	NS
Trypsin mean concentration (IU/ml)	17.2± 3.8	22.2	9.6	18.5± 9.1	NS	3.3± 1.8	0.001
Lipase mean concentration (U/ml)	93.7± 22.4	23.9	48.9	119.7± 55.2	NS	47.0± 29.5	0.001

*$\bar{X}\pm$SD represents mean and standard deviation; VC, variation coefficient in percent; LLN, lower limit of normal (mean − 2 SD); P, level of significance; NS, not significant.

was surprising. This could be explained, to some extent, by the limited number of control patients. In addition, they did not represent a completely healthy group (Table 1). Occasional technical difficulties in the collection of duodenal juice, such as temporary gastric reflux and slight displacement of the tube, may have added to the variance.

Enzyme measurements did not contribute essentially to the diagnostic value of the secretin

Table 4. Pancreatic Tests on Patients with Pancreatic Disease

Patient	Attacks (N)	Time between 1st attack and test (wk)	Secretin test HCO_3PC* (mEq/liter)	Secretin test Trypsin (IU/ml)	Lundh test Trypsin MC† (IU/ml)	Lundh test Lipase MC (U/ml)
Acute pancreatitis						
1 BW	2	3.5	59	16.5	22.1	193.4
2 JC	2	2	80	15.5	6.8	78
3 RB	2	10	50	9.5	21.4	146.4
4 AH	2	4	70	9.9	15.2	70.6
5 RR	1	4	60	10.0	6.2	73.0
6 BB	2	1	65	18.5	13.7	41.1
7 JD	2	8	40	14.8	14.8	169.9
8 CM	1	1	51	14.0	36.3	167.6
9 HD	2	3	52	11.7	33.7	170.3
10 AH	1	1	79	16.9	21.3	101.9
11 FJ	2	10	66	18.3	19.5	196.4
12 JL	1	4	45	9.8	11.2	76.1
13 JM	2	2	68	7.1	21.7	70.9
Chronic pancreatitis						
14 RP			26	3.5	2.3	46.7
15 JH			51	5.9	2.5	65.9
16 DW			33	<2	<2	12.3
17 SC			45	4.1	6.3	86.0
18 RR			38	<2	2.5	13.0
19 SP			55	6.5	4.4	57.8

*PC = peak concentration.
†MC = mean concentration.

test. However a drop in the enzyme secretion to below normal appears to indicate advanced destruction of acinar tissue (25). Among the enzymes determined in the Lundh test, trypsin has been widely used (15) and is often employed as the sole test (7–9) because of its stability in the lower pH ranges and because it can be determined chemically with relative ease (20). In contrast, lipase is unstable at body and room temperature; a considerable amount of its activity is probably lost during the collection period if the flow rate is low (2). Our results may partly reflect this fact. Amylase may be inactivated at a pH below 5.5 (2, 15). The latter most likely caused the erroneous results in some samples from control patients after stimulation by test meal. Furthermore the determinations of amylase and lipase require more time than that of trypsin.

Despite the postulated parallelism in the secretion of enzymes, (2, 3, 7) certain discrepancies were noted concerning the secretion of lipase and trypsin in our series (Figure 1, Table 3). In fact, although statistically not significant, a more pronounced increase of LMC than TMC in the Lundh test was found in patients with acute pancreatitis. Whether this dissociation is of diagnostic significance in acute pancreatitis, remains to be established. However, the determination of at least two enzymes seems advisable as suggested by Zieve et al (13).

The pH of the collected samples dropped below 5.0 after the meal in some of the controls. The mechanism involved is probably a sudden, rapid gastric emptying in people with a high output of hydrochloric acid (9). The use of the Dreiling tube, instead of a smaller tube, has possibly contributed to the disturbance of gastric emptying.

The two tests gave meaningful results in all 6 patients with chronic and in 8 of 13 patients with acute pancreatitis. The latter group included 2 patients with an abnormal secretin test and obvious hypersecretion of trypsin and lipase in the Lundh test (Table 4, patient 8 and 9). Such hypersecretion in acute pancreatitis has been reported (5, 9, 15, 26) but not much value was attributed to it until recently (27). 2 patients showed an abnormal Lundh test only, which could be explained by a longer recovery phase for trypsin than for bicarbonate (7, 26). In the 3 patients with abnormal secretin and normal Lundh test, the bicarbonate secretion after secretin administration. Two of the patients showed abnormally high lipase secretion in the Lundh test. These 3 persons may have had a milder form of acute pancreatitis.

The wide variation in results in patients with acute pancreatitis is well known (25). The value of tests in this stage is therefore questionable. The secretin test seems to be more sensitive to acute and milder disturbances of the pancreas than is the Lundh test. On the other hand, this may render the Lundh test more reliable in excluding acute pancreatitis as an episode of chronic pancreatic disease. Follow-up testing with proof of recovery or persistent deficiency is of great importance in this problem. An easy and truly sensitive test is still lacking to cover the gap between acute and chronic pancreatitis.

The few reports in the literature directly comparing the two procedures emphasize the good agreement between Lundh and pancreozymin-secretin test, especially in chronic pancreatitis (11, 13, 15). Some authors recognize a higher sensitivity for the pancreozymin-secretin test (11) and for the augmented secretin test (12). Zieve et al (13) and Fiore et al (14) found the test meal more reliable. All of these authors consider the Lundh test worthy, economic, and simple, without side effects. This agrees with the results of our study. However, the Lundh test does not help in differentiating between carcinoma of the pancreas and chronic pancreatitis as does the secretin test. Therefore, the suspected diagnosis is of great importance in the choice of test procedure.

ACKNOWLEDGMENTS

The author wishes to thank Dr. E.B. Ferguson for reviewing this manuscript and Mr. R. Fonseca, Mrs. A. Amos, and Mr. W. Anderson for their technical assistance.

REFERENCES

1. Lundh G: Diagnostic investigation of the external pancreatic secretion. Bull Soc Chir 2:169–176, 1965
2. Lagerlöf HO: Pancreatic function and pancreatic disease. Acta Med Scand (Suppl) 128:1–289, 1942
3. Dreiling DA, Janowitz HD: The measurement of pancreatic secretory function, The exocrine pancreas. Ciba Foundation Symposium, Boston, Little, Brown and Co, 1962
4. Burton P, Evans DG, Harper AA et al: A test of pancreatic function in man based on the analysis of duodenal contents after administration of secretin and pancreozymin. Gut 1:111–124, 1960
5. Sun DCH: The use of pancreozymin-secretin test in the diagnosis of pancreatitis and tumors of the pancreas. Gastroenterology 45:203–208, 1963
6. Dreiling DA: The early diagnosis of pancreatic cancer. Scand J Gastroenterol (Suppl) 6:115–122, 1970
7. Lundh G: Pancreatic exocrine function in neoplastic and inflammatory disease: a simple and reliable new test. Gastroenterology 42:275–280, 1962
8. Kayasseh L, Stalder GA: Zur Diagnostik der Pankreasinsuffizienz. Schweiz Med Wschr 101:1624–1628, 1971
9. Cook HB, Lennard-Jones JE, Sherif SM et al: Measurement of tryptic activity in intestinal juice as a diagnostic test of pancreatic disease. Gut 8:408–414, 1967
10. Ventzke LE, Davidson WA, Grossman ML: Diagnostic value of pancreatic enzymatic response to a test meal. Gastroenterology 46:765, 1964
11. Moeller DD, Dunn GD, Klotz AP: Comparison of the pancreozymin-secretin test and the Lundh test meal. Am J Dig Dis 17:799–805, 1972
12. Hartley RC, Gambill EA, Engstrom GW, et al: Pancreatic exocrine function. Comparison of response to augmented secretin stimulus, augmented pancreozymin stimulus and test meal in health and disease. Am J Dig Dis 11:27–39, 1966
13. Zieve L, Mulford B, McHale A: Secretion of pancreatic enzymes. II. Comparative response following test meal or injection of secretion and pancreozymin. Am J Dig Dis 11:685–694, 1966
14. Fiore E, Dal Monte PR, Sasdelli M: Studio comparativo della secrezione pancreatica esocrina dopo stimulazione con pancreazimina e secretina e dopo pasto di prova. G Clin Med 48:1194–1203, 1967
15. Lurie B, Brom B, Bank S, et al: Comparative response of exocrine pancreatic secretion following a test meal and secretin-pancreozymin stimulation. Scand. J Gastroenterol 8:27–32, 1973
16. Schoen H, Rico-Irles J, Henning N: Ueber die Untersuchung der excretorischen Pancreasfunktion. II. Vergleichende Untersuchungen von Pancreasprovokationsmitteln. Klin Wschr 40:15–18, 1962
17. Worning H: Pancreatic secretion of amylase as compared to the amylase concentration in the intestinal contents after ingestion of a meal. Scand J Gastroenterol 6:257–260, 1971
18. Cherry IS, Crandall LA: The specificity of pancreatic lipase: its appearance in the blood after pancreatic injury. Am J Physiol 100:266–273, 1932
19. Johnson TA, Bockus HL: Diagnostic significance of determinations of serum lipase. Arch Intern Med 66:62–77, 1940
20. Wiggins HS: Simple method of estimating trypsin. Gut 8:415–416, 1967
21. Sigma Chemical Co: Sigma Chrome. The colorimetric determination of amylase. Sigma Technical Bulletin No. 550, St Louis, 1973
22. Somogyi M: Micromethods for the estimation of diastase. J Biol Chem 125:399–414, 1938
23. Remington RD, Schork MA: Statistics with applications to the biological and health sciences. Prentice Hall Inc, Englewood Cliffs NJ, 1970
24. Zieve L, Silvis SE, Mulford B, Blackwood WD: Secretion of pancreatic enzymes. I. Response to secretin and pancreosymin. Am J Dig Dis 11:671–684, 1966
25. Dreiling DA, Janowitz HD, Perrier CV: Pancreatic inflammatory disease. Harper and Row Publishers, New York, 1964
26. Wormsley KG: Pancreatic function tests. Clin Gastroenterol 1:27–51, 1972
27. Dreiling DA, Greenstein AJ, Bordalo O: The hypersecretory states of the pancreas. Am J Gastroenterol 59:505–511, 1973