

An evaluation of ⁷⁵Se Selenomethionine scanning as a test of pancreatic function compared with the secretin-pancreozymin test

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SUMMARY The uptake of ⁷⁵Se Selenomethionine by the pancreas has been evaluated in 102 patients and compared with the secretin-pancreozymin test of pancreatic function. In groups of patients with chronic pancreatitis and cancer of the pancreas abnormal scans closely parallel the diminished exocrine secretion, especially bicarbonate output, following a submaximal dose of secretin. Thirty per cent of the group with no pancreatic abnormality have abnormal scans, though the secretin-pancreozymin test is normal. Though a normal scan excludes the presence of chronic pancreatitis and cancer of the pancreas with a probability greater than 90%, an abnormal scan is found so frequently in normal subjects that it does not provide a reliable index of impaired pancreatic function.

In the decade since Blau and Bender (1962) introduced ⁷⁵Se Selenomethionine to scan the pancreas, numerous reports have confirmed its use in delineating the structure and position of the pancreas (Sodee, 1966; Centi Colella and Pigorini, 1967; Melmed, Agnew, and Bouchier, 1968). The evidence that the scan also reflects pancreatic function rests on three studies. The first was confined to 19 diabetics (Lähdevirta, 1967); the second showed good general agreement between pancreatic function assessed by a secretin-pancreozymin test and ⁷⁵Se Selenomethionine scans in 20 patients, though no details of the functional test were provided (Brown, Sircus, Smith, Donaldson, Dymock, Falconer, and Small, 1968); and the third compared duodenal tryptic activity following a Lundh-Borgström meal with ⁷⁵Se Selenomethionine scans of the pancreas in 54 subjects (McCarthy and Brown, 1969). In the present study we have assessed ⁷⁵Se Selenomethionine scanning as a test of pancreatic function by comparing it with the results of the secretin-pancreozymin test, considered to be the most useful test of pancreatic function currently available in clinical practice.

Methods

One hundred and thirty-six consecutive patients

who attended between 1967 and 1971 for the investigation of suspected pancreatic disease were included in the study. All patients were examined clinically and a gastroenterological investigation was undertaken to establish the diagnosis. Laparotomy findings interpreted by the same surgical team were available in 57 patients. The secretin-pancreozymin test (Burton, Evans, Harper, Howat, Oleesky, Scott, and Varley, 1960) and the ⁷⁵Se Selenomethionine scan of the pancreas (Charlesworth, Testa, Pullan, and Torrance, 1970) were usually performed within a week of each other. In each case liver scanning using 99m Technetium colloid was carried out before the pancreatic scan. Thirty-four patients were subsequently omitted from the study for the reasons indicated in table I.

<i>Reason for Omission</i>	<i>No. of Cases</i>
Incomplete follow up	5
Gastro-jejunostomy	2
Incomplete record of data from secretin-pancreozymin test	11
Patient intolerant of gastroduodenal tube	3
Specimen lost or broken	2
No liver scan	11
Total	34

Table I *Reasons for omitting 34 patients from the study*

Interpretation of the Scan

Scans were assessed by four observers independently in a two-stage procedure, initially blind, and subsequently, after an interval in the light of all the available clinical, biochemical, and radiological information. Scan abnormalities were recorded as focal or diffusely diminished uptake of the isotope or an absent pancreatic image. Visual subtraction of the hepatic and pancreatic images was employed to interpret the pancreatic photoscans. When a pancreatic image could not be defined adequately because of hepatic enlargement or increased bowel uptake of isotope the pancreatic scan was deemed to be unreadable.

Results

Three of the four observers agreed in 84% of cases at the initial assessment of the scans, and in 88% of cases at the second evaluation (table II).

	Agreement			
	4 : 0	3 : 1	2 : 2	2 : 1 : 1
Blind	52 (51%)	34 (33%)	11 (11%)	5 (5%)
Informed	73 (72%)	17 (16%)	9 (9%)	3 (3%)

Table II Comparison between 'blind' and 'informed' assessment of 102 pancreatic scans by four observers

NORMAL PANCREAS

Fifty-six patients were included in the control group in whom from all the available information, including laparotomy in 23 patients, the pancreas was considered to be normal. These patients were arbitrarily split into five subgroups (table III) to ascertain whether scan or secretin-pancreozymin test abnormalities occurred more frequently in any one section of this group. The scan was normal in 61% of the whole group, abnormal in 30%, and

Normal Pancreas	No. of Patients	Scan Reports		
		Normal	Abnormal	Unreadable
Abdominal pain	24	12	10	3
Biliary disease	14	9	5	—
Adult coeliac disease	3	3	—	—
Cirrhosis	3	2	1	—
Jaundice	11	8	1	2
Total	56	34 (61%)	17 (30%)	5 (9%)
Laparotomy	23	16 (70%)	6 (26%)	1 (4%)

Table III Scan reports in the control group of 56 patients

unreadable in 9%, while in the 23 patients in whom the condition of the pancreas was assessed during laparotomy, the scan was normal in 70%, abnormal in 26%, and unreadable in 4%. Of the five patients who had a focal defect in the head of the pancreas (table IV), three suffered from spastic colon, one had systemic sclerosis, and the fifth cancer of the bile ducts. Diffusely diminished uptake of isotope was recorded in 11 patients, three of whom were diabetic, three had gallstones, three a spastic colon, one cirrhosis of the liver, and one Vaterian stenosis. No pancreatic image was detected in only one patient in this group of 56—a diabetic woman with chronic cholecystitis in whom the pancreas proved to be normal at laparotomy.

Normal Pancreas	Abnormal Scan			
	Poor Uptake			
	Focal	Diffuse	Absent	Unreadable
Abdominal pain 25	4	6	—	3
Biliary disease 14	—	4	1	—
Adult coeliac disease 3	—	—	—	—
Jaundice 11	1	—	—	2
Cirrhosis 3	—	1	—	—
Total 56 patients	5	11	1	5

Table IV Details of 22 abnormal scans in the control group of 56 patients

Normal values for the secretin-pancreozymin test in health are shown in table V and the results of the

	Mean \pm SE of Mean	Lower Limit of Normal	
		Mean—2 SD	Percentile Estimate (PE) Method
Volume (ml) D1-6	251 \pm 10.96	151	148
Maximum bicarbonate concentration (mMole%)	10.47 \pm 0.054	6.97	
Bicarbonate output D1-3 (mMoles)	11.35 \pm 0.6	6.25	4.29
Amylase output (units) D4-6	525 \pm 44	131	182
Trypsin output (units) D4-6	4715 \pm 363	1549	1970

Table V Secretin-pancreozymin test (Burton *et al*, 1960)¹

¹Normal values of the secretin-pancreozymin test: D1-3, three 10-min samples following secretin (1.7 Crick, Harper, Raper units/kg); D4-6, three 10-min samples following pancreozymin (2.0 CHR units/kg); D1-6, total 60-min collection.

secretin-pancreozymin test in the 56 patients in table VI. There were four abnormal tests (7%) in this group of 56. One patient with the clinical diagnosis of spastic colon secreted a marginally reduced volume of pancreatic juice. In the patient with cirrhosis of the liver the concentration of bicarbonate was reduced though the bicarbonate output was normal. A patient with Vaterian stenosis and another with cancer of the bile ducts had both reduced concentration and output of bicarbonate.

Normal Pancreas	No. of Patients	Decreased		
		Volume	Maximum HCO ₃ Concentration	Amylase Output after Pancreozymin
Abdominal pain	25	1	0	0
Biliary disease	14	1	1	0
Adult coeliac disease	3	0	0	0
Cirrhosis of liver	3	0	1	0
Jaundice	11	0	1	0

Table VI Results of the secretin-pancreozymin test in the normal group of 56 patients

PATHOLOGICAL PANCREAS

In this group of 46 patients (table VII) 32 patients had chronic pancreatitis and cancer of the pancreas and 12 patients had suffered from one or more attacks of acute pancreatitis. The pancreas was inspected at laparotomy or necropsy in 34 of these 46 patients.

	46 Cases	Laparotomy or Necropsy (34 Cases)
Chronic pancreatitis	18	10
Cancer of the pancreas	14	14
Pancreatic agenesis	1	1
Pancreatic atrophy	1	1
Postacute pancreatitis	12	8

Table VII Results in 46 cases of pancreatic disease

CHRONIC PANCREATITIS (TABLES VIII AND IX)

A diagnosis of chronic pancreatitis was confirmed by laparotomy in 10 patients and by the presence of diffuse pancreatic calcification radiologically in three patients. An additional five patients had clinical features of chronic pancreatitis associated with impaired exocrine secretion. The scan showed diffuse abnormalities in 15 patients, a focal abnormality in two patients, but was normal in one. The secretin-pancreozymin test was abnormal in 16 of the 18 patients in this group.

CANCER OF THE PANCREAS (TABLES VIII AND IX)

Fourteen patients had cancer of the pancreas proved by laparotomy or at necropsy. The tumour was located in the head of the gland in 11 cases, in the body and tail in one patient, and in the tail of the pancreas in two cases. Both the scan and the secretin-pancreozymin test were abnormal in 11 patients. In one patient in whom the tumour was located in the tail of the pancreas both tests were normal. The

Diagnosis	No. of Cases	Scan Reports			Secretin-pancreozymin Test	
		Normal	Abnormal	Unreadable	Normal	Abnormal
Chronic pancreatitis	18	1 (5.5%)	17 (94.5%)	—	2 (11%)	16 (89%)
Cancer of the pancreas	14	2 (14%)	11 (79%)	1 (7%)	2 (15%)	12 (85%)
Pancreatic agenesis atrophy	2	0	2	—	0	2
Total	34	3 (9%)	30 (88%)	1 (3%)	4 (12%)	30 (88%)

Table VIII Results of pancreatic scanning and secretin-pancreozymin test in 34 patients with pancreatic disease

Diagnosis	No. of Patients	Decreased				Total Abnormal Tests
		Volume (D1-6)	Maximum HCO ₃	HCO ₃ Output after Secretin	Amylase Output after Pancreozymin	
Chronic pancreatitis and relapsing chronic pancreatitis	18	7	12	15	9	16
Cancer of the pancreas	14	9	7	12	7	12
Pancreatic agenesis and atrophy	2	2	1	2	1	2
Postacute pancreatitis and relapsing acute pancreatitis	12	1	1	1	1	1

Table IX Secretin-pancreozymin test in 46 patients with pancreatic disease

scan was unreadable in a patient in whom the secretin-pancreozymin test was normal, and normal in another with impaired exocrine secretion. In both patients with a normal scan the tumour was about 5 cm in diameter.

PANCREATIC AGENESIS AND ATROPHY

The scan of an elderly patient in whom the exocrine secretion was markedly reduced due to primary atrophy of the pancreas showed no uptake of ^{75}Se Selenomethionine. A patient with partial agenesis of the head of the pancreas had a focal defect in the head of the gland on the scan, and an abnormal secretin-pancreozymin test.

Abnormal scans were recorded in 88% of this group of 34 patients with chronic pancreatic disease (table VIII) which compares with an 88% incidence of abnormal secretin-pancreozymin tests.

AFTER ACUTE PANCREATITIS

Of the 12 patients in this group, three who were scanned less than one month after the acute attack had diffuse abnormalities. In the nine patients scanned more than a month after the acute episode the scan was normal in six, and abnormal in three. One patient with a pseudocyst had a focal defect of the scan, in the other two uptake of ^{75}Se Selenomethionine was diffusely reduced. The secretin-pancreozymin test done more than three months after

the acute attack was normal in 11 patients. It remained abnormal in the patient with the pseudocyst.

COMPARISON OF PANCREATIC SCANNING WITH SECRETIN-PANCREOZYMIN TEST

Control group

The volume of duodenal juice aspirated during the secretin-pancreozymin test, the output of bicarbonate in response to secretin, and the output of amylase after pancreozymin have been compared with the abnormality in the scan, in an attempt to relate these abnormalities to impaired pancreatic exocrine

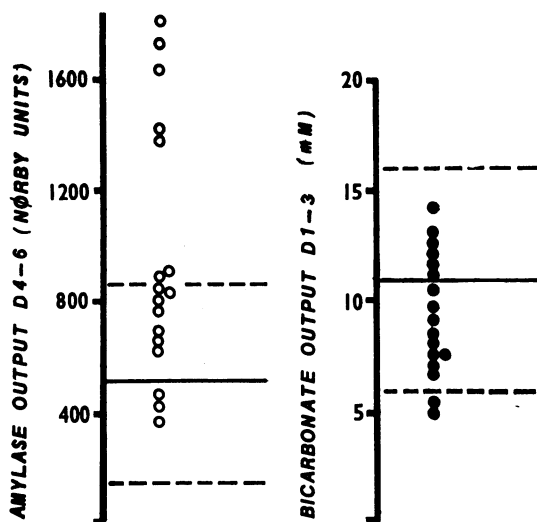


Fig 1 The output of amylase (○) after pancreozymin and of secretin after bicarbonate (●) in 17 patients with abnormal scans in the normal group of 56 patients. Horizontal lines represent the mean \pm 2 SD of the normal range.

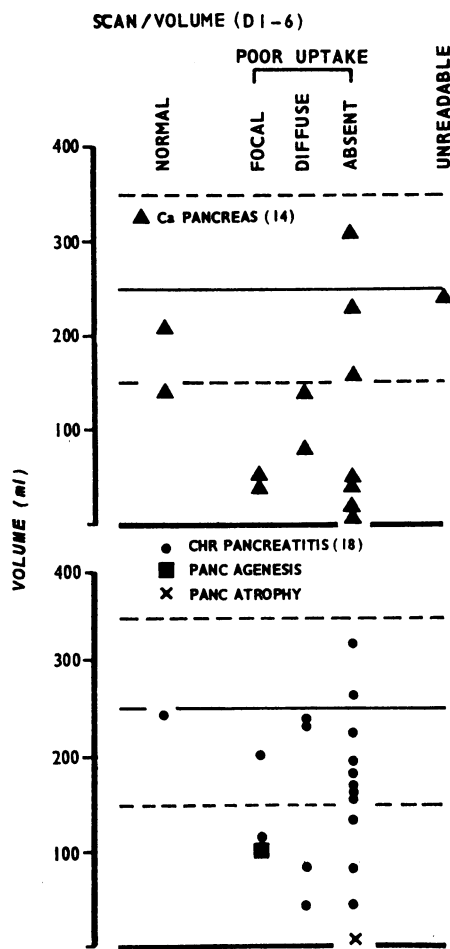


Fig 2 The relationship of scans to the volume of pancreatic juice obtained during the secretin-pancreozymin test in 14 patients with cancer (\blacktriangle), 18 patients with chronic pancreatitis (\bullet), a patient with agnesis of the head of the pancreas (\blacksquare), and a patient with pancreatic atrophy (\times). Horizontal lines are mean \pm 2 SD.

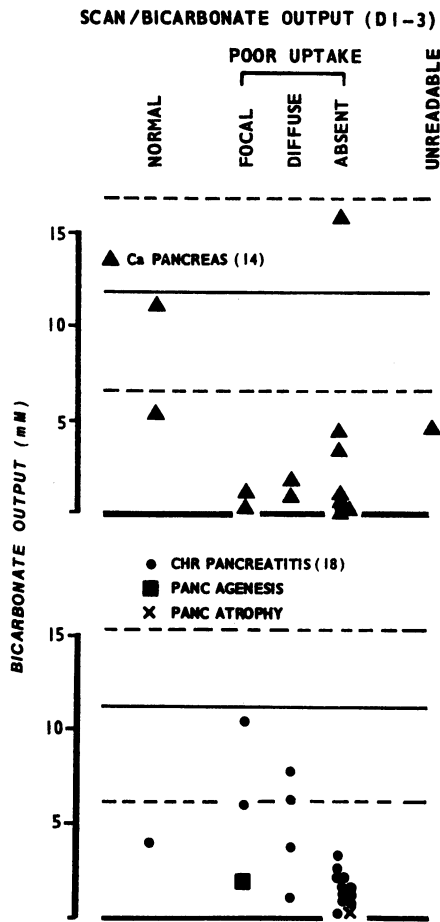


Fig 3 The relationship of scans to the output of bicarbonate after secretin in 14 patients with cancer (▲), 18 patients with chronic pancreatitis (●), a patient with agenesis of the head of the pancreas (■), and a patient with pancreatic atrophy (×).

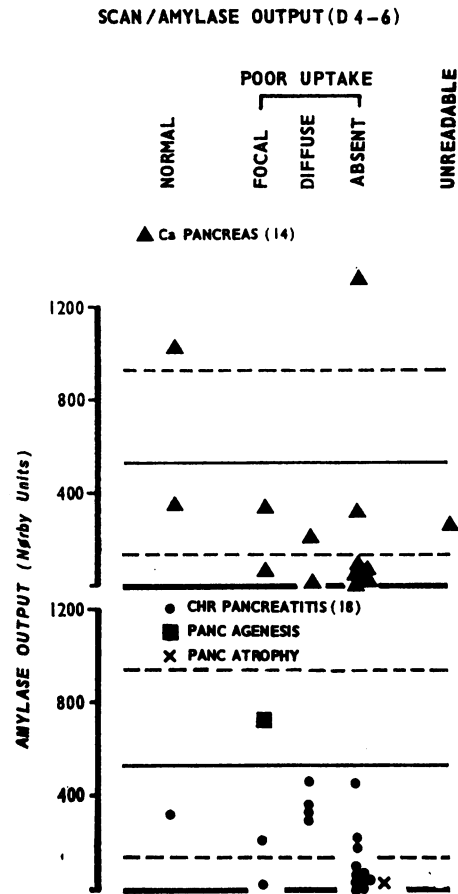


Fig 4 The relationship of scans to the output of amylase after pancreozymin in 14 patients with cancer (▲), 18 patients with chronic pancreatitis (●), a patient with agenesis of the head of the pancreas (■), and a patient with pancreatic atrophy (×).

secretion. The scan was normal in 34 of the 56 patients with a normal pancreas. Thirty-two of these 34 had normal exocrine function; one patient secreted a marginally reduced volume of juice of normal enzyme and bicarbonate content, in another the maximum concentration of bicarbonate was reduced but the bicarbonate and output were normal. All 17 patients with scan abnormalities in this group (fig 1) secreted a normal volume of pancreatic juice of normal enzyme content. The output of bicarbonate was reduced in one patient with Vaterian stenosis and in another with bile duct cancer in whom the pancreas was judged to be normal at laparotomy, though the primary site of cancer was not confirmed by necropsy.

Patients with chronic pancreatic disease

Abnormal scans were recorded in 30 of the 34 patients (88%) with chronic pancreatic disease. The volume of pancreatic juice was significantly reduced in 16 of these 30 patients (53%), the output of bicarbonate after secretion was low in 27 patients (90%), and amylase output after pancreozymin was reduced in 17 (57%) (figs 2, 3, and 4).

Discussion

A frequent criticism of pancreatic scanning is the lack of objectivity in reporting and the consequent variability of scan reports depending on the experience of the observer. In this study three or more

of the four observers agreed in 84% at the first reading and in 88% at the second. While these figures indicate consistency in reporting (table II) there was an increased incidence of unanimous reports (from 51 to 72) when the clinical details were made available to the observers.

In the 'control' group the incidence of abnormal scans was 30%. It should be appreciated that these patients in this control group were selected in that they all presented with abdominal symptoms to a clinical department. While such a population serves as a normal sample after pancreatic disease has been excluded, it may be that a few of these patients have had undetected pancreatic disease which may account for the abnormal scans. However, this is unlikely to be a major error since the proportion of abnormal scans was 26% in the subgroup of 23 patients in whom the pancreas was adjudged normal at laparotomy. In addition, all but two of the 17 patients with abnormal scans in this control group had normal exocrine function assessed by the secretin-pancreozymin test. McCarthy, Brown, Melmed, Agnew, and Bouchier (1972) list 32 conditions with a high incidence of abnormal scans in which the appearance does not reliably reflect pancreatic morphology or function. These cover many common clinical conditions including diabetes mellitus and peptic ulcer. In the present study four of the 17 patients with abnormal scans (25%) were diabetic, an association recognized by Lähdevirta (1967), and six of the seven patients with the clinical diagnosis of the spastic colon syndrome and one third of the patients with biliary disease had abnormal scans (table III). The reason why patients with a normal pancreas may have abnormal scans has not yet been explained in physiological terms.

Pancreatic scanning is of little diagnostic value during and immediately after an attack of acute pancreatitis but tends to reflect the return of pancreatic function to normal following the acute episode. Thus the appearance of scans vary with the timing of the scan in relation to the acute attack and no reliance should be placed on an abnormal scan within three to four weeks of an acute attack. We have followed the return of an abnormal scan to normal after acute pancreatitis in five of these cases. The scan may remain abnormal so long as a pseudocyst remains untreated.

The overall incidence of scans interpreted as normal in the group of 34 patients with chronic pancreatic insufficiency was 9%. While the incidence of abnormal scans in chronic pancreatitis and cancer of the pancreas was 95% and 79% respectively, the scan fails to differentiate between the two conditions.

Abnormal scans roughly paralleled diminished exocrine secretion in this group of patients. Since

⁷⁵Se Selenomethionine uptake and enzyme secretion depend on acinar cell mass and function, a particularly good relationship was expected between abnormal scans and diminished levels of enzyme after pancreozymin. The amylase output was diminished in 57% of patients with chronic pancreatitis and cancer of the pancreas with abnormal scans. In view of recent references which suggest that the amylase output in the normal population has a skew deviation (Sarles, Pastor, Pauli, and Barthelemy, 1963; Sun, 1963; Goldberg and Wormsley, 1970), we speculated that the lower limit of the normal range of Burton *et al* (1960a), which assumed that a Gaussian distribution might be too low and in part account for the relatively poor correlation obtained. We therefore computed the lower limit of the normal range for amylase in a group of 97 normal subjects using the non-parametric percentile estimate (Reed, Henry, and Mason, 1971). Using the PE lower limit the association between abnormal scans and decreased enzyme output in chronic pancreatic disease rose to 60% for amylase and 66% for trypsin. Corresponding values for volume and bicarbonate became 57 and 80% respectively. The interrelation between abnormal scans and decreased output of bicarbonate was greater than the interrelation between abnormal scans and diminished amylase or trypsin output, a difference which may reflect in part the relatively crude methods available to estimate enzyme activity.

The incorporation of ⁷⁵Se Selenomethionine into the acinar cells of the pancreas in the fed state may not correspond exactly to the output of enzyme excreted in the 30 minutes following pancreozymin in the secretin-pancreozymin test which is performed after a 12-hour fast, though Youngs, Agnew, Levin, and Bouchier (1971) found a reasonable correlation between radioactivity in the duodenal aspirate 90 to 120 minutes after ⁷⁵Se Selenomethionine and the mean concentration of tryptic activity in 30-minute samples over 120 minutes following a Lundh-Borgström meal. In their recent review of pancreatic scanning Bachrach, Birsner, Izenstark, and Smith (1972) have suggested that manipulation of the diet and the injection of the intestinal secretory hormones secretin and pancreozymin may possibly alter the optimal time for scanning but this still remains to be proved.

The incidence of abnormal secretin-pancreozymin tests in the normal group was 7% and the test was within normal limits in 12% of the patients with chronic pancreatic disease. While the secretin-pancreozymin test provides information essential for both the diagnosis and the management of the patients with chronic pancreatitis and cancer of the pancreas (Howat, 1968a, 1968b), it can prove

uncomfortable for the patient and requires the presence of a technically skilled physician throughout the test. In this group the secretin-pancreozymin test was incomplete or was abandoned in 14 patients.

Conclusions

Excellent acceptance by patients and ease of technique combine to ensure the continued use of ^{75}Se Selenomethionine scanning to screen patients for pancreatic disease in spite of its cost. In patients suspected of chronic pancreatitis and cancer of the pancreas a normal scan virtually eliminates the presence of pancreatic disease and no further investigations need be undertaken. When an abnormal scan is obtained, however, it is necessary to proceed to a specific test of pancreatic function to discriminate between a normal pancreas which has not taken up the isotope and a pathological gland, and to establish a definitive diagnosis. We use the secretin-pancreozymin test for this purpose.

In a group of patients with chronic pancreatitis and cancer of the pancreas there is a close interrelation between abnormal scans and diminished exocrine secretion, especially bicarbonate output following a submaximal dose of secretin. However, 30% of patients with a normal pancreas have abnormal scans. In this 30% pancreatic function assessed by the secretin-pancreozymin test is normal.

Until more is known of the factors and constraints which regulate the uptake and distribution of ^{75}Se Selenomethionine in abdominal and systemic disorders when the pancreas is normal, an abnormal scan cannot be equated with pancreatic malfunction.

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