THE AETIOLOGY, CLINICAL FEATURES AND DIAGNOSIS OF PANCREATITIS IN THE SOUTH WESTERN CAPE

A REVIEW OF 243 CASES

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Although the association between pancreatitis and both alcohol and gallstones was recognized shortly after the beginning of this century,[1-5] it is only in the past decade that attention has been focussed on the striking differences between these two forms of pancreatitis.[6-10] The wide use of alcohol probably contributed to the neglect of its role as a causative factor, and even the most authoritative workers,[11] as recently as 1953, were reluctant to accept cholelithiasis as an aetiological factor in pancreatitis. The conventional classification of pancreatitis into acute, relapsing and chronic types further minimized the importance of an aetiological approach, and tended to the institution of a standard medical and surgical attack on the disease irrespective of the specific cause in the individual patient. Little attempt was made to identify and eradicate the aetiologic factor in such patients.

The diagnosis of pancreatic disease is frequently dependent on various laboratory procedures. The relatively simple measurement of the serum amylase, although of value in the diagnosis of acute pancreatitis, is seldom helpful in the more chronic stages of the disease. In recent years 4 further parameters of pancreatic function have been introduced to assist in establishing a diagnosis of pancreatic disease. The pancreatic-function test, utilizing secretin and pancreozymin stimulation,[12-16] the provocative serum-enzyme test,[13-15,17] and chemical and radioactive measures of fat absorption, provide an index of the exocrine function of the pancreas, and the glucose-tolerance test is employed to assess the endocrine function of the gland.

The purpose of this paper is to stress the importance of establishing an aetiologic diagnosis and to draw attention to the marked differences that exist between alcoholic and gallstone pancreatitis with regard to the clinical, therapeutic and prognostic aspects. Clinical subdivisions of these groups will also be tentatively suggested. In addition, the relative value of the various tests employed in the diagnosis of pancreatic disease will be examined.

METHODS

The patients studied were referred to the Gastro-intestinal Service from the medical, surgical and paediatric divisions at Groote Schuur Hospital, the New Somerset Hospital, Victoria Hospital, Wynberg Military Hospital and Red Cross War Memorial Children's Hospital. The 243 patients with pancreatitis considered in the present paper were referred to the Service during the past 3 years. Their ages varied between 10 and 89 years.

Serum enzymes: Serum amylase was measured by the Wohlgemuth method[18] for the first 2 years of the study and thereafter by the method described by Pimstone.[19] Serum lipase[20] and trypsin[21] determinations were also carried out during the latter part of the study.

The pancreatic-function test (PFT), the provocative serum-enzyme test (PET), the glucose-tolerance test, and tests of fat absorption were carried out as described by Bank *et al.** The criteria of abnormality suggested by them were adopted.

Biliary disease and intraduodenal worm infestation: (*i*) Variations in the colour of the duodenal aspirate during the course of the pancreatic-function test provided an index of gallbladder function. (*ii*) An aliquot of the post-pancreozymin collection of duodenal aspirate was examined microscopically for biliary pigment, cholesterol crystals, *Giardia lamblia* and parasitic ova. (*iii*) The serum-bilirubin estimation, flocculation test and alkaline-phosphatase estimation were carried out as a routine in all patients during the pancreatic-function test.

Radiological examination: (*i*) Straight X-ray of the abdomen and chest was carried out in patients presenting with an acute attack of abdominal pain. An oblique view of the upper abdomen was taken to examine for pancreatic calcification. (*ii*) A barium-meal examination was made. (*iii*) Cholecystography and intravenous cholangiography was carried out.

Other investigations: (*i*) The haemoglobin, white blood count and erythrocyte sedimentation rate (ESR) were measured in all patients. The serum lipids were not measured, but gross hyperlipaemia (milky serum) was noted. (*ii*) The serum calcium and phosphorus levels were determined in all patients with pancreatitis in whom gallstones or alcohol could not be incriminated as an aetiologic factor. (*iii*) The sweat test was carried out in a few patients.

Laparotomy and *definitive pancreatic surgery* were carried out where indicated.

CLASSIFICATION

The conventional classification of pancreatitis into acute, relapsing, chronic and painless varieties has proved of only limited value in the understanding of proper management of the disease. These shortcomings prompted us to adopt a classification based on aetiologic factors rather than on clinical considerations (Tables I and II). Alcohol

TABLE I. CLINICAL CLASSIFICATION OF PANCREATITIS BASED ON AETIOLOGIC VARIETIES

Group	Aetiologic variety	Number of Patients: Pain	Painless	Total
I	Alcoholic pancreatitis	137	11	148
II	Pancreatitis and biliary disease	37	3	40
III	Miscellaneous	14	20	34
IV	Unknown	18	3	21
	Total	206	37	243

was considered to be responsible for 61% of the 243 cases and biliary disease for a further 16%. Miscellaneous causes accounted for 14%, and the aetiology in the remaining 9% could not be ascertained. Pancreatic disease unassociated with pain was present in 37 patients.

I. ALCOHOLIC PANCREATITIS

Our experience with 148 cases of pancreatitis associated with a moderate to heavy intake of alcohol offers strong support for the view that alcoholic pancreatitis is a defi-

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*See article by Bank *et al.* on p. 1061 of this issue of the *Journal*.

nite entity, differing markedly from other varieties of pancreatitis with regard to natural history, liability to pancreatic insufficiency and response to therapy.

Alcoholic pancreatitis is predominantly a disease of males, developing in early adulthood or soon after. Only 8 of our 148 cases occurred in females. The age at onset of attacks in the 137 cases of painful pancreatitis was calculated by subtracting the duration of symptoms from the age of the patient when first seen at the Gastro-intestinal Service; 30·5% of these patients began having attacks before the age of 30 and 71% before the age of 40, while only 8% of patients had their first attack when over the age of 50. No racial difference was noted among the 148 patients. Bantu patients constituted 10% of the group, a figure which agrees closely with the proportion of Bantu admissions to the medical and surgical wards of the hospital.

The majority of patients began drinking excessively in their late teens or early twenties. Many started drinking while in the armed forces during World War II; others acquired the habit working in the hotel and liquor trades or at sea, while farm labourers had the habit foisted on them by the 'tot system' (free supply of fortified cheap wines). The type and amount of alcohol consumed varied considerably in different patients. Cape Coloured patients tended to use cheap wines, whereas Europeans seemed to prefer brandy. Whisky drinkers constituted a distinct minority. The drinking pattern ranged from 'round the clock' drinking of 2 - 4 bottles of wine or ½ - 1 bottle of spirits a day, to little or no drinking except during weekends. A few patients drank as much as 15 bottles of wine each weekend, their thirst limited only by financial factors. A striking feature was the long time interval between the commencement of alcoholic indulgence and the onset of the first attack of clinical pancreatitis. This first attack usually occurred against a background of a heavy alcoholic intake of about 5 - 15 years' duration. Despite the foregoing, most patients were considered to be 'heavy drinkers' rather than 'chronic alcoholics'.

A fairly characteristic alcohol-pancreatic-pain pattern occurred in the majority of patients, but in many the clinical picture was sufficiently different to warrant the consideration of alcoholic pancreatitis under separate subheadings.

Clinical Subgroups:

1. *Typical Alcoholic Pancreatitis*

This well-recognized clinical entity, comprising the acute and relapsing varieties of the disease, was found in 116 of the 148 cases of alcoholic pancreatitis. At the time of writing 101 of these patients had had recurrent acute and subacute attacks and only 15 a single acute attack. Relationship of the attack to an alcoholic binge or a night's over-indulgence was of paramount importance, but in many the amount of alcohol consumed was not necessarily greater than, or indeed as much as, that taken with impunity on previous occasions. Another point which tended to detract from the significance of the alcohol in the causation of the attack was that the pain usually commenced some 12 - 48 hours after the end of the drinking bout. A few patients admitted to early morning nausea and headache on the 'morning after', but most remained quite well until the onset of the attack of abdominal pain during the afternoon, evening or following day. The onset of persistent abdominal pain on the 'afternoon after the night before' was found to be characteristic of alcoholic pancreatitis.

The severity of the attack varied greatly from patient to patient. In the relapsing group individual attacks in the same patient also showed marked variations. Of the 116 patients, 82 were sent into hospital on at least 1 occasion with the diagnosis of 'acute abdomen'. The pain was usually fairly widespread over the upper abdomen, but a few patients had pain localized to the right or left upper quadrants. Pain radiation through to the back was commonly present, and some patients volunteered that the pain was less severe when sitting or bending forwards. Patients with the more acute attacks had excruciatingly severe generalized abdominal pain with little radiation through to the back and no postural relief. The pain was persistent, increasing in severity over the first 24 hours,

TABLE II. CLINICAL CLASSIFICATION OF PANCREATITIS USED IN THE PRESENT SERIES (243 PATIENTS)

	No.
I. *Alcoholic pancreatitis* (148 cases):	
Typical attacks	
Non-calcific	
Single acute attack	15
Relapsing acute or subacute attacks	64
Calcific	
Relapsing	37
Atypical attacks	
Non-calcific	
'Executive' type	6
Other varieties	15
Painless	
Non-calcific	
Associated with cirrhosis	8
Unassociated with cirrhosis	2
Calcific	1
II. *Pancreatitis caused by biliary disease* (40 cases):	
Painful attacks	
Acute gallstone pancreatitis	16
Pain not necessarily due to pancreatitis	
Gallstones and chronic pancreatic disease	14
Postcholecystectomy syndrome	4
Post-sphincterotomy pancreatitis	2
Choledochal cyst and pancreatitis	1
Painless	
Postcholecystectomy disorder	3
III. *Miscellaneous causes* (34 cases):	
Painful pancreatitis	
Traumatic pancreatitis	3
Penetrating duodenal ulcer	3
Other causes	8
Painless pancreatitis	
Non-alcoholic cirrhosis	6
Small bowel disease	6
Haemochromatosis	5
Fibrocystic disease	1
Other causes	2
IV. *Unknown causes* (21 cases):	
Painful attacks	
Non-calcific	18
Painless	
Non-calcific	1
Calcific	2

and then remaining constant for a few days before passing off. It was aggravated by food in some patients, but was unassociated with heartburn, was not relieved by alkalis, and seldom woke the patient up at night. Anorexia was usually present, and nausea and vomiting were features of the more severe cases. However, vomiting rarely preceded the onset of the pain and did not occur in some patients. Blood-streaked vomitus was sometimes noted, and 11 of the patients with typical attacks gave a history of frank gastro-intestinal bleeding. The bleeding in 8 occurred later than the onset of abdominal pain, often several days after the last drinking bout. The bowels were usually costive, and a few patients noted that their urine had become dark. One patient with severe left quadrant pain and haematuria was transfered from the urological ward after investigations there had proved negative.

Examination during the attack sometimes revealed an acutely ill patient with fever, tachycardia, abdominal tenderness, and guarding (most marked in the epigastrium or right or left upper quadrant) and absent or diminished bowel sounds; tenderness in the left lumbar region was sometimes noted and mild jaundice was occasionally present. In others, physical examination was non-contributory apart from upper abdominal tenderness. Although the liver was sometimes palpable, overt evidence of cirrhosis was distinctly rare. Patients were seldom inebriated on admission. A few showed evidence of peripheral neuritis.

A mild leukocytosis, a raised ESR and an elevated serum-amylase level were usually present. Many patients with severe relapsing pancreatitis were found to have a normal serum-amylase level during acute attacks, however. A frankly milky serum occurred in 4 patients. Glycosuria was often noted, but the urine became sugar-free in many, once the attack subsided. A proportion had diabetes as a result of previous attacks. The serum bilirubin was slightly elevated in many patients and the urine in these usually contained bile. Straight X-ray of the abdomen often showed one or more dilated loops of bowel in the upper abdomen, and an occasional patient showed elevation of the diaphragms, a small pleural effusion, or signs at one or other lung base. Calcification in the region of the pancreas was of obvious diagnostic value. Barium studies were usually non-contributory, but widening and pressure deformity of the duodenal loop and external compression of the stomach were sometimes noted. Deformity of the duodenal cap suggestive of duodenal ulceration was seen in 6 patients, but slight abnormality of the second part of the duodenum was also noted when the barium study was repeated in 2 patients.

The acute attacks tended to settle within a few days of commencing conventional medical treatment. This treatment included gastric suction, intravenous fluids, anticholinergics, antibiotics and analgesics; 'trasylol'* was also used on occasions. Many patients required little more than bed rest and analgesics. A few had more persistent pain associated with a leukocytosis and an increasing ESR. Some of these developed an ill-defined mass in the upper abdomen, caused by a pseudocyst of the pancreas. The hospital course was occasionally complicated by delirium tremens or gout. A small proportion of patients were extremely ill, but the attack rarely constituted a threat to life; only 2 patients succumbed from acute fulminating pancreatitis; one of these showed tetany, encephalopathy, and Grey-Turner's and Cullen's signs. These features did not occur in any of the other patients with alcoholic pancreatitis.

* Kindly supplied by FBA Pharmaceuticals Ltd.

Calcific pancreatitis: Calcification of the pancreas was present in 37 of the 116 patients with typical alcoholic pancreatitis. All gave a history of relapsing pancreatitis, but 8 of them were referred to us many years after the last attack of alcoholic pancreatitis for investigation of diabetes or steatorrhoea. There were 3 additional cases of calcific pancreatitis unassociated with a history of typical alcoholic pancreatitis. These comprised 2 patients with painless pancreatitis in whom alcohol could not be incriminated as an aetiological factor and one 65-year-old patient with radiological evidence of pancreatic calcification noted during routine examination for a recent ulcer dyspepsia; he had taken an excessive amount of spirits for many years until some 30 years previously, but could not remember having had attacks of abdominal pain at the time. The pancreatic calcification in the 40 cases in the present series usually involved the head or the entire organ, but was occasionally confined to the tail. The radiological appearances varied from a diffuse, fine distribution to discrete, nodular areas ranging up to 1 cm. in diameter. Larger areas of calcification tended to be confined to the head of the pancreas.

Recurrent attacks in the 37 patients with relapsing alcoholic pancreatitis associated with calcification were usually precipitated by alcoholic binges. Chronic pancreatic pain eventually supervened in a large number of chronic alcoholics and in them the clinical picture was further complicated by drug addiction. However, 5 patients in the calcific group suffered persistent pain following a typical attack, despite complete alcohol withdrawal subsequent to the attack. The pain in 2 of these patients was attributed to the development of pancreatic cysts, since it disappeared after surgical drainage of these cysts. A few patients had occasional attacks of pancreatic pain despite alcohol withdrawal. Overt evidence of pancreatic insufficiency—diabetes, marked weight loss and steatorrhoea—was very much more common in the calcific than in the non-calcific groups of alcoholic pancreatitis. Low-grade or marked jaundice associated with a raised serum alkaline-phosphatase level was present in a few patients with calcific pancreatitis; chronic obstruction of the lower end of the bile duct by the diseased pancreas was found in all patients subjected to laparotomy. Histologic evidence of biliary cirrhosis was found in 2 of these patients. Although biochemical jaundice was not infrequently present during attacks in patients with non-calcific alcoholic pancreatitis, the development of chronic biliary obstruction as manifested by persistent jaundice and a raised alkaline-phosphatase level was rare.

2. *Atypical Alcoholic Pancreatitis*

Of the 148 patients with alcoholic pancreatitis, 21 suffered abdominal pain which did not conform to typical attacks of pancreatitis. They could be divided into the following sub-groups:

(*a*) *'Executive type':* The 6 patients in this sub-group

had recurrent attacks of persistent upper abdominal discomfort or pain, invariably related, as in the case of patients with typical attacks of alcoholic pancreatitis, to a night's over-indulgence. The patients usually admitted to a moderate, but socially acceptable, intake of alcohol over many years. This usually amounted to about 2 - 8 tots of whisky or brandy on most evenings, with considerably greater amounts being taken whenever the pretext of a party presented itself. The patients seldom showed any ill-effects from the alcohol, apart from an occasional episode of diarrhoea following a party. Many prided themselves on their ability to drink most other people 'under the table' without suffering any harmful effects themselves. The eventual development of recurrent bouts of upper abdominal discomfort some 12 - 48 hours after a party was not usually attributed to the party. Medical advice was seldom sought during an attack, since severe pain and vomiting were only rarely present, and the patients were usually able to continue at work. The discomfort or pain was persistent, and tended to last for a few days; in many it radiated through to the back and was eased by a forward posture. Most patients in this sub-group were either business executives or manufacturers' representatives. Three further patients who developed typical alcoholic pancreatitis against a background of 'executive pancreatitis' were included in the typical group.

(*b*) *Persistent pain with or without exacerbations:* This sub-group consisted of 15 patients in whom a definite relationship between abdominal pain and alcoholic over-indulgence could not be elicited; all used excessive amounts of alcohol and many were confirmed alcoholics. Six of these patients had persistent pain and 9 suffered from attacks of pain not particularly suggestive of pancreatic disease. Two of the 9 presented with early morning upper abdominal pain relieved by the passage of watery stools. The associated and complicating features noted in the typical pancreatitis group were present in some of these patients.

3. *Painless Alcoholic Pancreatitis*

Eleven patients with a strong history of alcoholism had pancreatic disease unassociated with pain. They comprised the following sub-groups:

(*a*) *Cirrhosis or transient hepatomegaly:* Of 20 patients with alcoholic liver disease, 8 showed disturbed pancreatic function. These included 2 patients with cirrhosis of the liver and glycosuria, 5 with cirrhosis unassociated with clinical diabetes, and 1 who presented with acute diabetes and hepatomegaly. The mean age of the patients in this sub-group was 53 years, with a range of 41 - 62 years, and was greater than that found in the typical pancreatitis group.

(*b*) *Painless pancreatitis unassociated with cirrhosis:* One patient presented with diabetes and another with obstructive jaundice of 6 months' duration. The third patient in this sub-group was the 65-year-old male with pancreatic calcification found during radiological investigations of a recent ulcer dyspepsia, mentioned earlier.

Overt Pancreatic Insufficiency and Complications in Alcoholic Pancreatitis

The incidence of these features among the different groups of patients with alcoholic pancreatitis is shown in Table III. Twenty-nine of the 148 patients had been diagnosed as having diabetes before they were referred to the Gastro-intestinal Service; 18 of these patients had calcific pancreatitis. The diabetes was considered to be pancreatic in origin in all 29 patients, although 3 gave a family history of diabetes.

Eighteen patients had a clinical history of steatorrhoea, but advanced liver disease associated with deep jaundice undoubtedly contributed to the steatorrhoea in one of them; 14 of the remaining 17 patients had calcific pancreatitis. Pancreatic replacement therapy improved the character of the stools in these patients.[22]

Twenty-one of the 137 patients with painful alcoholic pancreatitis developed pseudocysts of the pancreas, the incidence in the calcific group again being slightly higher than in the non-calcific groups.

Gastro-intestinal bleeding occurred in 17 patients, 4 of whom were considered to have bled from oesophageal varices, peptic ulceration or acute erosion, and one of whom bled following pancreatic surgery. The bleeding in the remaining 12 patients occurred following the onset of attacks of pancreatitis, and a few of these had recurrent bleeds with subsequent attacks. Three of the 12 patients were admitted to hospital with a haemoglobin level of less than 5 G. per 100 ml., and a fourth also required blood transfusion. Detailed investigations, including laparotomy in 3 failed to establish the cause of the bleeding.

Cirrhosis of the liver was a feature in 17 patients, 8 of whom had no clinical evidence of pancreatitis, and a further 2 who had biliary cirrhosis complicating involvement

TABLE III. COMPLICATIONS AND INCIDENCE OF PORTAL CIRRHOSIS IN 148 PATIENTS WITH ALCOHOLIC PANCREATITIS

		Typical attacks			*Atypical attacks*		*Painless*		
	Total	*Non-calcific*		*Calcific*	*Non-calcific*		*Non-calcific*		*Calcific*
		1 attack	*Relapsing*		*Executive*	*Atypical*	*Cirrhosis*	*No cirrhosis*	
	148	*15*	*64*	*37*	*6*	*15*	*8*	*2*	*1*
Diabetes*	29	0	6	18	0	1	3	1	0
Steatorrhoea†	17 (1)	0	3	14	0	0	0 (1)	0	0
Cyst formation	21	1	10	7	0	3	0	0	0
Bleeding	12 (5)	0	3 (3)	5	0	4 (1)	0 (1)	0	0
Cirrhosis	17§	0	4	4§	0	1	8	0	0
Carcinoma	2	—	1	—	—	1	—	—	—

* Known diabetics; † Clinical steatorrhoea; Numbers in brackets refer to complications not caused by the pancreatitis *per se*; § Includes 2 patients with biliary cirrhosis.

of the lower end of the common bile duct by the pancreatic disease. Thus only 7 of the 137 patients with painful alcoholic pancreatitis had alcoholic cirrhosis. The diagnosis of portal cirrhosis could be established in only 2 of the 38 patients with calcific pancreatitis, the most protracted and severe form of the disease. Investigations included serum-protein estimations, flocculation tests, and bromsulphalein excretion. Liver biopsy carried out in 12 patients confirmed the presence of portal cirrhosis in 2 with undoubted cirrhosis, showed normal histology in 8, and mild siderosis in 2.

Carcinoma of the pancreas was an unexpected complication in 2 patients who had suffered recurrent attacks of alcoholic pancreatitis for 5 and 10 years respectively; both patients ultimately developed pancreatic cysts which appeared to be benign at operation. The carcinoma was found in a routine biopsy of the cyst contents in one and of the cyst wall in the other.

Biliary Disease or Disorder in Patients with Alcoholic Pancreatitis

The following disturbances were encountered:

(*i*) Transient slight elevation in the serum-bilirubin level, and the presence of bile in the urine occurred in a sufficiently large group of patients to render these findings of value in supporting a clinical diagnosis of pancreatitis. The alkaline-phosphatase level was elevated in 3 patients with non-calcific pancreatitis and in 6 with calcific pancreatitis; 4 of these 9 patients presented with obstructive jaundice and, of these, 2 had histologic evidence of biliary cirrhosis. Involvement of the lower end of the common bile duct by the disease process in the pancreas was responsible for the findings in all patients.

(*ii*) Bile pigment aggregates were occasionally recovered from the duodenal aspirate in patients tested within 3 weeks of the last attack of pancreatitis. Subsequent cholecystography failed to confirm the presence of gallstones in these patients.

(*iii*) Cholecystography frequently failed to show gallbladder filling when carried out during or immediately after an attack of pancreatitis, but was almost invariably normal when done some weeks after an attack. Only 1 patient in the group had cholecystographic evidence of gallstones; a large cholesterol stone was found at laparotomy, but the clinical history and laboratory findings prompted our retaining him in the alcoholic group.

(*iv*) Biliary pigment stones were found at laparotomy in a further 2 patients, both of whom gave a typical history of long-standing alcoholic pancreatitis. Transient jaundice, non-function of the gallbladder on cholecystography and biliary pigment stones in the gallbladder were considered to be secondary to pancreatic disease with common bile duct hold-up and biliary stasis.

Diagnosis of Pancreatic Disease in Alcoholic Pancreatitis

A confident clinical diagnosis could usually be made in patients presenting with typical relapsing alcoholic pancreatitis. The history was less typical or indeed atypical in others, and in some the correct history was not elicited when the patient was first seen. Thus, only those patients in whom the diagnosis of pancreatic disease could be made on laboratory tests or operative findings were included in the present series. Many patients were subjected to detailed investigation after the diagnosis had already been established by means of laparotomy, and others were investigated before operation.

Table IV shows the diagnostic criteria employed in 86 fully investigated patients with non-calcific alcoholic pancreatitis associated with pain. The PFT was abnormal in 59 patients, 54 of whom showed, in addition, abnormality of one or more of the other tests, comprising the PET, the serum-amylase level noted during an attack of pain, the glucose-tolerance test (GTT), and the fat-absorption test. Of the 5 in whom the PFT was the only abnormality, 4 showed an impaired bicarbonate and enzyme response,

TABLE IV. LABORATORY DIAGNOSIS OF PANCREATIC DISEASE IN 86 PATIENTS WITH PAINFUL NON-CALCIFIC ALCOHOLIC PANCREATITIS, SUBJECTED TO DETAILED INVESTIGATION

Abnormal test	*Number*	*Operative confirmation*
PFT abnormal (59 patients):		
PFT only	5	2
+ 1 other test *	21	5†
+ 2 other tests *	27	10
+ 3 other tests *	6	3
PFT normal (27 patients):		
Only 1 other test abnormal		
PET	8	2
GTT	6**	1
Serum-amylase level	5**	0
Two of above abnormal *	5	2
Three of above abnormal *	3	1

PFT = pancreatic-function test, PET = provocative serum-enzyme test, GTT = glucose-tolerance test.

*Refers to one or more of the following—PET, serum-amylase level during attack, GTT, and fat-absorption tests.
** Associated transient jaundice in 2 patients.
† Laparotomy negative in a 6th patient.

and the fifth a grossly impaired enzyme response. Laparotomy confirmed the diagnosis in 20 of the 21 patients with abnormal pancreatic-function tests who were subjected to operation. The negative laparotomy was in a patient who had developed a mass in the right iliac fossa some months after his last attack of alcoholic pancreatitis; the tests had been carried out a few days after this attack. Eight other patients had previously had an 'interval appendicectomy' for what, in retrospect, must have been relapsing pancreatitis. The pancreas in these patients had not been examined at operation.

Twenty-seven of the 86 patients showed no abnormality in the PFT, and laboratory confirmation in these was obtained by means of one or more of the less-specific tests of pancreatic disease. Three showed an abnormal PET and GTT, and an elevated serum-amylase level during an attack, and a further 5 an abnormality of 2 of these 3 tests. In 19 the laboratory diagnosis was based on the finding of an abnormality in only 1 of these tests. Transient jaundice associated with a mild leukocytosis strengthened the diagnosis in 4 of these 19 cases. Laparotomy confirmed the diagnosis in 6 of the 27 patients.

The diagnosis in a further 14 patients with acute or relapsing non-calcific pancreatitis not subjected to detailed investigations was established by means of laparotomy in

6, a markedly elevated serum-amylase level in 6, an elevated serum-amylase level associated with disturbed glucose tolerance and jaundice in 1, and by disturbed glucose tolerance and jaundice in 1 (see Table VII).

Calcific pancreatitis: Pancreatic investigations were hardly necessary to confirm the diagnosis of pancreatic disease in the 37 patients with calcific pancreatitis. The results of these investigations are discussed below under the heading of 'the reliability of the pancreatic-function test in 200 patients tested'.

Painless pancreatitis: The diagnosis in the 11 patients with painless alcoholic pancreatitis was made by means of laparotomy in 1 and detailed pancreatic investigations in 10. One of these 10 had calcification of the pancreas; 8 of the remaining 9 had abnormal pancreatic function associated, in 5, with abnormal glucose tolerance or a positive PET. Only 1 patient had a normal PFT, but both the PET and glucose tolerance were abnormal.

The Role of Surgery in Alcoholic Pancreatitis

Seventy-seven abdominal operations were carried out on 52 of the 137 patients with painful alcoholic pancreatitis. Most of these operations had been performed before the present study began. They included laparotomy, cholecystectomy, sphincterotomy and choledochostomy, cholecystectomy combined with sphincterotomy and choledochostomy, cholecyst-enterostomy, left and right splanchnicectomy, Whipple's operation, distal pancreatectomy and pancreatico-jejunostomy, total pancreatectomy, various gastric operations, drainage of retroperitoneal abscess, and various cyst drainage procedures. Apart from total pancreatectomy, all these procedures proved of doubtful value in preventing attacks, except where the patient abandoned alcohol completely. On the other hand, the results of medical treatment based on alcohol withdrawal were highly satisfactory in most patients. Furthermore, ablation procedures on the pancreas invariably aggravated signs of pancreatic insufficiency, and frequently added diabetes and steatorrhoea to the burden of pancreatic pain. The drainage of a retroperitoneal abscess or pancreatic cyst was clearly justified.

The persistence of pancreatic pain for weeks or months following alcohol withdrawal posed a difficult problem in management and prompted laparotomy in some patients to exclude a pancreatic cyst, pancreatic duct obstruction, malignant disease or unrelated abdominal disease. The finding of carcinoma on routine biopsy in 2 patients with pancreatic cysts underlined the importance of routine biopsy in patients operated on for chronic pancreatic pain.

II. PANCREATITIS CAUSED BY BILIARY DISEASE

Although biliary disease accounted for only 40 of the 243 cases of pancreatitis in the present series, it was undoubtedly the most important single cause of pancreatitis in non-alcoholic patients, in females and in the elderly. Twenty-three of the 40 patients were over the age of 50, the mean age being 58 years. Twenty-eight of the patients were female and only 12 male. No racial difference was noted.

Clinical Subgroups

1. *Acute Gallstone Pancreatitis*

The 16 patients in this sub-group included those with the most severe and indeed the most lethal pancreatitis in the series. Two of the 16 died during the acute attack, and a further 4 were critically ill for some weeks before recovering from it. The fact that 8 of the 16 patients were subjected to immediate laparotomy after admission to hospital offered further evidence of the severity of the attacks and the acuteness of the condition. Apart from the severity of the attack, however, the clinical picture of gallstone pancreatitis was similar to other varieties of acute or relapsing pancreatitis. The patient, often a female and usually over the age of 50, sometimes gave a history of previous attacks of biliary colic or pancreatitis. The pain was described as persistent and progressively severe, starting in the upper abdomen and spreading to involve the whole abdomen. Severe vomiting usually followed the onset of pain, and pain radiation through to the back was sometimes a feature. Three of the 16 patients had diabetes which antedated the onset of abdominal pain.

The patients were often acutely ill on examination; tachycardia, fever and marked abdominal distension were usually present. A few were dyspnoeic and many were shocked. Abdominal tenderness and guarding was sometimes diffuse. Clinical jaundice was sometimes present and occasionally marked, but mild or moderate elevation of the serum-bilirubin level was the rule. The serum-amylase level was invariably elevated, often markedly.

Emergency laparotomy was carried out in 8 patients, and 3 of these had definitive biliary surgery for gallstones. One of these 3 had a stone at the lower end of the common bile duct and died a few days later, but the remaining 7 patients settled, within about 10 days, on intravenous drip, gastric suction, antibiotics and anticholinergics. The 8 patients not subjected to immediate laparotomy included 5 who settled satisfactorily on the above medical regime within a few days to a week, 2 in whom operation was deemed necessary after the attack had failed to respond to a fortnight's conservative therapy, and 1 who remained critically ill until her death on the sixth day; she had developed acidotic breathing and Cullen's and Grey-Turner's signs a few days before her death. The 2 severely ill patients operated on a fortnight after admission both had stones in the lower end of the common bile duct; 1 had a large necrotic cyst involving the greater part of the body of the pancreas.

The diagnosis of pancreatitis in these patients was made by laparotomy or by the finding of a raised serum-amylase level. Emergency laparotomy always showed the recognized changes of acute pancreatitis, but the gallstones were missed despite careful palpation of the gallbladder in no fewer than 5 of the 8 patients operated on in an emergency. The temperate habits, age and, to a lesser extent, sex of these 5 patients prompted a detailed investigation during the convalescent period for possible gallstones. Cholecystography revealed filling defects in the gallbladder in 2, non-function in 2 and an apparently nor-

mal cholecystogram in 1. Biliary drainage yielded cholesterol crystals, with or without biliary pigment, in 4, and biliary pigment alone in 1. This last patient was a 74-year-old female in whom cholecystography showed non-function of the gallbladder; an intravenous cholangiogram showed a normal common bile duct, but there was again no filling of the gallbladder. These 5 patients were each subjected to a second operation—elective cholecystectomy on the basis of these results—and the presence of gallstones was confirmed in all.

Of the remaining 8 patients not subjected to immediate laparotomy, 2 had cholecystographic evidence of gallstones, and a further 3 showed a non-functioning cholecystogram; the diagnosis in 1 of these 3 was suggested by the result of routine biliary drainage which yielded cholesterol crystals. Biliary drainage was negative in the remaining 2. Laparotomy carried out after recovery from the acute attack confirmed the presence of gallstones in 5 patients. In the 2 patients who failed to respond to a fortnight's conservative therapy, operation revealed stones in the gallbladder and the lower end of the common bile duct. Autopsy confirmed the clinical impression of gallstones in the eighth patient.

The role of surgery in acute gallstone pancreatitis: None of the 14 patients with acute gallstone pancreatitis submitted to biliary surgery suffered a recurrence of pancreatitis during the 6 months—3 years during which they were followed-up. This highly satisfactory response to operation contrasts strongly with the poor results following operation in patients with alcoholic pancreatitis.

2. *Gallstones Associated with Chronic Pancreatic Disease*

Clinical evidence of acute pancreatitis was absent in this sub-group of 14 patients with cholelithiasis. The serum-amylase level was not found to be elevated in any of the 8 patients tested. Four of the 14 patients were known to be diabetic before the onset of abdominal symptoms, and diabetes or abnormal glucose tolerance was discovered in 3 of the remaining patients. Two patients showed abnormal fat absorption, and the finding of abnormal pancreatic function in 2 others with silent gallstones pointed to associated pancreatic disease. Twelve patients presented with a history suggestive of cholelithiasis, cholecystitis or obstructive jaundice. The PFT was abnormal in 8 of the 10 patients tested, and the pancreas was abnormal on palpation in 7 of 10 patients subjected to operation. The postoperative course was uneventful in 8 patients, but the remaining 2 died from cholaemia and uraemia respectively.

3. *Pancreatic Disease following Biliary Surgery*

Postcholecystectomy syndrome with pain: Four postcholecystectomy subjects investigated for upper abdominal pain were found to have evidence of pancreatic disease. One gave a clinical history of acute pancreatitis associated with a raised serum-amylase level some months after cholecystectomy; he was investigated 4 years later for what was probably a functional condition. The 3 remaining patients had recurrent attacks of pain in the right upper quadrant unassociated with a raised serum-amylase level. Pancreatic function was abnormal in 3 of the 4, and the fourth was found to have an abnormal pancreas at laparotomy. One of the patients had steatorrhoea and abnormal glucose tolerance in addition to an abnormal PFT.

Painless postcholecystectomy disorder: Evidence of pancreatic disease was found in a further 3 postcholecystectomy subjects in whom pain was not a feature. Two had obstructive jaundice caused by stones in the common bile duct, and 1 had recurrent episodes of vomiting unassociated with organic disease of the bile duct. Pancreatic function was abnormal in the 2 former cases, and the PET was positive in the latter.

Post-sphincterotomy pancreatitis: One patient developed typical acute pancreatitis a few days after sphincterotomy and cholecystectomy. The postoperative course in another was complicated by high fever and right-sided abdominal pain associated with slight elevation of the serum-amylase and trypsin levels; this patient died and autopsy revealed a retroperitoneal abscess caused by perforation of the duodenum at the sphincterotomy site.

Choledochal cyst and pancreatitis: One patient who had had a previous operation on a choledochal cyst developed recurrent attacks of typical pancreatic pain. Pancreatic function was clearly abnormal, but it is of interest that the pancreas appeared normal at operation carried out a few days later.

III. MISCELLANEOUS CAUSES OF PANCREATIC DISEASE

This group consisted of 34 patients in whom a definitive aetiologic diagnosis other than alcohol or biliary disease could be established as the cause of the pancreatic disease. Only 14 of these, however, had pancreatitis associated with pain; 20 had painless pancreatic disease.

Clinical Sub-groups

1. *Pancreatitis Associated with Pain*

(*a*) *Traumatic pancreatitis:* Three patients with closed abdominal injuries had clinical and operative evidence of pancreatitis. One patient presented with an 'acute abdomen' shortly after falling from a height; laparotomy revealed laceration of the liver in addition to pancreatic damage. The postoperative course was complicated by a pancreatic fistula which closed spontaneously after 2 weeks. Another presented with a haematoma of the anterior wall after a motor-scooter accident. At laparotomy he was found to have a transection of the tail of the pancreas, and a pancreatic fistula again complicated the postoperative course. Spontaneous closure of the fistula after 4 weeks was associated with abdominal pain and an abnormal increase in serum enzymes. Further laparotomy revealed a cyst in the tail of the pancreas, and an uneventful recovery followed removal of the transected distal end of the pancreas. The third patient was a 13-year-old girl who was injured by the handlebars while falling forwards over her bicycle. This accident was followed by a long pyrexial illness associated with hyperamylaseaemia and complicated by subcutaneous and medullary fat necrosis.[23] Laparotomy some weeks after the onset confirmed the presence of pancreatitis and fat necrosis. Pancreatic function was abnormal in only 1 of the 3 patients, all of whom were tested, and only 1 patient, the 13-year-old girl, showed transient glycosuria during the acute state of illness; her glucose tolerance was abnormal when tested a year later.

(*b*) *Penetrating duodenal ulcer:* Three patients with a long history of periodic ulcer dyspepsia complicated by severe pain radiation through to the back, which was eased slightly by bending forwards, were investigated. Pancreatic function was normal in all 3, but the PET was positive in 2. Laparotomy revealed a duodenal ulcer penetrating into the head of the pancreas in each case.

(*c*) *Other causes:* (*i*) Pregnancy pancreatitis—2 patients had acute pancreatitis during the latter part of pregnancy. One developed a large pseudocyst of the pancreas, clearly evident on inspection of the abdomen within a few days of admission; the PFT was abnormal, and diabetes was present. The other presented with an acute abdomen associated with a serum-amylase level of 2,370 Pimstone units and transient glycosuria; glucose tolerance was normal when tested 10 days later. (*ii*) Disseminated lupus erythematosus (DLE)—1 patient with DLE, receiving steroids for associated thrombocytopenia, collapsed with acute abdominal pain. She died 2 days later, and autopsy revealed acute haemorrhagic pancreatitis. (*iii*) Porphyria—1 middle-aged Bantu female with porphyria and diabetes was found to have abnormal pancreatic function. There was no history of alcoholism. However, 4 patients with painful alcoholic pancreatitis had hepatic porphyria in addition. (*iv*) Ascaris infestation—3 patients developed acute pancreatitis secondary to presumed infestation of the common bile duct. A roundworm was found in the bile duct in an adult female operated on for acute pancreatitis, and severe roundworm infestation of the upper bowel was present in 2 13-year-old children presenting with acute pancreatitis. (*v*) Obstructive 'pancreatosis' caused by carcinoma—laparotomy in a patient with a recent history of fever, jaundice and abdominal pain showed a diffusely hard pancreas. Biopsy taken from the body of the pancreas showed evidence of pancreatitis, and was complicated by the development of a large pseudocyst causing pyloroduodenal obstruction. The underlying carcinoma of the pancreas became apparent over the ensuing few months when the patient developed superficial vein thrombosis associated with an increased serum trypsin, and hepatomegaly caused by multiple liver secondary deposits. He died within 8 months of the onset of his illness.

2. *Painless Pancreatitis*

(*a*) *Non-alcoholic hepatitis or cirrhosis:* Six of 13 patients with non-alcoholic disease of the liver showed evidence of pancreatic disorder. The PFT was abnormal in 5, and a positive PET, associated with abnormal glucose tolerance, was present in the sixth. Pancreatic function was abnormal with regard to both bicarbonate and amylase response in 1 of the 5 patients; the remaining 4 showed only an impaired amylase response. Laparotomy confirmed the presence of cirrhosis and pancreatic disease in 1 of these 4, but autopsy failed to provide histologic evidence of pancreatic disease in another who died in cholaemia following operation.

(*b*) *Steatorrhoea caused by small-bowel disorder:* Six of 12 patients with small-bowel malabsorption showed abnormal pancreatic function. Both the bicarbonate and amylase response were abnormal in 2, and the amylase only was impaired in 4. A flat glucose-tolerance curve was found in 3 and a normal curve in 2 patients. Two of the 6 patients had idiopathic steatorrhoea, and 3 of the remaining 4 had Whipple's disease, massive resection of the small bowel, and lymphoma of the small bowel respectively.

(*c*) *Haemochromatosis:* Five patients with haemochromatosis investigated in the present series all showed evidence of abnormal pancreatic function. The PFT showed impaired bicarbonate and amylase responses with regard to concentration, but the volume responses were usually large in all 5 patients. The 80-minute volume ranged from 463 to 1,164 ml.; the mean value of 703 ml. was more than 3 times greater than the value found in control subjects. Four of the 5 patients had had diabetes for some years, and the fifth showed a diabetic glucose-tolerance curve when tested. None of the patients tested showed abnormal fat absorption.

(*d*) *Fibrocystic disease of the pancreas:* A 23-year-old male admitted for investigation of bronchiectasis, gave a recent history suggestive of steatorrhoea. This was confirmed, and pancreatic function was found to be grossly impaired. A positive sweat test further supported the clinical diagnosis of fibrocystic disease of the pancreas. He was not diabetic, but glucose tolerance was abnormal. There was no family history of the condition.

(*e*) *Other causes:* One patient with *Toxacara canis* infestation of the liver diagnosed by liver biopsy, showed grossly abnormal pancreatic function. Another patient presenting with vomiting and weight loss from a carcinoma of the third part of the duodenum, was found, at laparotomy, to have an abnormally hard pancreas clearly distinct from the duodenal lesion; pre-operatively the PFT was found to be abnormal, and the PET positive.

IV. PANCREATIC DISEASE OF UNKNOWN AETIOLOGY

An underlying or precipitating cause of the disease could not be established in 21 of the 243 cases of pancreatitis (Table V). Eight of the 21 admitted to taking moderate amounts of alcohol at times, but the attacks could not be related to alcohol intake. Gallstones were excluded as far as possible in all cases; biliary drainage in 2 of 16 patients so tested revealed biliary pigment and cholesterol crystals respectively, but cholecystography was normal in both and careful inspection of the gallbladder at operation in the one from whom biliary pigment was recovered showed no evidence of gallstones. None of the patients had hypercalcaemia or hyperlipaemia.

The group comprised 18 patients with painful pancreatitis and 3 with painless pancreatitis. Of the former, 10 patients presented with an acute abdomen and 8 gave a history of persistent or recurrent bouts of upper abdominal pain. The diagnosis was established or confirmed by operation in 13 of the 18 patients. Laboratory tests pointed to the diagnosis in the remaining 5. Gross pancreatic insufficiency was present in the 3 patients with painless pancreatitis, 2 of whom showed pancreatic calcification. One of the latter, a 23-year-old teetotaller, had diabetes, steatorrhoea, and bilateral cataracts and parotid swellings. He was considered to have developed pancreatic disease on a nutritional basis. The other, a 40-year-old woman, had diabetes, steatorrhoea, diabetic retinopathy, intercapillary glomerulosclerosis, and hypertension with peripheral vascular disease.

TABLE V. FINDINGS IN 21 PATIENTS WITH PANCREATITIS OF UNKNOWN CAUSE

Patient number	*Sex*	*Age*	*Alcohol intake*	*Clinical findings*	*Laboratory tests*					*Operation*	
					Serum amylase	*PFT*	*PET*	*GTT*	*Steat.*	*Definitive pancreatic surgery*	*Laparo-tomy*
1	M	38	±	ACP		—	—				+
2	M	23	±	RP	—	+	—	—	+		
3	F	24	±	RP	—	+	—	A	+	+	
4	M	52	±	RP	—	—	+	—	—		
5	M	46	±	ACP	+	—	+	A	—		
6	F	37	—	ACP	+	+	+	D	—		+
7	F	28	—	ACP	—	+	—	D*	—		
8	M	50	—	Chr. P.		—	+				
9	F	69	—	ACP		—	+	A			+
10	F	58	—	RP		+	—	A	—	+	
11	F	72	—	ACP		+	+				+
12	F	55	±	ACP		+	+	D	—		+
13	F	51	—	ACP		—	—				+
14	M	40	—	Chr. P.†	—			A		+	
15	M	41	±	RP						+	
16	F	50	—	ACP	+					+	
17	F	76	—	ACP	+						+
18	M	70	±	Chr. P.	+					+	
19	M	40	—	Painless		+	+	D	+		
20	M	25	—	Painless§		+	—	D	+		
21	F	43	—	Painless§		+	—	D	+		

PFT = pancreatic-function test, PET = provocative serum-enzyme test, GTT = glucose-tolerance test, Steat. = steatorrhoea, ACP = 'acute abdomen' not necessarily first attack, RP = relapsing pancreatitis, Chr. P. = chronic pancreatitis with previous history of relapsing pancreatitis, D = diabetes, A = abnormal glucose tolerance, D* = diabetes not caused by pancreatitis.

†Histological evidence of carcinoma of the pancreas—patient died subsequently.

§Pancreatic calcification.

The clinical picture in the 18 patients presenting with pain varied from the recurrent bouts of mild to moderately severe attacks seen in alcoholic pancreatitis to fulminating acute attacks suggestive of gallstone pancreatitis. This type of pancreatitis could not be excluded with certainty in 4 patients in the group, 1 of whom died shortly after a laparotomy which showed haemorrhagic pancreatitis.

The role of surgery in pancreatitis of unknown cause: The fairly reasonable results of operation in this group are indicated in the last column of Table V. Distal pancreatectomy appeared to be helpful in 1 case, while sphincterotomy with or without cholecystectomy and common duct drainage failed to influence the symptoms in 1 of 3 patients. A further patient who relapsed after sphincterotomy was found to have histologic evidence of carcinoma when subjected to distal pancreatectomy 3½ years later, and died shortly afterwards. Two other patients died within a few days of operation.

PEPTIC ULCERATION

Peptic ulceration was a most unusual finding in our series. Nine patients, all alcoholic, showed radiological evidence of ulcer, 3 gastric and 6 duodenal. Operation confirmed the presence of gastric ulceration in 2, but a high lesser-curve pocket of barium had been misinterpreted as gastric ulceration in the third. Only 1 of the 6 patients with alleged duodenal ulceration gave a history compatible with ulcer dyspepsia, but the diagnosis was suspect because of the finding of marked acid hyposecretion. The remaining 5 patients did not respond to intensive alkali therapy and the diagnosis of peptic ulcer in 3 of these was further excluded by operation in 2 and autopsy in 1. A repeat barium-meal examination in another showed indentation of the first and second parts of the duodenum. In addition to the above, the series included 3 patients with localized pancreatitis caused by posterior penetrating duodenal ulceration.

GASTRO-INTESTINAL BLEEDING

Gastro-intestinal bleeding occurred in 20 patients with pancreatitis. Oesophageal varices, peptic ulceration, and gastric erosions accounted for the bleeding in 5 of the patients, and a sixth died after a massive bleed following pancreatic surgery; autopsy failed to reveal the site of bleeding in this patient. Extensive investigations, which sometimes included laparotomy and gastrotomy, failed to establish a cause for the bleeding in the remaining 14, 12 of whom, including 1 with a histamine-fast achlorhydria, had alcoholic pancreatitis.

Bleeding in patients with alcoholic pancreatitis tended to occur after the onset of the attack, often 24 - 48 hours after the end of the last alcoholic debauch rather than immediately afterwards, as might have been anticipated if it were on the basis of alcoholic gastritis. Furthermore, an autopsy on a patient who died shortly after admission from acute fulminating alcoholic pancreatitis showed a large submucosal haemorrhage in the duodenum adjacent to a necrotic and haemorrhagic head of the pancreas.

MORTALITY

Twenty-eight of the 243 patients died during the 3-year period of the study. Seventeen of the deaths were clearly related to pancreatitis, and the remaining 11 to associated or incidental causes. Six patients died from acute haemorrhagic pancreatitis, but 1 of these had recently been given steroids for disseminated lupus erythematosus; 2 of these 6 patients had fulminating alcoholic pancreatitis and another 2 gallstone pancreatitis. Death in 5 patients with

calcific pancreatitis, diabetes and steatorrhoea, was attributable to the frail and indeed precarious metabolic balance found in some of them; 2 died of irreversible hypoglycaemia, and difficulty in insulin control was a feature in 2 others who died of uncertain causes, while the fifth had hypertension and developed irreversible hypotension after an oral dose of 10 mg. of 'mevasine', when 5 mg. daily had failed to control the hypertension. Two patients appeared to have developed carcinoma of the pancreas on the basis of chronic pancreatitis of 3½ and 10 years' duration respectively. Four deaths were attributable to operation; 3 patients died from complications of pancreatic surgery and the fourth developed retroperitoneal leak at the site of sphincterotomy. Associated liver disease or other incidental conditions were responsible for the deaths in 11 patients, 9 of whom had painless pancreatitis.

THE RELIABILITY OF THE PANCREATIC-FUNCTION TEST IN 200 PATIENTS TESTED

Two hundred of the 243 patients included in the present series were subjected to pancreatic function (PFT) and provocative serum enzyme (PET) tests* and, of these, 160 had glucose-tolerance tests and 130 fat-absorption studies; serum-amylase data obtained during recent or previous hospital admissions were available for 137 patients. The value of these tests in the diagnosis of pancreatic disease is presented in Fig. 1 and Table VI. The PFT was abnormal in 146 patients and the PET positive in 73. The serum-amylase level was elevated in 58 of the patients tested during an attack. Glucose tolerance was abnormal in 109, excluding 7 in whom diabetes clearly antedated the clinical onset of pancreatitis, and steatorrhoea was noted in 33, excluding 6 with small-bowel steatorrhoea and 1 with advanced cirrhosis and deep jaundice. Thus the PFT was abnormal in 73% and the PET in 36% of the patients, and the serum enzymes, glucose tolerance and fat absorption were abnormal in 42%, 71% and 26% respectively of the patients so tested. Either one of the PFT or PET was abnormal in 85%, and this figure was increased to 93% when serum-enzyme levels obtained during the attack were taken into consideration. Disturbed glucose tolerance, though usually associated with an abnormal PFT, was the only abnormality in a further 5·5% of cases, and increased the combined diagnostic yield to 98%. There were no patients in whom pancreatic steatorrhoea was the sole abnormality; it was invariably associated with abnormal pancreatic function and glucose tolerance. Laparotomy confirmed the diagnosis of pancreatitis in the remaining 2% of patients in whom the PFT, PET and, in some, the glucose-tolerance and fat-absorption tests were normal when tested, but for whom data on serum-amylase levels during the attack were not available. The reliability of the PFT in the diagnosis of various types of pancreatic disease included in the above analysis is shown in Fig. 2.

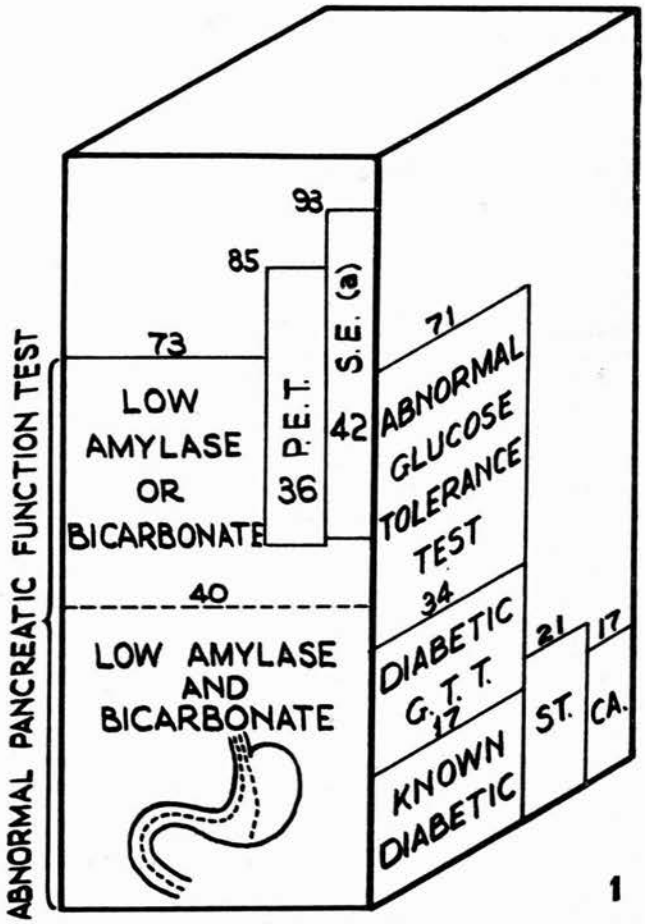

Fig. 1. The relative value of the various diagnostic tests employed in 200 patients with pancreatitis. The numbers refer to the percentage of positive results. P.E.T. = provocative serum-enzyme test; S.E. (a) = serum-amylase elevation during attack; ST. = impaired fat absorption; CA.=calcification of pancreas seen radiologically. The results of the glucose-tolerance test (G.T.T.), fat-absorption test and serum-amylase estimation during an attack have been corrected to allow for tests not done.

Calcific Pancreatitis (34 Patients)

The PFT was normal in only 1 patient. Twenty-six of the 33 patients with an abnormal PFT had gross insufficiency as shown by an impaired volume (less than 150 ml.), amylase and bicarbonate response, and a further 2 had an abnormal amylase and bicarbonate response associated with a normal volume. The remaining 5 patients had an abnormality in either the amylase or bicarbonate concentration.

The PET was positive in 21% of cases and the serum-amylase level during an attack of pancreatitis was elevated in 38% of patients tested. Fat absorption was abnormal in more than 50% of the patients in this group. Glucose tolerance was abnormal in all 33 patients tested, but the test in 1 of these patients was normal when repeated after the attack. Sixteen patients were known to be diabetic when first seen at the Gastro-intestinal Service, and a further 8 were found to be diabetic when tested.

Non-calcific Alcoholic Pancreatitis with Pain (86 Patients)

The PFT was abnormal in 59 of the 86 patients. Eighteen of these 59 had gross insufficiency, as shown by an impaired volume, amylase and bicarbonate response, and a further 8 showed an abnormal amylase and bicarbonate response associated with a volume greater than 150 ml. The remaining 33 patients showed either an impaired amylase or bicarbonate response.

The PET was positive in 38 patients, including 13 in whom the PFT was normal. Supportive or confirmatory evidence of pancreatic disease was obtained in 7 of the 13 patients by means of a raised serum-amylase level during the acute attack, an abnormal glucose-tolerance test, or laparotomy findings. The serum-amylase level was abnormally high in 58% of the patients tested, and fat absorption was abnormal in 14%. Glucose tolerance was abnormal in 61% of those tested. The diagnosis could be made by means of the PFT and PET in 82% of the patients and consideration of the serum-amylase level during an attack increased the diagnostic yield to 93%. The glucose-tolerance test was the sole abnormality in the remaining 7% of cases.

Gallstone Pancreatitis (10 Patients)

Five of the 10 patients were tested after an operative diagnosis of acute pancreatitis had already been made, usually within a month of operation. The PFT was normal in these 5 patients, but the PET was positive in 2 and glucose tolerance

*Secretin and pancreozymin, used in this study, are available from Boots Pure Drug Co. Ltd., Nottingham, UK.

TABLE VI. LABORATORY FINDINGS IN 200 PATIENTS WITH PANCREATITIS, SUBJECTED TO DETAILED INVESTIGATIONS

Condition	No.	Laboratory investigations															
		PFT		PET		GTT					Steatorrhoea			Serum enzymes		
		Abn.	N	Abn.	N	D	DT	Abn.	N	ND	Abn.	N	ND	Abn.	N	ND
Alcoholic pancreatitis:																
(i) Painful attacks																
Non-calcific:																
1 attack	11	7	4	5	6	0	1	5	2	3	0	8	3	10	1	0
Relapsing	55	38	17	24	31	5	7	20	16	7	6	32	17	21	15	19
Executive	6	3	3	3	3	0	0	2	4	0	1	4	1	0	5	1
Atypical	14	11	3	6	8	1	2	5	3	3	1	6	7	2	3	9
Calcific	31	30	1	7	24	14	8	9	0	0	14	14	3	10	15	6
(ii) Painless pancreatitis																
Non-calcific:																
Alcoholic cirrhosis	8	7	1	2	6	3	0	1	3	1	1(1)*	1	5	0	8	0
Non-cirrhotic	1	1	0	0	1	1	0	0	0	0	0	0	1	0	1	0
Calcific	1	1	0	0	1	0	0	0	0	1	0	1	0	0	0	1
Biliary diseases:																
(i) Painful attacks																
Gallstone pancreatitis	10	1	9	2	8	(3)	0	2	3	2	0	5	5	9	0	1
Gallstones and pancreatic disease	10	8	2	2	8	(3)	2	1	0	4	2	3	5	0	8	2
Postcholecystectomy syndrome with pancreatic disease	4	3	1	0	4	0	0	2	1	1	1	1	2	2	0	2
Choledochal cyst and pancreatitis	1	1	0	0	1				1		1					1
(ii) Painless																
Postcholecystectomy pancreatitis	3	2	1	1	2				1	2		2	1	1		2
Miscellaneous:																
(i) Painful attacks																
Traumatic pancreatitis	3	1	2	1	2			1	1	1			3	1		2
Penetrating duodenal ulcer	3	0	3	2	1				1	2		2	1		2	1
Others	3	3	0	2	1	1				2			3		1	2
(ii) Painless pancreatitis																
Non-alcoholic cirrhosis	6	5	1	1	5		1			5		1	5		3	3
Small-bowel disease	6	6	0	3	3				5	1	(6)				6	
Haemochromatosis	5	5	0	3	2	4	1					3	2		5	
Fibrocystic disease	1	1	0	0	1			1			1				1	
Others	2	2	0	1	1				1	1		1	1			2
Unknown:																
(i) Painful attacks																
Non-calcific	13	7	6	7	6	(1)	2	4	2	4	2	6	5	2	3	8
(ii) Painless																
Non-calcific	1	1	0	1	0	1					1	0				1
Calcific	2	2	0	0	2	2					2	0		0	2	

PFT = pancreatic-function test; PET = provocative serum-enzyme test; GTT = glucose-tolerance test; Abn. = abnormal, N = normal, D = known diabetic; DT = diabetic on testing, N/D = not done.
* Numbers in brackets = abnormality caused by associated condition.

was abnormal in 1. The gallstones had not been noted at laparotomy in any of these patients, and it was only after the diagnosis had been suggested by the results of biliary drainage that cholecystography and subsequent cholecystectomy were carried out. The second operation confirmed the presence of gallstones in each of the 5 patients. Only 1 of the 10 patients in the group had an abnormal PFT. On the other hand, *the serum-amylase level was markedly elevated during the attack in all patients tested.*

Pancreatic Disorder Associated with Biliary Disease, Excluding Acute Gallstone Pancreatitis (15 Patients)

The PFT was abnormal in 12 patients included in this group, and the glucose-tolerance test was the only abnormality in the remaining 3. The pancreas was considered abnormal at operation in 8 out of 9 patients, including 2 in whom the PFT was normal.

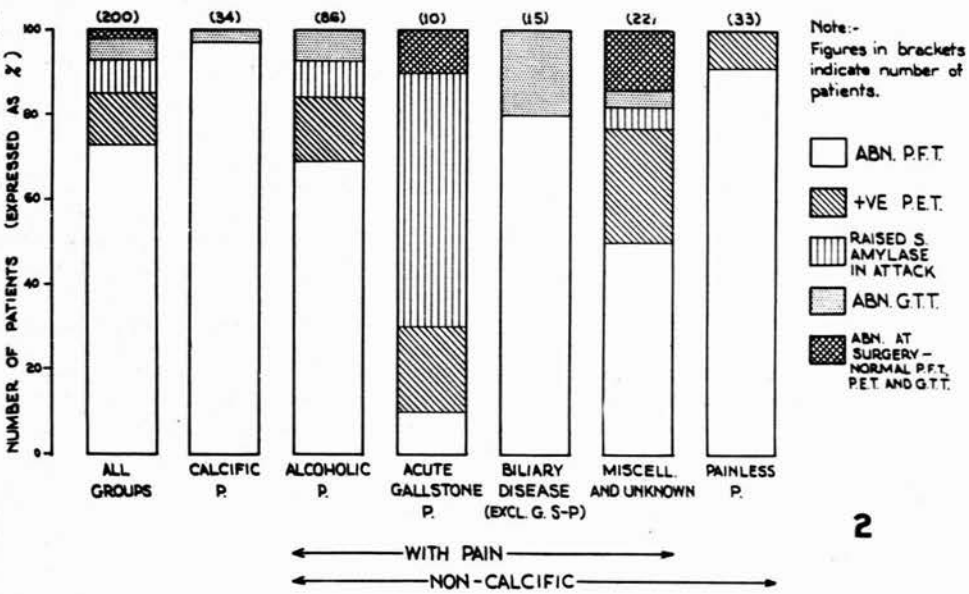

Fig. 2. The value of the pancreatic function test in the diagnosis of different varieties of pancreatic disease. P.=pancreatitis, ABN.=abnormal, P.F.T.=pancreatic function test, +ve=positive, P.E.T.=provocative serum-enzyme test, S.=serum, G.T.T.=glucose-tolerance test. G. S-P=gallstone pancreatitis.

Non-calcific, Painful Pancreatitis from Miscellaneous and Unknown Causes (22 Patients)

The PFT was abnormal in 11 patients and the PET positive in 12, 6 of whom showed a normal PFT. Two of these 6 patients had abnormal glucose tolerance, and operation confirmed the diagnosis in a further 2. In 5 patients both the PFT and the PET were normal; 1 of these had a markedly elevated serum-amylase level during the attack and another had abnormal glucose tolerance. Laparotomy evidence of pancreatic disease was obtained in 12 patients, 3 of whom had a normal PFT and PET when tested subsequently; the serum-amylase level was not measured during the attack, however, and glucose tolerance data were also not available for these 3 patients.

TABLE VII. LABORATORY FINDINGS IN THE 43 PATIENTS NOT SUBJECTED TO DETAILED INVESTIGATION

	No.	GTT				Serum enzymes		
		D	Abn.	N	ND	Abn.	N	ND
Alcoholic pancreatitis:								
(i) Painful attacks								
Non-calcific								
1 attack	4		1	1	2	3	1	
Relapsing	9	1	3	1	4	5	2	2
Atypical	1				1			1
Calcific	6	4	2					6
(ii) Painless pancreatitis								
Non-calcific								
Non-cirrhotic	1				1			1
Biliary disease:								
Painful attacks								
Acute gallstone pancreatitis	6		1		5	5		1
Gallstones and pancreatic disease	4	(1)*						
Postsphincterotomy pancreatitis	2			1	1	2		
Miscellaneous:								
Painful attacks	5		2		3	4		1
Unknown:								
Painful attacks								
Non-calcific	5		1		4	3		1

GTT = glucose-tolerance test, D = known diabetic, Abn. = abnormal, N = normal, ND = not done.
* Number in brackets refers to diabetes not caused by the pancreatitis *per se*.

Non-calcific Painless Pancreatitis (33 Patients)

The diagnosis in these patients was obviously dependent on abnormal laboratory findings. The PFT was abnormal in 30 patients, and the diagnosis in 11 of these was supported by the finding of abnormal glucose tolerance. The laboratory diagnosis in the remaining 3 patients was made on the grounds of an abnormal PET, associated with disturbed glucose tolerance in 2 and an elevated serum-amylase level during a previous attack of nausea in the third. Laparotomy or autopsy evidence of pancreatic disease was found in 8 of 9 patients. Autopsy revealed no macroscopic or microscopic evidence of pancreatic disease in the ninth patient, a middle-aged female who died after 3 months' jaundice of unknown cause; the PFT done some weeks previously was clearly abnormal.

Remainder of Series

The laboratory findings in the 43 patients not subjected to detailed investigation are shown in Table VII.

DISCUSSION

The present study was based on the findings in 243 patients with pancreatitis referred to the Gastro-intestinal Service during the past 3 years. Stringent diagnostic criteria were employed and operation afforded further confirmation of the diagnosis in over a third of the patients. The large number of patients seen during this relatively short period was due mainly to the high incidence of alcoholic pancreatitis in the South Western Cape, the increasing awareness of pancreatitis as a cause of abdominal symptoms and diabetes, the excellent liaison between the staffs of Groote Schuur and the associated hospitals and the Gastro-intestinal Service, and the facilities of the Service for the routine investigation of pancreatic function. The large number of patients diagnosed as having alcoholic pancreatitis in the present series was due largely to the ready availability of cheap wines and the relative frequency of alcoholism in the Cape and, to some extent, to recognition of the significance of the typical alcohol—pain sequence in such patients. Alcohol appeared to be the major aetiologic factor in 61% of patients, a figure similar to that quoted in a few American reports,[24-26] but greater than that found in Australia[27] and most American centres,[8,28-30] and considerably greater than in Britain, where acute alcoholic pancreatitis has virtually ceased to exist.[31,32,54]

Our experience with alcoholic and acute gallstone pancreatitis offered strong support for the view expressed by Howard and Ehrlich[8-10] that each of these varieties constitutes a distinct clinical entity. Alcoholic pancreatitis was predominantly a disease of males, and over 70% of patients developed their first attack before the age of 40. Nearly all patients gave a 5 - 15 year history of alcoholic overindulgence before the onset of the first attack. In addition, we noted that attacks of pancreatitis characteristically developed some 12 - 48 hours after the end of an alcoholic binge or party; the majority developed their pain 'on the *afternoon* after the night before'. This contrasted with symptoms of alcoholic gastritis present in a few patients, which almost invariably manifested on waking up 'on the *morning* after the night before'. It is interesting to speculate on the reason for this delayed onset of clinical pancreatitis following alcoholic insult, but it is unlikely that vomiting played a significant role in precipitating attacks,[33] since it seldom preceded the onset of pain. The alcohol—pain pattern was often the only clinical clue to the diagnosis in mild cases of pancreatitis and, when overlooked, frequently resulted in an incorrect diagnosis of alcoholic gastritis, peptic ulceration, hepatitis, chronic appendicitis or even perinephric abscess. A few patients had been given as many as 4 of these labels at different times before being correctly diagnosed as having alcoholic pancreatitis. This applied to all groups of alcoholic pancreatitis, but was particularly evident in the 'executive pancreatitis' group in whom excessive 'social drinking' was often considered to be incidental rather than aetiologic. Pancreatic function was usually impaired when tested shortly after or between attacks, and evidence of overt pancreatic insufficiency was present in a third of all patients. Most of those with overt insufficiency had radiological evidence of pancreatic calcification. Complete

alcohol withdrawal was unquestionably the most important, and indeed the only worth-while, measure in preventing future attacks. Biliary or ablative pancreatic surgery or sphincterotomy proved most unsatisfactory in the prophylaxis of further attacks, unless accompanied by alcohol withdrawal.

Acute gallstone pancreatitis, on the other hand, was found in an older age group and tended to affect females slightly more frequently than males. The patients usually presented with an 'acute abdomen', and the disease was generally more severe than the alcoholic variety. The 2 deaths among the 16 patients in our series fail to give an adequate reflection of the severity of the attack, since the acute illness often persisted for several weeks despite enthusiastic therapy in those that survived. Despite this, pancreatic function, when tested within a month of the attack, was usually normal. Biliary surgery invariably halted subsequent attacks of pancreatitis in these patients, at least during the period of follow-up.

The series included 40 patients with pancreatic calcification, 38 of whom gave a past or recent history of alcohol over-indulgence. These findings thus support a further observation made by the Philadelphia workers[8] that the presence of pancreatic calcification affords almost *prima facie* evidence of alcoholic pancreatitis. The incidence of pancreatic calcification among the 148 patients with alcoholic pancreatitis was 26%, exactly half the incidence reported in the Philadelphia series.[8] The lower incidence in our series probably reflects the greater number of patients with mild or moderately severe non-calcific pancreatitis diagnosed by means of the pancreatic-function and glucose-tolerance tests. While pancreatic calcification was frequently diffuse, or localized to the head of the pancreas, 2 patients showed localized calcification of the body and tail. Diffuse calcification was noted in 2 patients within a year of the onset of symptomatic pancreatitis. Diabetes was present in 60%, and steatorrhoea in 40% of patients with calcific pancreatitis. Weight loss was often striking, amounting in some patients to 33% of their weight before the onset of the disease. Eight of the 38 patients were investigated because of the development of diabetes or steatorrhoea many years after their last attack of painful pancreatitis. Indeed, pancreatic calcification was found in the majority of patients in whom steatorrhoea developed against a background of relapsing alcoholic pancreatitis. Overt steatorrhoea in alcoholic pancreatitis was almost invariably associated with diabetes, although the converse did not hold true. The 2 patients with non-alcoholic calcific pancreatitis both showed diabetic complications only rarely[34,35] ascribed to pancreatic diabetes. The first, a 40-year-old woman, showed diabetic angiopathy and the second, a 23-year-old youth, had bilateral cataracts. Neither of these patients had a family history of diabetes. The past history, coupled with bilateral enlargement of the parotid glands in the youth, suggested a nutritional basis for the pancreatic disease, possibly similar to that reported in Java[36] and Uganda.[37]

Persistent pain in patients with established pancreatic disease posed a difficult diagnostic problem, particularly in those in whom continued alcohol intake and drug addiction could be excluded. Persistent pain associated with a markedly elevated ESR pointed to the possibility of a pseudocyst of the pancreas, the presence of which was sometimes confirmed by barium studies. In any event, laparotomy was usually undertaken to exclude *i.a.* the possibility of a pseudocyst or carcinoma of the pancreas. The importance of pancreatic biopsy was underlined by the unexpected histologic diagnosis of carcinoma in 3 such patients who, at operation, showed no obvious evidence of malignancy. Chronic pancreatitis appears to carry an increased risk of malignant change.

The term 'painless pancreatitis' may appear paradoxical; however, our findings clearly show that 37 of the 243 patients in this series had definite evidence of pancreatic disease without any history of upper abdominal pain. This evidence was biochemical in the majority, but pancreatitis was also confirmed by operation or autopsy in some. The term 'pancreatopathy' might better be applied to the pathological condition in this group of patients. The group constituted 15% of the overall series, and comprised patients with alcoholic and non-alcoholic cirrhosis, haemochromatosis, post-cholecystectomy states, fibrocystic disease of the pancreas, small-bowel malabsorption and other conditions. The relatively high incidence of painless pancreatitis in patients with liver disease[38] is in keeping with autopsy data,[25] which revealed chronic pancreatic lesions in 49% of patients with portal cirrhosis. As observed by others,[16,38] the volume of the duodenal aspirate following secretin and pancreozymin stimulation was often excessively high in patients with haemochromatosis. The fact that a similar, although less consistent or dramatic, increase in volume was found in patients with portal cirrhosis, supports Howat's view[39] that the increased volume response in haemochromatosis is hepatic rather than pancreatic in origin. The pancreatic disturbance in patients with small-bowel malabsorption, on the other hand, manifested as an impaired amylase response. Since these patients invariably had low serum-albumin levels, the possibility exists that the pancreatic disorder in this group is secondary to protein-calorie malnutrition, analogous to that reported in kwashiorkor in children.[40]

The remarkably low incidence of alcoholic cirrhosis in patients with alcoholic pancreatitis associated with pain was perhaps unexpected in view of their long history of heavy drinking. Boyer and MacKay,[27] however, noted that the duration of alcoholism in patients with alcoholic cirrhosis was even longer than in those with alcoholic pancreatitis. Since alcoholism usually starts in early adulthood, the average age of patients with cirrhosis is usually, as in our experience, about 10 - 15 years greater than in pancreatitis. Our data suggest that alcohol may be responsible for a wide spectrum of pancreatic disorders, including the acute fulminating, acute, relapsing, mild and painless varieties. Most of the patients with painless alcoholic pancreatitis had associated alcoholic cirrhosis, whereas only 5% of the patients with painful varieties of alcoholic pancreatitis had alcoholic cirrhosis. These clinical data are supported by autopsy findings in chronic alcoholics. Weiner and Tennant[25] reported that 47% of patients with chronic alcoholism and 49% of patients with portal cirrhosis had pancreatic lesions—practically all of a chronic nature. Conversely, Clarke[4] found that only

2 of 15 alcoholics who died of acute haemorrhagic pancreatitis had cirrhotic changes in the liver. The rarity of acute pancreatitis in patients with alcoholic cirrhosis raises the question whether the chronic pancreatic changes so frequently found in these patients confers a relative immunity to these acute attacks. This contrasts with the frequency of fulminating attacks in patients with gallstone pancreatitis in whom the pancreas is presumably normal before the onset of the first attack. One may argue that the relatively less severe attacks in patients with acute and relapsing alcoholic pancreatitis is dictated, in part at least, by the extent of chronic, subclinical changes in the pancreas consequent on alcohol insult over a long period of time.

No aetiologic factor could be established in 9% of patients in the present series, an incidence somewhat lower than that found by other workers. A further 3 patients (1%) originally labelled as having pancreatitis of unknown aetiology were subsequently shown to have gallstones. A third of the patients in the group with unknown aetiology gave a history of occasional alcoholic excesses, but alcohol could hardly be held responsible for the pancreatitis. None of the attacks appeared to arise on the basis of hyperparathyroidism,[42,43] steroid and chlorothiazide therapy, a hereditary tendency,[44] familial hyperlipaemia[45] or mumps.[8]

The pancreatitis could be regarded as 'familial' in 4 patients in the series—2 brothers had calcific pancreatitis and a mother and son non-calcific pancreatitis—but alcohol was clearly the aetiologic factor in each case. Four other alcoholics presenting with fulminating pancreatitis or acute diabetes showed gross but transient hyperlipaemia. Two of 4 patients who developed diabetes shortly after an attack of mumps had abdominal pain during the attack. These 4 patients were excluded from the series because a pancreatic basis for the diabetes could not be established with certainty; serum-lipase and trypsin levels were not measured during the acute attack and pancreatic function was normal when tested several months later. The observations of Rich and Duff[46] and Yotuyanagi,[47] extended by Birnstingl,[48] suggested that pancreatic ductal obstruction by squamous metaplasia or columnar epithelial metaplasia may be invoked as the cause of the pancreatitis in at least a proportion of patients in whom an aetiologic factor could not be ascertained. Birnstingl,[48] in his excellent pancreatographic and histologic study on 150 routine autopsies, found a 29% incidence of columnar epithelial hyperplasia and a 10% incidence of squamous metaplasia; dilation and irregularity of the secondary pancreatic ducts were commonly present, and closely reflected the development of these ductal changes. Sub-clinical focal pancreatic necrosis was noted in 5 of the specimens, in which it was apparently related to the presence of hyperplastic epithelial lesions of the ducts.

Pancreatic diabetes occurred in 25% of patients in the present series and was particularly common (75%) in patients with calcific pancreatitis. The pancreatic nature of the diabetes in a few patients had been unsuspected for many years, but the majority of these admitted to a past history of alcoholism associated with recurrent attacks of abdominal pain. Alcohol was, in fact, responsible for 75% of the total number of pancreatic diabetics. Our findings suggest that the presence of diabetes in a patient with cirrhosis should make one suspect pancreatic disease. Two Bantu alcoholics presenting with diabetes were also found to have cutaneous porphyria acquired on the basis of liver disease;[49] both patients had grossly abnormal pancreatic function.

The remarkably low incidence of peptic ulceration in the present series contrasts with the increased incidence of 15%, claimed by Howard and Jordan.[50] Of special interest was the relatively large number of patients in whom pressure deformity and distortion of the duodenal cap by the underlying pancreatic lesion simulated duodenal ulceration. The total number of such patients and those with proved ulceration showed good agreement with the 6% incidence of ulceration reported by the Australian workers.[27] Upper gastro-intestinal bleeding in patients with acute and relapsing pancreatitis also presented diagnostic difficulties. Peptic ulceration and oesophageal varices could be excluded in the majority and the relationship of the bleed to the attack of pain in patients with alcoholic pancreatitis suggested that acute erosions were not the cause of the bleed. While it is conceivable that acute erosions could have been overlooked in a few patients, we believe that our clinical and autopsy findings suggest a more direct causal relationship between acute pancreatitis *per se* and upper gastro-intestinal bleeding.

The mortality in the present series was 12%; it could be ascribed to the pancreatic disease in 7% and to miscellaneous causes and the effects of liver disease in the remaining 5%. Pancreatic causes included deaths due to acute pancreatitis, chronic pancreatic insufficiency, the development of malignant change in the pancreas, and pancreatic surgery. As in other series,[50] the incidence of fatal acute pancreatitis was greater in the gallstone than the alcohol group, whereas deaths ascribed to chronic pancreatic insufficiency occurred only in the calcific pancreatitis group. Control of diabetes in those with calcification was often difficult, particularly when they continued to take moderate amounts of alcohol. Alcohol appeared to be responsible for a marked reduction in insulin requirements in a few patients, and 2 actually died of irreversible hypoglycaemia following an alcoholic debauch.

This study has confirmed[51] the value of the combined use of the pancreatic-function test, the provocative enzyme test and the glucose-tolerance test in the diagnosis of pancreatic disease, particularly in patients with chronic, relapsing or painless pancreatitis unassociated with calcification. While the serum-enzyme levels often provide adequate laboratory confirmation of a diagnosis of acute pancreatitis, they cannot be relied upon for diagnosis of the less acute varieties of the disease. Indeed, serum-enzyme levels were not infrequently normal even in acute attacks of alcoholic pancreatitis.

The PFT proved to be the most reliable of all the diagnostic procedures and clearly justified the tedium of intubation and the laboratory load inherent in it. Although the test *per se* was of little diagnostic value in patients with gallstone pancreatitis, the frequent finding of cholesterol crystals in the duodenal aspirate obtained from these patients again justified its use. The glucose-tolerance test was of value in that it occasionally provided the only laboratory confirmation of a clinical diagnosis of pan-

creatitis. Fat-absorption tests were of limited diagnostic value, since they were invariably associated with abnormalities of one of the other parameters of pancreatic function. However, the development of clinical steatorrhoea in a diabetic often provided the first pointer to the pancreatic basis of the diabetes.

The usual sequence of abnormal pancreatic function as measured by the PFT, followed by diabetes and eventual steatorrhoea in patients with progressive pancreatic insufficiency is not invariable, particularly in patients with haemochromatosis and fibrocystic disease of the pancreas. Steatorrhoea is seldom found in patients with long-standing diabetes associated with haemochromatosis, whereas diabetes is only rarely found in patients with steatorrhoea caused by fibrocystic disease of the pancreas.[52] Although it is conceivable that the islets of Langerhans are preferentially involved (haemachromatosis) or spared (fibrocystic disease) in some forms of pancreatic disease, it is probable that the discrepancies noted can best be explained on the basis of distribution of the lesion within the pancreas; MacLean and Ogilvie[53] have found that the number of islets per unit area of pancreas is far greater in the neck, body and tail than in the head. Selective damage to the body and tail of the pancreas following an attack of pancreatitis may also explain the occasional finding of abnormal glucose tolerance in those patients in whom the PFT is found to be normal.

SUMMARY

The aetiology, clinical features, diagnosis and treatment of 243 cases of pancreatitis seen during a 3-year period are reviewed.

Attention has been drawn to the high incidence of alcoholic pancreatitis and characteristic time relationship between the onset of an acute attack and the recent intake of alcohol in such patients.

The importance of establishing an aetiologic diagnosis is stressed, particularly with regard to alcoholic and gallstone pancreatitis. The former will respond to total withdrawal of alcohol in practically all patients, whereas biliary surgery is mandatory in the latter.

The various causes of painless pancreatitis (pancreatopathy) are presented, and the rarity of acute attacks in patients with alcoholic cirrhosis is noted.

The possible relationship of gastro-intestinal bleeding to acute pancreatitis is considered, and the low incidence of peptic ulceration in the present series is discussed.

The relative value of the tests of pancreatic function carried out in this series is examined, and the reliability of the secretin-pancreozymin pancreatic-function test in the diagnosis of chronic, relapsing or painless pancreatitis is confirmed. The glucose-tolerance test is useful as part of the work-up in cases with suspected pancreatic disease and is impaired or frankly diabetic in about 70% of patients.

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MEMORABILIA

We are very anxious to learn if any of our South African confreres have given a trial to the pancreatic treatment of malignant disease. If so, will they favour us with their results, however crude?

'Passim' in the* South African Medical Record, *25 August 1907, p. 249.