Exocrine pancreatic function tests: A review

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ABSTRACT: Exocrine pancreatic function tests (PFTs) remain of value in the diagnosis and assessment of chronic pancreatic disease. Direct intubation PFTs, using secretin/cholecystokinin or secretin/caerulein as the stimulants, continue to be the 'gold standard', although they are invasive, expensive and time consuming. Tubeless indirect tests, ie, the N-benzoyl-L-tyrosyl-para-aminobenzoic acid and pancreolauryl test, have gained increasing acceptance particularly as screening tests. The fecal measurement of chymotrypsin remains a useful screening test for pancreatic insufficiency and fecal fat testing standard for steatorrhea. Radioisotope tests are now outdated. Estimation of pancreatic markers in serum, urine and body fluids are useful when abnormal but miss mild disease. Combining PFTs with imaging techniques provides a rational approach to early diagnosis and gives a better assessment of the patient with chronic pancreatic disease. *Can J Gastroenterol* 1989;3(4):153-161

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Tests de l'exploration fonctionnelle pancréatique exocrine

RESUME: Les tests de l'exploration fonctionnelle pancréatique exocrine (PFTs) restent utiles dans le diagnostic et l'évaluation des affections chroniques du pancréas. Les épreuves par intubation directe qui utilisent la sécrétine/CCK ou la sécrétine/céruleïne comme stimulants, continuent à être de rigueur bien qu'elles soient invasive, coûteuses et longues. Les épreuves indirectes sans tubage, au NBT-PABA et le test pancreolauryl, par exemple, gagnent en popularité, au niveau du dépistage surtout. L'examen coprologique reste utile: la mesure de la chymotrypsine sert à déceler l'insuffisance pancréatique et celles des graisses fécales, à reconnaître la stéatorrhée. Les épreuves aux radioisotopes sont aujourd'hui dépassées. L'estimation des marqueurs pancréatiques dans le sérum, l'urine et les liquides organiques est utile en cas d'anomalie mais ne dépiste pas les affections peu graves. Combiner les PFTs et les techniques d'imagerie fournit une approche rationnelle au diagnostic rapide et donne une meilleure évaluation du patient atteint d'une affection chronique du pancréas.

SINCE THE PIONEER STUDIES OF Chiray et al and Lagerlof reported in 1930 (1) and 1942 (2), a variety of exocrine pancreatic function tests (PFTs) including intubation and tubeless techniques have been developed and applied to clinical practice. For the diagnosis of pancreatic disease, PFTs are needed to assess the amount of functional damage (3). In the past two decades, the development of new imaging techniques such as ultrasound, computed tomography, endoscopic retrograde pancreatography (ERP), arteriography and magnetic resonance imaging have made possible new approaches to the diagnosis of pancreatic disease. However, exocrine pancreatic function may be impaired before morphological changes are seen with these techniques (4-8); PFTs may thus detect dysfunction at an earlier stage. In some circumstances the discrepancies between functional tests and morphological alterations are remarkable (9,10), the combination of PFTs and imaging techniques may improve their individual sensitivity (4,11,12).

Recently a series of comprehensive reviews regarding PFTs have been published (3,13-16). This paper will briefly review the roles of PFTs but discuss more extensively the new developments of tubeless PFTs.

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TABLE 1
Exocrine pancreatic function tests

Intubation tests

Direct secretory tests

- Secretin test
- Secretin-CCK test
- Secretin-caerulein test
- Secretin-bombesin test

Lundh meal

Direct synthetic tests

- ⁷⁵Se-methionine test

Determinations in pure pancreatic juice or duodenal aspiration

- Viscosity
- Enzymes
- Isoenzymes
- Lactoferrin

Tubeless tests

Indirect tests

- NBT-PABA test
- Pancreolauryl test

Fecal tests

- Microscopic sedimentation
- Fat and nitrogen determination
- Chymotrypsin estimation

Radioisotope methods

- Triolein test
- Breath test
- Dual-label Schilling test

Estimation of blood, urine or body fluids

- Evocative test
- Parotid saliva test
- Trypsin-like immunoreactivity
- Pancreatic isoamylase
- Plasma pancreatic polypeptides
- Plasma CCK
- Serum cationic trypsinogen
- Plasma amino acids

CCK Cholecystokinin; NBT-PABA *N*-benzoyl-L-tyrosyl-para-aminobenzoic acid

INTUBATION TESTS

Direct secretory tests: Although intubation tests are invasive, expensive and time consuming, direct secretory tests continue to provide the 'gold standard' for the estimation of exocrine pancreatic function (3). For optimal performance, the tests require: the complete collection of secreted pancreatic juice into the duodenum without contamination by gastric juice; and the administration of secretagogue or combination of secretagogues, which can stimulate maximal pancreatic secretion.

The complete collection of uncontaminated duodenal juice remains a major problem but several techniques have been generally accepted. Separate aspiration can be achieved by the com-

bination of a vented gastric tube (Salem gastric tube) and a duodenal tube (Anderson duodenal tube), or a single double-lumen air vented tube with gastric and duodenal aspiration holes (Dreiling gastroduodenal tube). It has been proven that careful positioning of the gastric tube in the most dependent part of the antrum can achieve a near complete collection of the gastric content and that duodenal reflux is negligible (17-19). A recovery rate of above 85% from duodenal aspiration is widely accepted as indicating a satisfactory collection (3,13,14). When this recovery is achieved, perfusion of non-absorbable or radiolabelled markers to indicate completeness of duodenal collection may be unnecessary (14,20). Balloon occlusion of the pylorus and the distal duodenum has been considered, but interferes with motility and secretion (13). Endoscopic cannulation of the pancreatic duct to collect pure pancreatic juice alone allows only intermittent sampling (21) and the results are likely to be affected by pre-endoscopy medication, thus it is not recommended for routine use.

There is considerable disagreement about which secretagogue or combination of secretagogues and which dose and route of administration, should be used to obtain the best evaluation of pancreatic insufficiency. Several direct tests have been suggested (Table 1). Procedures from each centre are so different that only a few of them are comparable (Table 2). The sensitivity and specificity reported for different studies are affected by the severity of disease in differing study arms and the quality of the controls. False negatives are most likely to derive from mild cases; whereas false positives are seen in patients with celiac sprue, diabetes mellitus, subtotal gastrectomy, hepatic cirrhosis and biliary diseases (22-27).

Obviously there is a need to standardize procedures, but the most satisfactory technique has not been clearly defined. The European Pancreatic Club has tried to standardize the test procedures, but the pilot study of this project showed that the enzyme assays from multiple centres agreed too poorly to make any comparison (28). Currently

the most commonly used direct test in clinical practice is the secretin-cholecystokinin (CCK) test with sensitivity and specificity ranging from 74 to 97% and 80 to 98%, respectively (3,13-15). The secretin-CCK test provides additional information of enzyme output compared to the secretin test alone, in which only pancreatic flow, bicarbonate concentration and output can be estimated. In some pancreatic disorders impaired secretion of enzymes occurs earlier than an effect on volume and bicarbonate output (29,30), so that the sensitivity of the secretin-CCK test may be expected to be higher than that of the secretin test. However, crossover comparisons of these two tests are lacking. Caerulein has been extensively used in Europe to replace CCK in the secretin-CCK test and provides a similar stimulation of pancreatic enzyme secretion. It can be obtained in pure form and is cheaper than CCK. A secretin-bombesin test has been introduced but the role of this procedure remains to be established (3,13).

Lundh meal: The Lundh meal is an indirect PFT involving the assessment of the pancreatic secretory response to the test meal and thus to the endogenous release of gut hormones. The procedure is simpler than those of direct secretory tests, because only enzyme activity is measured and sampling of a small fraction is reliable (14). The test perhaps provides more physiological information than direct tests, however, the results are influenced by such non-pancreatic factors as gastric emptying, intraduodenal pH and the endogenous release of gut hormones (3,13). In the presence of intestinal mucosal disease, eg, celiac sprue, the test may be invalid because of the impairment of mediator hormone released from the abnormal mucosa (31,32). In comparison with the secretin-CCK test, the Lundh meal has usually been shown to be less sensitive, especially in detecting mild pancreatic insufficiency (33,34). Furthermore, it cannot provide pancreatic juice for cytology if carcinoma is suspected.

Direct synthetic tests: Radiolabelled amino acids have been used to estimate

TABLE 2
Data of the exocrine pancreatic function tests

PFTs	Sensitivity	Specificity	Key elements being tested	Comments
Intubation tests				
Secretin	80-90%	80-90%	1 volume 2 bicarbonate	Initial test
Secretin-CCK	74-97%	80-98%	1 volume 2 bicarbonate 3 enzymes	Gold standard
Secretin-caerulein		Similar to secretin-CCK test		
Secretin-bombesin		Similar to secretin-CCK test		Needs evaluation
Lundh meal	66-94%	Lower than above	Enzymes	Less expensive Less sensitive
Radio-methionine	Poor	Poor	Synthetic capacity	More invasive
*Tubeless indirect tests				
PABA	60-90%	70-90%	Chymotrypsin	Screening test
FDT	75-93%	46-97%	Esterases	Screening test
*Fecal tests				
Fat or nitrogen tests	Low	Low	Lipases Trypsin Chymotrypsin Chymotrypsin	Standard test for steatorrhea Inconvenient Screening test
Chymotrypsin test	41-100%	62-97%		
Radioisotope methods				
Triolein tests	>90%? (in steatorrhea)	>90%?	Lipases	Outdated
Breath test	>90%? (in steatorrhea)	>90%?	Lipase	Outdated
Estimation of serum, urine and body fluids				
Trypsin-like RIA	33-65%	?	Trypsin	Convenient Insensitive
Isoamylase	13-71%	?	Isoamylase	Same as above
Pancreatic polypeptide	90-100% (in steatorrhea)	?	Pancreatic	Same as above
Cationic trypsinogen	>90% (in steatorrhea)	86%	Trypsinogen	Convenient New study
Amino acids	67-91%	?	Amino acids	Convenient New study

*The sensitivity and specificity are compared with 'gold standard' intubation test; FDT Fluorescein dilaurate test; PABA Para-aminobenzoic acid; RIA Radioimmunoassay

the capacity of the pancreas to synthesize digestive enzymes. ^{75}Se -methionine, given intravenously is rapidly taken up by pancreatic acinar cells and incorporated into newly synthesized pancreatic enzymes, subsequently secreted into the duodenum. Pancreatic secretion may be stimulated by either a Lundh meal or secretin-CCK. The protein bound ^{75}Se radioactivity in the duodenal aspirate is used as an index of exocrine pancreatic function. Some studies have reported satisfactory discrimination between healthy

controls and patients with pancreatic disease (35,36), but other studies failed to confirm the sensitivity of the test (37,38). Moreover, it is more invasive because both intubation and radioactivity are involved, thus this test seems to confer no advantage unless an estimation of the capacity of pancreatic synthesis is required (3).

Determination in pure pancreatic juice or duodenal aspirates: Determinations of the viscosity (39-41), enzymes (21,42-44), isoamylase (45) or lactoferrin (46-50) in duodenal juice or

in pure pancreatic juice aspirated via ERP with or without secretin-CCK stimulation, provide an ideal approach for research studies but not for routine practice, because of the invasive nature of the procedures and considerable overlap in the measured indices between normal and abnormal (3).

TUBELESS TESTS

Tubeless indirect tests: Two tubeless indirect PFTs are frequently used: the N-benzoyl-L-tyrosyl-para-aminobenzoic acid test (NBT-PABA, bentiromide) and the fluorescein dilaurate test (FDT, [pancreolauryl test, PLT]). In both procedures, the patients are given orally a substrate metabolized by pancreatic enzymes into two or more products, one of which is absorbed from the intestine, conjugated in the liver and excreted in urine where it can be measured. The excretion rate of the tracer elements in urine over time reflects the intraluminal enzyme activity and, indirectly, the exocrine pancreatic function. These tubeless tests require no medical supervision, are less expensive, more convenient and more acceptable to patients than intubation procedures. They have been gaining increasing interest and have been widely used as screening tests (13,16,51).

The NBT-PABA test was initially reported in man in 1976 (52-54) and is valuable for the diagnosis of pancreatic insufficiency. The test substrate, NBT-PABA (Chymex; Adria Laboratories), a synthetic tripeptide is cleaved by pancreatic chymotrypsin into N-benzoyl-L-tyrosine (NBT) and para-aminobenzoic acid (PABA). PABA excreted in urine can be determined and used as an index of exocrine pancreatic function. Test procedures have not been completely standardized, but most studies are done according to the following protocol.

The test is performed after an overnight fast and pancreatic enzyme supplements should be discontinued at least five days prior to the study. Drugs or food resulting in a high urinary excretion of aromatic amino acids must be avoided beforehand. The NBT-PABA given in a dose between 0.5 and 1 g provides the greatest sensitivity (55-

57). A test meal is recommended to stimulate pancreatic secretion (52,54,58-60); tea or mineral water is encouraged to ensure sufficient diuresis and urine collection over 6 h is generally sufficient (60,61).

Sensitivity of the test ranges from 37 to 100%, with most studies between 60 and 90%. Specificity ranges from 39 to 100%, with the majority of tests over 70% against the 'gold standard', the direct intubation tests (13,16). Several nonpancreatic factors such as gastrectomy, small bowel diseases (celiac sprue, Crohn's disease), impaired liver or renal function and diabetes mellitus may cause false positive results (58,62-67).

Some modifications of the test have been developed to overcome the high incidence of the false positives. A control test on an additional study day by administering free PABA instead of NBT-PABA is commonly used (58). From the PABA excretion rate on a test day (T) and a control day (C), the PABA excretion index (PEI) is derived ($PEI = T/C$). Nonpancreatic disease will influence both T and C, while pancreatic dysfunction only T, thus by using PEI, false positives can be minimized. A PEI value of greater than 82% is considered normal (20). A single day NBT-PABA test has been developed as an alternative in order to obtain a PEI from one study day. The subjects are given free ^{14}C -PABA (67-70) or para-aminosalicylic acid (PAS) (71,72) in addition to the normal administration of NBT-PABA. The excretion rate of PABA and ^{14}C -PABA or PAS are determined respectively. PEI is the ratio of PABA: ^{14}C -PABA or PABA:PAS. But the assay techniques in these tests are more complex and results can be invalidated by drug or isotopic interference (16). The measurement of PABA in serum at between 90 and 150 mins after the administration of NBT-PABA is a convenient alternative to that of urine collection, especially in children, elderly patients or those with renal disorders. In most studies results have been satisfactory (73-79) while the simultaneous serum and urinary measurements of PABA may also improve the specificity but not the sensitivity of the NBT-PABA test (56,80).

The fluorescein dilaurate test (FDT [pancreolauryl test, PLT]) was first described in 1969 (81), but has only recently attracted widespread interest. The principle of the test is similar to that of the NBT-PABA test. Fluorescein dilaurate, a poorly water soluble synthetic ester, is given orally and cleaved by pancreatic esterases to lauric acid and free fluorescein, which is water soluble and excreted in urine. In comparison with the NBT-PABA test, FDT undergoes less interference from drugs or serum components, only requires simple hydrolysis and is more independent of renal function (16). The FDT test has been standardized and is commercially available (Temmler; Marburg, West Germany).

The test is performed after fasting, and pancreatic supplements or vitamin B preparations, which interfere with fluorescein measurements, have to be stopped. On the test day a capsule containing 0.5 mmol fluorescein dilaurate is administered together with breakfast, while on the control day 0.5 mmol free fluorescein is given. Free fluids and a normal lunch are encouraged to maintain an adequate diuresis. Urine is collected over 10 h. Urinary fluorescein on the test (T) and control day (C) is measured photometrically or fluorometrically and the fluorescein excretion index (FEI) obtained ($FEI = T/C$). An FEI over 30% indicates normal; less than 20% abnormal; between 20 and 30% requires a repeated test. If the repeated test shows a ratio of less than 30%, it is considered abnormal. Recent studies of FDT indicate a sensitivity ranging from 46 to 100% with most studies between 75 and 93%, and specificity between 46 and 97% (13,16). Diseases associated with false positive results are similar to those for the NBT-PABA test. Most studies show the sensitivity of FDT to be superior to that of NBT-PABA test (59,82-84).

In order to shorten the test period and avoid the need to collect urine, fluorescein determinations in serum have been developed. Optimal fluorescein serum concentrations are found between 4 and 6 h after oral ingestion. Serum testing seems to offer sensitivity and specificity similar to those of the

urine test (79,85-87). A modified FDT with fluorescein serum determination following metoclopramide to enhance gastric emptying and secretin stimulation appears superior to the urine test (88).

Fecal tests: Fecal microscopic examination of a random stool sample is simple but unreliable. Fecal fat and nitrogen tests have continued as routine tests for assessing steatorrhea, but they cannot distinguish pancreatic from nonpancreatic disease. Steatorrhea and azotorrhea are late symptoms of pancreatic disease, and only occur when the lipase output falls below 10% of normal (99). The degree of pancreatic impairment, as measured by the intubation tests, may not reflect the severity of steatorrhea. Therefore, for sophisticated evaluation of the functional reserve capacity of the exocrine pancreas both intubation tests and fecal tests have been considered necessary (90). Fecal fat estimation of 72 h stool collection remains the standard test to quantify fat malabsorption (3,13,91). The measurement of fecal nitrogen does not improve further the sensitivity, since pancreatogenic azotorrhea occurs only in patients with steatorrhea (89,92,93). In order to overcome the time consuming and unpleasant laboratory methods of quantifying stool fat, nuclear magnetic resonance (NMR) spectrometry has been recently introduced (94).

Fecal chymotrypsin measurements can be done on random stool samples (95-97), although a 24 h collection of feces may provide slightly better results (98,99). From the present data the measurements still remain a useful screening test for exocrine pancreatic insufficiency. Recently, new photometric methods using standard laboratory equipment have been developed, which make this test even more accessible than the traditional titrimetric method (100-103). The sensitivity of the test ranges from 72 to 90% and specificity from 62 to 90% (3-13). Stool samples collected from outpatients can be mailed to the diagnostic centre performing the assay without affecting test results. The test may, therefore, be particularly helpful in follow-up studies.

Radioisotope methods: Triolein tests have been investigated in an attempt to replace the more cumbersome fecal fat tests. The oral administration of double labelled radioactive fats include the easily measured ^{131}I -triolein/ ^{131}I -oleic acid given on separate days or more recently the stable ^{14}C -triolein/ ^3H -oleic acid given simultaneously. Lipase deficiency in pancreatic disease would only affect triglyceride hydrolysis but not fatty acid absorption, thus pancreatic steatorrhea could be distinguished from other disorders. Some studies have reported a favourable sensitivity and specificity of about 90% in the detection of steatorrhea (104-106). To avoid fecal collection, measurements of serum radioactivity have been developed, but the results are sometimes distorted by kinetics unrelated to the assimilation of the label (105).

The $^{14}\text{CO}_2$ breath test is another alternative to fecal fat testing. Several radiolabelled triglycerides have been recommended as test substrates, of which ^{14}C -triolein showed the best sensitivity and specificity (107). It is given orally together with a standard breakfast and is digested by pancreatic lipase. The exhalation of $^{14}\text{CO}_2$ measured in breath reflects the malabsorption of fat. Sensitivity and specificity have been reported to reach over 90% in steatorrhea (106). False positive results come from non-pancreatic factors such as intestinal mucosal absorption, hepatic metabolism, pulmonary disorders and metabolic disorders, eg, hyperthyroidism, diabetes mellitus and obesity (106). Modifications, such as repeating the test on a separate day together with the administration of pancreatic enzymes (108) or replacing the test substrate by a 'mixed' triglyceride that consists of one medium chain fatty acid in position 2 and two long chain fatty acids in positions 1 and 3 (109), have been developed to improve the specificity. A recently developed cholesteryl octanoate breath test shortens the study duration from 6 h to between 60 and 90 mins (110).

The dual label Schilling test measures the ratio of urinary $^{57}\text{Co}/^{58}\text{Co}$ after the administration of intrinsic

^{57}Co -cobalamine and hog-R-protein ^{58}Co -cobalamine together with free intrinsic factor (111), but has not been further evaluated.

In general, because of the unreliability of the tests and the involvement of elaborate isotope techniques, radioisotope methods have been out-dated by other tubeless PFTs (3,106).

Estimation of serum, urine and body fluids: Estimation of exocrine pancreatic function by measuring the levels of enzymes, hormones or other components in serum, urine or saliva is attractive, because it is simple and non-invasive. Measuring serum enzymes after intravenous stimulation with pancreatic secretagogues, the 'evocative tests', has proven neither sensitive nor specific (29,112,113). Measuring salivary bicarbonate and amylase outputs is also of little diagnostic value (114,115).

Fasting serum trypsin-like immunoreactivity is significantly lower in patients with chronic pancreatitis, but the sensitivity of this test only reaches 33 to 65%. Measuring fasting pancreatic isoamylase in serum or other body fluids and measuring secretagogue stimulated pancreatic polypeptide in plasma has similar problems of low sensitivity (3,13). Therefore, these tests are only reliable in severe exocrine pancreatic insufficiency with steatorrhea.

Plasma CCK concentrations are elevated in patients with pancreatic insufficiency (116-119), but this has not been confirmed by a study using sequence specific radioimmunoassay (120). Several reports have shown that serum immunoreactive cationic trypsinogen measurement may be promising. In patients with pancreatic insufficiency the levels decline with age and are low or undetectable after five to six years of age. At that time low levels occur in patients with moderately or severely impaired exocrine pancreatic function irrespective of the original disease. The sensitivity of the test extends above the steatorrheic threshold. In the presence of steatorrhea of unknown etiology, low levels of cationic trypsinogen indicate a pancreatic etiology (121-124). Serum immunoreactive pancreatic lipase levels also decrease in a similar way in patients with exocrine

pancreatic insufficiency and can be used as an index, although less sensitive than cationic trypsinogen (123).

One study reported a lower reduction of plasma amino acid levels in patients with exocrine pancreatic insufficiency than in controls after stimulation by secretin-CCK. The sensitivity of this test was reported to be 67% in mild cases and 91% in moderate or severe cases. The sensitivity improves if several individual amino acids are measured (125).

CONCLUSION

Direct secretory tests, using secretin-CCK or the secretin-caerulein as stimulants, remain the 'gold standard' for the assessment of exocrine pancreatic function. The pancreolauryl test and the NBT-PABA test (or perhaps the determinations of fecal chymotrypsin) can be recommended as screening tests. The other tests miss almost all patients with pancreatic dysfunction without steatorrhea and are only useful in the assessment of advanced disease. The estimation of pancreatic markers in serum, urine or body fluids can supply information when abnormal, and require better evaluation.

It is apparent that no one test is entirely satisfactory, thus the diagnosis should be based on a combination of PFTs with other techniques. A rational approach to the diagnosis of chronic pancreatic disease is detailed below, although each centre can assess its own resources and requirements. For the diagnosis of patients with chronic abdominal pain suspected of having pancreatic disease, a suitable screening procedure might be ultrasonography initially, if negative, then a tubeless test, (NBT-PABA or pancreolauryl test) or fecal chymotrypsin which are non-invasive and relatively inexpensive. A positive result warrants confirmation by either computed tomography scan, ERP or a secretin-CCK test. Arteriography could be substituted for ERP in the event of failure or unavailability of ERP, when pancreatic carcinoma is suspected. Ultrasound or computed tomography guided fine needle biopsy and cytologic evaluation in pancreatic

juice from ERP should be performed. For functional assessment of a patient with chronic pancreatic insufficiency, if

there is steatorrhea, fecal fat may be used to monitor enzyme replacement; if there is no steatorrhea, then either the

NBT-PABA, pancreolauryl test or fecal chymotrypsin may be used, and can be followed by a secretin-CCK test.

REFERENCES

- Chiray M, Jeandel A, Salmon A. L'exploration clinique du pancréas et l'injection intraveineuse de sécrétine purifiée. *Presse Med* 1930;38:977-82.
- Lagerlof HO. Pancreatic function and pancreatic disease: Studied by means of secretin. *Acta Med Scand* 1942;128(Suppl): 1-289.
- Lankisch PG. Exocrine pancreatic function tests. *Gut* 1982;23:777-98.
- Braganza JM, Hunt LP, Warwick F. Relationship between pancreatic exocrine function and ductal morphology in chronic pancreatitis. *Gastroenterology* 1982;82:1341-7.
- Ammann RW, Deyhle P, Fumagalli I, Hofmann K. Diagnostischer Wert der endoskopischen pankreatographie (ERP) bei pankreatitis, Korrelation mit exokriner funktionsdiagnostik. *Z Gastroenterol* 1974;12:20-1.
- Dobrilla G, Fratton A, Valentini M, et al. Endoscopic retrograde pancreatography and secretin-pancreozymin test in diagnosis of chronic pancreatitis: A comparative evaluation. *Endoscopy* 1976;8:118-23.
- Nakano S, Horiguchi Y, Takeda T, Suzuki T, Nakajima S. Comparative diagnostic value of endoscopic pancreatography and pancreatic function tests. *Scand J Gastroenterol* 1974;9:383-90.
- Tympner F, Schaffner O, Koch H, et al. Wertigkeit der endoskopischen retrograden pankreatikografie, des volumenverlustkorrigierten sekretin-pankreozymin tests und der sonografie in der diagnostik der chronischen pankreatitis. *Leber Magen Darm* 1979;9:1-4.
- Malfertheiner P, Buchler M, Stanescu A, Ditschuneit H. Exocrine pancreatic function in correlation to ductal and parenchymal morphology in chronic pancreatitis. *Hepatogastroenterology* 1986;33:110-4.
- DiMaggio EP, Malagelada JR, Go VLW. The relationship between pancreatic ductal obstruction and pancreatic secretion in man. *Mayo Clin Proc* 1979;54:157-62.
- DiMaggio EP, Malagelada JR, Taylor WFL, Go VLW. A prospective comparison of current diagnostic tests for pancreatic cancer. *N Engl J Med* 1977;297:737-42.
- Foster PN, Mitchell CJ, Robertson DRC, et al. Prospective comparison of three non-invasive tests for pancreatic disease. *Br Med J* 1984;289:13-6.
- Niederau C, Grendell JH. Diagnosis of chronic pancreatitis. *Gastroenterology* 1985;88:1973-95.
- Wormsley KG. Tests of pancreatic secretion. *Clin Gastroenterol* 1978;7:529-44.
- Arvanitakis C, Cooke AR. Diagnostic tests of exocrine pancreatic function and disease. *Gastroenterology* 1978;74:932-48.
- Scharpe S, Lliano L. Two indirect tests of exocrine pancreatic function evaluated. *Clin Chem* 1987;33:5-12,16.
- Petersen H, Eerstad A. Comparison of response to intravenous injection and infusion of secretin in man. *Scand J Gastroenterol* 1972;7:453-9.
- Wormsley KG. Aspects of duodenogastric reflux in man. *Gut* 1972;13:243-50.
- Petersen H, Myren J. Secretin dose-response in health and chronic pancreatic inflammatory disease. *Scand J Gastroenterol* 1975;10:851-61.
- Boyd EJS, Wormsley KG. The assessment of pancreatic exocrine function. In: Misiewicz JJ, Pounder RE, Venables CW, eds. *Diseases of the Gut and Pancreas*. Oxford: Blackwell Scientific Publications, 1987:489-98.
- Denyer ME, Corten PB. Pure pancreatic juice studies in normal subjects and patients with chronic pancreatitis. *Gut* 1979;20:89-97.
- Regan PT, DiMaggio EP. Exocrine pancreatic insufficiency in celiac sprue: A cause of treatment failure. *Gastroenterology* 1980;78:484-7.
- Novis BH, Bank S, Marks IN. Exocrine pancreatic function in intestinal malabsorption and small bowel disease. *Dig Dis Sci* 1972;17:489-94.
- Lankisch PG, Manthey G, Otto J, et al. Exocrine pancreatic function in insulin-dependent diabetes mellitus. *Digestion* 1982;25:211-6.
- Pollard HM, Miller L, Brewer WA. The external secretion of pancreas and diabetes mellitus. *Am J Dig Dis* 1943;10:20-3.
- Forell MM, Stahlheber M, Otte M. Erkrankungen der verdauungsorgane und ihr einfluss auf die verdauungssekretion. *Dtsch Med Wochenschr* 1969;94:1097-101.
- Renner IG, Rinderknecht H, Wisner JR. Pancreatic secretion after secretin and cholecystokinin stimulation in chronic alcoholics with and without cirrhosis. *Dig Dis Sci* 1983;28:1089-93.
- Duerr HK, Bode HCh, Ammann RW, et al. Interlaboratory quality control of laboratory data in the secretin-pancreozymin test. Report of a pilot study. *Ir J Med Sci* 1977;146:(Suppl 1):11-2.
- Otte M. Pankreasfunktionsdiagnostik. *Internist* 1979;20:331-40.
- Gullo L, Costa PL, Fontana G, Labo G. Investigation of exocrine pancreatic function by continuous infusion of caerulein and secretin in normal subjects and in chronic pancreatitis. *Digestion* 1976;14:97-107.
- DiMaggio EP, Go VLW, Summerskill WHJ. Impaired cholecystokinin-pancreozymin secretion, intraluminal dilution and maldigestion of fat in sprue. *Gastroenterology* 1972;63:25-32.
- Worning H, Mullertz S, Hess Thaysen E, Bang HO. pH and concentration of pancreatic enzymes in aspirates from the human duodenum during digestion of standard meal in patients with intestinal disorders. *Scand J Gastroenterol* 1967;2:81-9.
- Moeller DD, Dunn GD, Klotz AP. Comparison of the pancreozymin-secretin test and Lundh test meal. *Am J Dig Dis* 1972;17:799-805.
- Gry K, Agrawal NM, Felsenfeld O, et al. Comparison study of secretin and Lundh tests. *Am J Dig Dis* 1975;20:506-12.
- Youngs GR, Agnew JE, Levin GE, Bouchier IAD. Radioselenium in duodenal aspirate as an assessment of pancreatic exocrine function. *Br Med J* 1971;2:252-5.
- Shichiri M, Etani N, Yoshida M, et al. Radioselenium pancreozymin-secretin test for pancreatic exocrine function. *Am J Dig Dis* 1975;20:460-8.
- Pointner H, Kletter H. Evaluation of Se-selenomethionine test for pancreatic disease. *Digestion* 1980;20:225-33.
- Pointner H, Kinast H, Flegel U. Se-selenomethionine excretion in bile and pancreatic juice. *Digestion* 1975;12:61-4.
- Tympner F, Rosch W. Viskosität des reinen pankreassekretes bei chronischer pankreatitis. *Klin Wochenschr* 1978;56:421-2.
- Tympner F, Rosch W. Viscosity and trypsin activity of pure pancreatic juice in chronic pancreatitis. *Acta Hepatogastroenterol* 1978;25:73-6.
- Leonhardt H, Reinhardt I. Viscosity of duodenal juice examined in patients with excretory pancreas insufficiency by the pancreozymin secretin test compared to a control group and patients

- with cholelithiasis. *Acta Hepatogastroenterol* 1978;25:45-8.
42. Kawanishi H, Sell JE, Pollard HM. Combined endoscopic retrograde collection and retrograde pancreatography. *Gastroenterology* 1975;68:1033.
 43. Carr-Locke DL. Pancreatic juice analysis, carcinoembryonic antigen (CEA) and endoscopic retrograde cholangiopancreatography (ERCP) in the diagnosis of pancreatic disease. *Gut* 1977;18:A980-1.
 44. Cotton PB. ERCP. *Gut* 1977;18:316-41.
 45. Lankisch PG, Otto J. Salivary isomylase in duodenal aspirates. *Dig Dis Sci* 1986;31:1299-302.
 46. Estevenon JP, Sarles H, Fiagrella C. Lactoferrin in duodenal juice of the patients with chronic pancreatitis. *Scand J Gastroenterol* 1975;10:327-31.
 47. Fedail SS, Harvey RF, Salmon PR, Read AE. Radioimmunoassay of lactoferrin in pancreatic juice as a test for pancreatic disease. *Lancet* 1987;i:181-2.
 48. Tympner F, Gutmann W. Lactoferrin konzentration im reinen pankreassekret bei chronischer pankreatitis. *Z Gastroenterol* 1979;17:858-61.
 49. Hayakawa T, Harada H, Noda A, Kondo T. Lactoferrin in pure pancreatic juice in chronic pancreatitis. *Am J Gastroenterol* 1983;79:222-4.
 50. Multigner L, Fiagrella C, Sarles H. Diagnosis of chronic pancreatitis by measurement of lactoferrin in duodenal juice. *Gut* 1981;22:350-4.
 51. Lankisch PG, Lembcke B. Indirect pancreatic function tests: Chemical and radioisotope methods. *Clin Gastroenterol* 1984;13:717-37.
 52. Arvanitakis C, Greenberger NJ. Diagnosis of pancreatic disease by a synthetic peptide. A new test of exocrine pancreatic function. *Lancet* 1976;i:663-6.
 53. Bornschein W, Goldmann FL, Otte M. Methodische und erste klinische untersuchungsergebnisse mit einem neuen indirekten pankreasfunktionstest. *Clin Chim Acta* 1976;67:21-7.
 54. Gyr K, Stalder GA, Schiffman I, Fehr C, Vonderschmitt D, Fahrlander H. Oral administration of a chymotrypsin-labile peptide: A new test of exocrine pancreatic function in man (PFT). *Gut* 1976;17:27-32.
 55. Thienhaus R, Niederau C. Die untersuchung der exokrinen pankreasfunktion mit N-Benzoyl-L-Tyrosyl-P-Aminobenzoesaure. *Z Gastroenterol* 1979;17:187-94.
 56. Wakasugi H, Funakoshi T, Ibayashi H. Evaluation of exocrine pancreatic function by oral administration of N-benzoyl-L-tyrosyl-P-aminobenzoic acid (PFD test) in primary diabetes mellitus. *Digestion* 1983;26:1-9.
 57. Buehler H, Ammann RW. PABA-test versus chymotrypsin und fettbestimmung im stuhl in der pankreas-funktionsdiagnostik. *Schweiz Med Wochenschr* 1979;109:597-8.
 58. Mitchell CJ, Humphrey CS, Bullen AW, et al. Improved diagnostic accuracy of modified oral pancreatic function tests. *Scand J Gastroenterol* 1979;14:737-41.
 59. Lankisch PG, Schreiber A, Otto J. Pancreolauryl test. Evaluation of a tubeless pancreatic function test in comparison with other indirect and direct tests for exocrine pancreatic function. *Dig Dis Sci* 1983;28:490-3.
 60. Sacher M, Kohsa A, Shmerling DH. PABA screening test for exocrine pancreatic function in infants and children. *Arch Dis Child* 1978;53:639-41.
 61. Toskes PP. Bentiromide as a test of exocrine pancreatic function in adult patients with pancreatic exocrine insufficiency. Determination of appropriate dose and urinary collection interval. *Gastroenterology* 1983;85:565-9.
 62. Arvanitakis C, Greenberger NJ. The use of BT-PABA (PFT) in chronic pancreatitis and other diseases. The experience in USA. In: Madusa M, ed. *Pancreatic Function Diagnostant*. New York: Igaku-Shoin, 1980:60-9.
 63. Harada H, Shundo T, Ikubo I. Exocrine pancreatic function test by a synthetic peptide. In: Masuda M, ed. *Pancreatic Function Diagnostant*. New York: Igaku-Shoin, 1980:101-7.
 64. Freise J, Hofmann R. Zur spezifitaet des peptid-paba-tests. *Z Gastroenterol* 1979;17:310-7.
 65. Lankisch PG, Ehrhardt-Schmelzer S, Koop H, Caspary WF. Der NBT-PABA-test in der diagnostik der exokrinen pankreasinsuffizienz. Ein vergleich mit dem sekretin-pankreozymin-test, den stuhlenzymbestimmungen und der quantitativen stuhlfett-analyse. *Dtsch Med Wochenschr* 1980;105:1418-23.
 66. Imamura R, Miyazawa T, Abe Y, Bab T, Nakamura T, Takebe K. Evaluation of new pancreatic function test (PFT) for determination of pancreatic function in pancreatic diseases. In: Masuda M, ed. *Pancreatic Function Diagnostant*. New York: Igaku-Shoin, 1980:47-54.
 67. Tanner AR, Fisher D, Smith CL. An evaluation of one day NBT-PABA/¹⁴C-PABA in the assessment of pancreatic exocrine insufficiency. *Digestion* 1984;29:42-6.
 68. Tetlow VA, Lobley RW, Herman H, Braganza JM. A one-day oral pancreatic function test using a chymotrypsin-labile peptide and radioactive marker. *Clin Trials J* 1980;17:121-30.
 69. Tetlow VA, Key G, Herman H, Braganza JM. Diagnostic accuracy of the PABA excretion index (using ¹⁴C-PABA) *Gut* 1981;22:A441.
 70. Braganza JM, Kay GH, Tetlow VA, Herman H. Observations of the BT-PABA/¹⁴C-PABA tubeless test of pancreatic function. *Clin Chim Acta* 1983;130:339-47.
 71. Berg JD, Chesner IM, Allen-Narker RA, Buckley BM, Lawson N. Exocrine pancreatic function as determined in a same day test with use of bentiromide and P-aminosalicylic acid. *Clin Chem* 1986;32:1010-2.
 72. Hoek FJ, Van-den-Bergh FA, Klein-Elhorst JT, et al. Improved specificity of the PABA test with p-aminosalicylic acid (PAS). *Gut* 1987;28:468-73.
 73. Dockter G, Nacu I, Kohlberger E. Determination of protease cleaved p-aminobenzoic acid (PABA) in serum after oral administration of N-benzoyl-L-tyrosyl-P-aminobenzoic acid (PABA-peptide) in children. *Eur J Pediatr* 1981;135:277-9.
 74. Goode HF, Foster PN, Kelleher J, et al. Comparison of serum PABA measurement and the urinary PABA excretion index in the diagnosis of pancreatic insufficiency. *Digestion* 1984;30:111.
 75. Weizman Z, Forstner G, Gaskin K, Kopelman H, Wong S, Durie P. Bentiromide test for assessing pancreatic dysfunction using analysis of p-aminobenzoic acid in plasma and urine. *Gastroenterology* 1985;89:596-604.
 76. Gharbo SA, Boyer JA, Williamson MJ. Colorimetric plasma assay for the bentiromide test (BT-PABA) for exocrine pancreatic insufficiency. *Anal Biochem* 1985;148:228-32.
 77. Bellentani S, Grisendi A, Rinaldi M, et al. BT-paba test in the diagnosis of pancreatic exocrine insufficiency in cystic fibrosis: Urinary and serum determinations compared. *Eur J Pediatr* 1984;143:145-8.
 78. Takeda Y, Amatsu T, Tada H, et al. Value of the BT-PABA test with serum PABA as a pancreatic function test. *Nippon Shokakibyo Gakkai Zasshi* 1985;82:1742-7.
 79. Lankisch PG, Brauneis J, Otto J, Goke B. Pancreolauryl and NBT-PABA tests. Are serum tests more practicable alternatives to urine tests in the diagnosis of exocrine pancreatic insufficiency? *Gastroenterology* 1986;90:350-4.
 80. Delchier JC, Soule JC. BT-PABA test with plasma PABA measurements: Evaluation of sensitivity and specificity. *Gut* 1983;24:318-25.
 81. Kaffarnik H, Meyer-Bertenrath JG. Zur methodik und klinischen bedeutung eines neuen pankreaslipase-tests mit fluorescein-dilaurin-saurester. *Klin Wochenschr* 1969;47:221-3.
 82. Cavallini G, Piubello W, Brocco G, et al. Reliability of the Bz-Ty-PABA

- and the pancreolauryl test in the assessment of exocrine pancreatic function. *Digestion* 1983;27:129-37.
83. Ventrucchi M, Daniele C, Bartolucci C, et al. Evaluation of pancreolauryl test (PLT), PABA test and serum pancreatic enzymes in the diagnosis of exocrine pancreatic insufficiency. *Digestion* 1982;25:73.
 84. Ventrucchi M, Gullo L, Daniele C, Priori P, Labo G. Pancreolauryl test for pancreatic exocrine insufficiency. *Am J Gastroenterol* 1983;78:806-9.
 85. Cavallini G, Piubello W, Brocco G, et al. Behaviour of serum PABA and fluorescein (FL) in the course of BT-PABA and pancreolauryl (PL) test in exocrine pancreatic insufficiency (EPI) patients. *Digestion* 1983;28:17.
 86. Balaguer JV, Aparisi L, Rodrigo JM, et al. Influence of renal function on results in serum and urine of the PABA and pancreolauryl tests. *Digestion* 1984;30:114.
 87. Laggner A, Bastian L, Prager J, et al. Pankreas-funktions-dianostik vereinfachtes screening mit fluoresceindilaurat durch serumkonzentrationsbestimmungen. *Fortschr Med* 1981;99:589-91.
 88. Malfertheiner P, Buchler M, Muller A, Ditschuneit H. The fluorescein dilaurate serum test following metoclopramide and secretin stimulation for evaluating pancreatic function. Contribution to the diagnosis of chronic pancreatitis. *Z Gastroenterol* 1987;25:225-32.
 89. DiMagno EP, Go VLW, Summerskill WHJ. Relations between pancreatic enzyme outputs and malabsorption in severe pancreatic insufficiency. *N Engl J Med* 1973;288:813-5.
 90. Lankisch PG, Lembcke B, Wemken G, Creutzfeldt W. Functional reserve capacity of exocrine pancreas. *Digestion* 1986;35:175-81.
 91. Van de Kamer JH, Ten Bockel H, Weijers HA. Rapid method for the determination of fat in feces. *J Biol Chem* 1949;177:347-55.
 92. Dornberger GT, Comfort MW, Wollaeger EE, Power MH. Total fecal solids, fat and nitrogen. IV. A study of patients with chronic relapsing pancreatitis. *Gastroenterology* 1948;11:691-700.
 93. Henke WJ, Vacca JB, Van Goidsenhoven GE, Knight WA. Evaluation of pancreatic function tests in confirmed pancreatic disease. *Gastroenterology* 1961;41:233-41.
 94. Schneider MU, Demaling L, Jones SA, et al. NMR spectrometry. A new method for total stool fat quantification in chronic pancreatitis. *Dig Dis Sci* 1987;32:494-9.
 95. Ammann RW, Tagwercher E, Kashiwagi H, Rosenmund H. Diagnostic value of fecal chymotrypsin and trypsin assessment for detection of pancreatic disease. *Am J Dig Dis* 1968;13:123-46.
 96. Haverback BJ, Dyce BJ, Gutentag PJ, Montgomery DW. Measurement of trypsin and chymotrypsin in stool: A diagnostic test for pancreatic exocrine function. *Gastroenterology* 1963;44:588-97.
 97. Sale JK, Golbery DM, Thjodleifsson B, Wormsley KG. Trypsin and chymotrypsin in duodenal aspirate and faeces in response to secretin and cholecystokinin-pancreozymin. *Gut* 1974;15:132-8.
 98. Muller L, Wisniewski ZS, Hansky J. The measurement of faecal chymotrypsin: A screening test for pancreatic exocrine insufficiency. *Aust Ann Med* 1970;19:47-9.
 99. Dyck W, Ammann RW. Quantitative determination of fecal chymotrypsin as a screening test for pancreatic exocrine insufficiency. *Am J Dig Dis* 1965;10:530-45.
 100. Kasper P, Moller G, Wahlefeld AW, Staehler F. A new photometric method for determination of chymotrypsin in stool. *Fresenius Zeitschrift fur Analytische Chemie* 1982;311:391-2.
 101. Schlaeger R, Rohr A. Faecal chymotrypsin: A new photometric method using N-acetyl-L-tyrosine ethyl ester as substrate. *J Clin Chem Clin Biochem* 1982;20:147-50.
 102. Dockter G, Hoppe-Seyler F, Appel W, Sitzmann FD. Determination of chymotrypsin in feces by a new photometric method. *Pediatr Padol* 1985;20:257-65.
 103. Ehrhardt-Schmelzer S, Otto J, Schlaeger R, Lankisch PG. Faecal chymotrypsin for investigation of exocrine pancreatic function: A comparison of two newly developed tests with the titrimetric method. *Z Gastroenterol* 1984;22:647-51.
 104. Lembcke B, Losler A, Caspary WF, et al. Clinical value of a dual isotope fat absorption test system (FATS) using glycerol ¹²⁵I-trioleate and ⁷⁵Se-triether. *Dig Dis Sci* 1986;31:822-8.
 105. Pedersen NT, Halgreen H. Simultaneous assessment of fat maldigestion and fat malabsorption by a double-isotope method using fecal radioactivity. *Gastroenterology* 1985;88:47-54.
 106. Lankisch PG, Lembcke B. Indirect pancreatic function tests: Chemical and radioisotope methods. In: Creutzfeldt W, ed. *Clinics in Gastroenterology*. Vol 13, No 3. London: WB Saunders Co, 1984:717-37.
 107. Newcomer AD, Hofmann AF, DiMagno EP, Thomas PJ, Carlson GL. Triolein breath test: A sensitive and specific test for fat malabsorption. *Gastroenterology* 1979;76:6-13.
 108. Goff JS. Twostage triolein breath test differentiates pancreatic insufficiency from other causes of malabsorption. *Gastroenterology* 1982;83:44-6.
 109. Ghos YF, Vantrappen GR, Rutgeerts P, Schurmans PC. A mixed-triglyceride breath test for intraluminal fat digestive activity. *Digestion* 1981;22:239-47.
 110. Cole SG, Rossi S, Stern A, Hofmann AF. Cholesteryl octanoate breath test. Preliminary studies on a new noninvasive test of human pancreatic exocrine function. *Gastroenterology* 1987;93:1372-80.
 111. Brugge WR, Goff JS, Allen NC, et al. Development of the dual label Schelling test for pancreatic exocrine function based on the differential absorption of cobalamin bound to intrinsic factor and R protein. *Gastroenterology* 1980;78:937-49.
 112. Munch R, Kehl O, Buhler H, Medici T, Ammann RW. Change in the serum pancreas enzyme following i.v. stimulation with secretin in subjects with a normal pancreas. *Schweiz Med Wochenschr* 1987;117:756-60.
 113. Schmidt H, Witthoft C. Wert des Provokations (Evokations) tests fur die pankreasdiagnostik. *Leber Magen Darm* 1976;6:227-34.
 114. Lankisch PG, Chilla R, Luerssen E, Koop H, Arglebe C, Creutzfeldt W. Parotid saliva test in the diagnosis of chronic pancreatitis. *Digestion* 1979;19:52-5.
 115. Dobrilla G, Valentini M, Filippini M, et al. Study of parotid and mixed saliva in the diagnosis of chronic pancreatitis. *Digestion* 1979;19:180-5.
 116. Harvey RF, Dowsett L, Hartag M, Read AE. A radioimmunoassay for cholecystokinin-pancreozymin. *Lancet* 1973;ii:826-8.
 117. Harvey RF, Rey JF, Howard JM, et al. Serum cholecystokinin in pancreatic disease. *Gut* 1976;17:827.
 118. Harvey RF, Rey JF, Howard JM, et al. Bioassay and radioimmunoassay of serum cholecystokinin in patients with pancreatic disease. *Rend Gastroenterol* 1977;9:15-6.
 119. Elderle A, Vantini I, Harvey RF, et al. Fasting serum cholecystokinin levels in chronic relapsing pancreatitis. *Ir J Med Sci* 1977;146:30.
 120. Jansen JB, Hopman WP, Lamers CB. Plasma cholecystokinin concentrations in patients with pancreatic insufficiency measured by sequence-specific radioimmunoassays. *Dig Dis Sci* 1984;29:1109-17.

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121. Moore DJ, Largman C, Kopelman HR, Wong SS, Durie PR. Abnormalities of circulating immunoreactive pancreatic anionic trypsinogen in cystic fibrosis: An assay artefact due to cross-reacting serum antibodies. *Clin Biochem* 1986;19:303-7.
122. Cleghorn GJ, Benjamin L, Corey M, Forstner GG, Dati F, Durie PR. Age related alterations in immunoreactive pancreatic lipase and cationic trypsinogen in young children with cystic fibrosis. *J Pediatr* 1985;107:377-81.
123. Cleghorn GJ, Benjamin L, Corey M, Forstner GG, Dati F, Durie PR. Serum immunoreactive pancreatic lipase and cationic trypsinogen for the assessment of exocrine pancreatic function in older patients with cystic fibrosis. *Pediatrics* 1986;77:301-6.
124. Moore DJ, Forstner GG, Largman C, Cleghorn GJ, Wong SS, Durie PR. Serum immunoreactive cationic trypsinogen: A useful indicator of severe exocrine dysfunction in paediatric patients without cystic fibrosis. *Gut* 1986;27:1362-8.
125. Domschke S, Heptner G, Kolb S, Sailer D, Schneider MU, Domschke W. Decrease in plasma amino acid level after secretin and pancreozymin as an indicator of exocrine pancreatic function. *Gastroenterology* 1986;90:1031-8.
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