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Chronic pancreatitis with biliary obstruction

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In a 4-year review of 509 patients with chronic pancreatitis, the incidence of clinically manifest fixed common bile duct (CBD) stenosis was 9% (45 patients). In 76% this was alcohol related, and pancreatic calcification was present in 51%. All patients presented with unrelenting jaundice and five (11%) had cholangitis. The mean serum bilirubin (165 ± 108, normal 0–17 μmol/l), alkaline phosphatase (1790 ± 1143, normal 73–207 U/l) and gamma glutamyl transferase (798 ± 660, normal 7–64 U/l) were markedly raised. Diabetes occurred in 8 (18%). A biliary drainage operation was performed in 43 patients and 11 had concomitant pancreaticojejunostomy. Endoscopic retrograde cholangiopancreatography (ECRP) provided valuable information preoperatively in outlining both biliary and pancreatic disease in selecting patients for dual ductal drainage. Minor complications not related to biliary anastomosis occurred in 14%. Four patients died (9%), two from pseudocyst-related haemorrhage. Jaundice was successfully relieved in all and did not recur during follow-up. No secondary biliary cirrhosis was encountered, but varying degrees of portal fibrosis were present in 75% of liver biopsies. The commonest biliary pathogen was *E. coli*. It is recommended that a biliary bypass operation be performed when the diagnosis is radiologically confirmed and no improvement occurs within 1 month.

Chronic pancreatitis is usually due to excess alcohol intake. Some other conditions may contribute, such as hypercalcaemia, hyperlipidaemia, pancreatic trauma and congenital pancreatic abnormalities. Biliary tract disease rarely causes chronic pancreatitis. In alcoholic pancreatitis, deposition of proteinaceous material within the acini and ductules results in glandular destruction and replacement with fibrous tissue. The main pancreatic duct becomes distorted with varying degrees of narrowing, tortuosity and dilatation. Progressive damage to the gland eventually leads to loss of exocrine and endocrine function. Chronic inflammation and scarring may also involve nearby structures such as duodenum, colon and common bile duct. The latter is especially at risk as it traverses the pancreatic head for some distance.

Stenosis of the distal common bile duct in chronic pancreatitis is reported to occur from as low as 3% to as high as 62% (*1–9*). The precise indications for biliary drainage and its timing are unclear. We reviewed our recent experience with this complication.

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Patients and methods

The records of 509 patients with a final diagnosis of chronic pancreatitis admitted during the 4-year period 1986–1989 at King Edward VIII Hospital, Durban, were reviewed. The diagnosis was on the basis of information obtained by plain abdominal radiographs, ultrasonography, ERCP, CT-scanning, pancreatic function tests, operative findings or biopsy material. A total of 45 patients presented with unrelenting jaundice due to fixed stenosis of the distal common bile duct, an incidence of 9%. They form the basis of this analysis.

Sex and age

There were 38 males and 7 females with a median age of 39 years (range 25–80 years).

Table I. Presenting signs and symptoms ($n = 45$)

	n	%
Pain	43	95.6
Jaundice	45	100.0
Hepatomegaly	33	73.3
Abdominal tenderness	27	60.0
Malaise, vomiting	21	46.7
Malnutrition	16	35.6
Pruritus	15	33.3
Abdominal mass	8	17.8
Fever	5	11.1

Symptoms and signs

The usual presentation was with upper abdominal pains and jaundice and in one-third to one-half of the patients malaise, vomiting and pruritus. Most had epigastric tenderness and hepatomegaly on physical examination. Five patients (11%) had a fever and eight (18%) an abdominal mass (Table I). Twenty-three patients had previously been admitted with pancreatitis on one or more occasions. A relationship with alcohol consumption was present in 34 (76%), malnutrition occurred in 16 (36%) and diabetes in 8 (18%) of the patients. Pancreatic calcification was demonstrated in 23 (51%).

Laboratory results

The mean total serum bilirubin (165 ± 108 μmol/l), alkaline phosphatase (1790 ± 1143 U/l) and gamma glutamyl transferase (GGT, 798 ± 660 U/l) were markedly raised. The mean serum levels of aspartate transaminase (AST), alanine transaminase (ALT), lactic dehydrogenase (LDH), amylase and albumin were near normal and so were the international ratio of prothrombin time (INR) and partial thromboplastin time (PTT) (Table II).

Table II. Laboratory results

	Mean ± SD	*Distribution*	*Reference range*
Bilirubin	165 ± 108	>50: $n=40$ >100: $n=30$	0–17 μmol/l
Alk.phos	1790 ± 1143	>500: $n=40$ >1000: $n=32$	73–207 U/l
GGT	798 ± 660	>500: $n=27$ >1000: $n=10$	7–64 U/l
AST	111 ± 68		10–42 U/l
ALT	81 ± 71		10–60 U/l
LDH	302 ± 43		266–500 U/l
Amylase	233 ± 113		44–128 U/l
Albumin	30 ± 8.5		38–48 g/l
INR	1.13 ± 0.22		<1.2
PTT	33.4 ± 7.4		24–34 s

Alk.phos = Alkaline phosphatase
LDH = Lactic dehydrogenase
GGT = Gamma glutamyl transferase
AST = Aspartate transaminase
ALT = Alanine transaminase
INR = International ratio of prothrombin time
PTT = Partial thromboplastin time

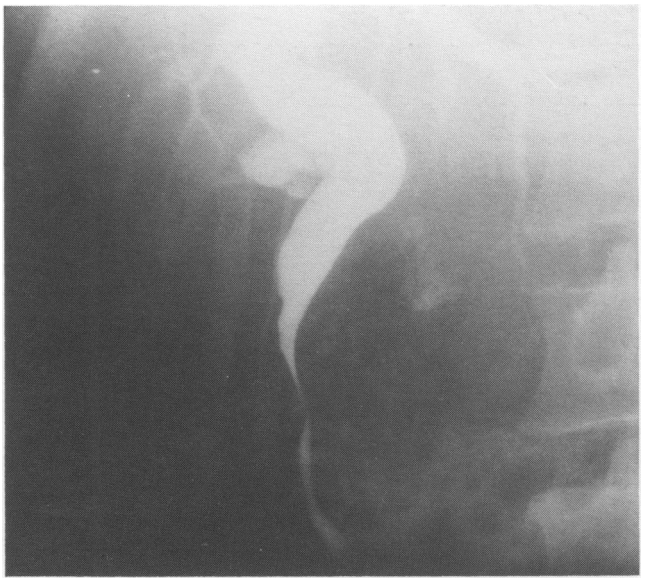

Figure 1. Smooth long stricture in the distal common bile duct, resulting from chronic pancreatitis. There is proximal dilatation of the bile duct. Note calcifications in the head of the pancreas.

Biliary-pancreatic imaging

The patients had a chest radiograph (pleural effusions present in five) and plain supine abdominal radiograph (pancreatic calcification present in 23) and all subsequently underwent ultrasonography, which demonstrated the features of extrahepatic biliary obstruction.

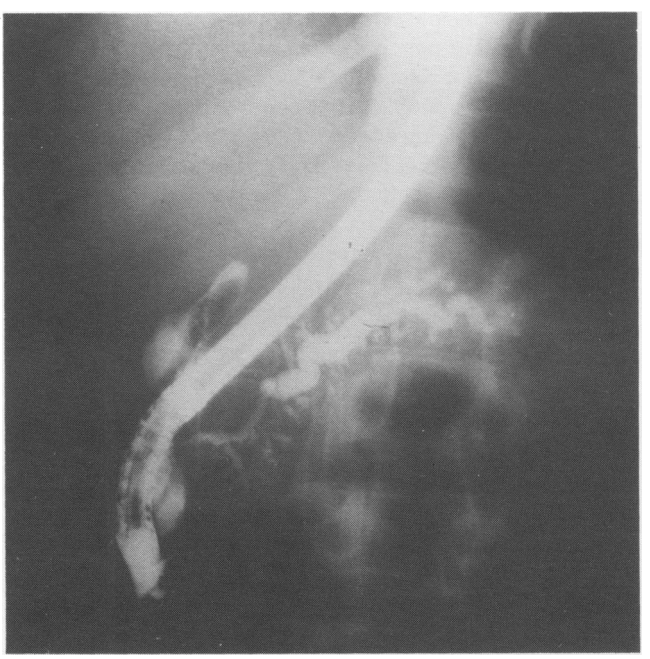

Figure 2. Chronic pancreatitis with ductal abnormalities, most obvious in the tortuous and dilated distal part.

Table III. ERCP findings ($n = 32$)

	n	%
Bile duct outlined (78%)	25	
Stenosis distal CBD	25	100
Dilated proximal CBD	20	80
Dilated IHBD	6	24
Dilated gallbladder	3	12
Stones	2	8
Pancreatic duct outlined (81%)	26	
Distorted MPD	19	73
Dilated MPD	16	62
Pseudocysts	5	19
Calcification	10	38

CBD = Common bile duct
IHBD = Intrahepatic bile duct
MPD = Main pancreatic duct

ERCP was performed in 32 patients and the bile duct was successfully cannulated in 25 (78%). A smooth stricture in the distal common bile duct related to the pancreas was present in all cases (Fig. 1). The pancreatic duct was outlined in 26 (81%) and main pancreatic duct dilatation demonstrated in 16 (62%) of these (Fig. 2). The ERCP findings are summarised in Table III. Where ERCP had been unsuccessful, a percutaneous transhepatic cholangiography (PTC) was carried out in nine patients, demonstrating a distal CBD stricture with proximal dilatation in them all. Preoperative CT scanning or a barium meal were obtained in 13 patients, while 19 underwent intraoperative cholangio- and/or pancreatography.

Operations (Table IV)

A total of 43 patients was operated on by various surgeons because of persistent jaundice. One of these patients had previously had a cholecystojejunostomy elsewhere. The two other patients declined operation. A biliary drainage procedure, most commonly a side-to-side choledochoduodenostomy was performed in 38 patients, and nine had internal or external drainage of a pseudocyst. In five of these, bile flow into the duodenum improved markedly as shown on intraoperative cholangiography and no further biliary drainage was undertaken. The other four patients required biliary drainage procedures. A cholecystectomy was performed in 20 instances. Eleven patients had a concomitant pancreaticojejunostomy for chronic pain associated with pancreatic duct dilatation on ERCP. Five patients had evidence of duodenal obstruction, for which a gastrojejunostomy was performed in three. Drainage of pseudocysts relieved the obstruction in the other two patients. One poorly nourished patient presented with an acute bleed into a pancreatic pseudocyst. For expediency and safety he was treated by arterial ligation within the pseudocyst, external tube drainage of the cyst and CBD decompression with a T-tube. He rebled in the intensive care unit and died. At operation, 22 patients had liver biopsies and 26 patients had pancreatic biopsies.

Table IV. Operations ($n = 43$)

Biliary drainage	
Choledochoduodenostomy	21
Choledochojejunostomy	4
Cholecystojejunostomy	12
Cholecystectomy	20
Choledochotomy + T-tube	1
Pancreatic drainage	
Pancreaticojejunostomy	11
Pseudocyst drainage	
Cyst–gastrostomy	4
Cyst–duodenostomy	2
External drainage	3

Results

All patients had their jaundice successfully relieved and there were no complications related to the biliary–digestive anastomosis.

Complications

Minor problems occurred in six patients (14%) and major in four, all resulting in death (9%). The causes of death were renal failure in a patient with pre-existing renal disease, haemorrhage from a cyst-gastrostomy on the 9th postoperative day, septicaemia after revision of a cholecystojejunostomy previously performed elsewhere, and uncontrollable haemorrhage from a false aneurysm related to the gastroduodenal artery. The average hospital stay was 25.9 (±15.7) days.

Histology

The 22 liver biopsies all showed evidence of large duct obstruction with widening of the portal tracts, bile duct proliferation, centrilobular cholestasis and mixed inflammatory infiltrates. Varying degrees of fibrosis, some with early bridging and cross-linking, were present in 16 patients (73%), but no definite secondary biliary cirrhosis was found. Cholangitis was present in three instances (14%). In all patients the appearances at operation suggested chronic pancreatitis, which was confirmed in all 26 pancreatic biopsies. No biopsies showed carcinoma. Chronic cholecystitis was present in 14 (70%) of the 20 gallbladders removed and acute cholecystitis in 3 (15%). Pigment stones were found in two.

Microbiology

Bile swabs from 36 patients yielded a variety of gut-associated organisms, most commonly *E. coli*, *Enterobact. cloacae* and *Strept. faecalis*. The only anaerobic organism isolated was *C. welchii*, and *Candida*

albicans was identified twice. Blood cultures were positive in two patients with cholangitis (*Str. pneumoniae* and *E. coli*). Organisms grown from pseudocyst collections were *Staph. aureus, Str. viridans* and *Klebsiella* sp.

Follow-up

Of the 39 patients who left hospital after operation, 26 (66.7%) were available for follow-up assessment, with a mean duration of 25.6 months. None developed recurrence of clinical obstructive jaundice. In addition to the four hospital deaths there were three late deaths. One patient died 3 months after a combined biliary and pancreatic drainage procedure with undiagnosed lower intestinal haemorrhage. Another died 8 months after operation with pneumonia on the basis of pre-existing pulmonary tuberculosis. He had no jaundice. One patient died after 1.5 years in liver failure with encephalopathy, ascites, portal hypertension and deep jaundice. At the initial operation the liver did not appear cirrhotic, but no information was available from histology or post-mortem. Two patients developed cholangitis 1.5 and 4 years, respectively, after a cholecystojejunostomy and were treated conservatively with antibiotics. After biliary drainage, nine patients had significant persistent pain in association with continued alcohol intake. Two patients underwent ERCP and a widened main pancreatic duct was demonstrated in both, one of whom underwent a pancreaticojejunostomy with good result. Seven patients returned for follow-up after their pancreaticojejunostomy and had marked pain relief. In the remaining patients pain was minimal or tolerable. Pseudocysts occurred in two patients with spontaneous resolution; diabetes and malabsorption developed in three and adhesive intestinal obstruction was treated non-operatively in another patient.

Discussion

The distal common bile duct is at risk of involvement in pancreatic disease due to its intrapancreatic course. Temporary narrowing of the duct may result from oedema in acute pancreatitis or compression by a pseudocyst, but on resolution of these conditions the bile duct reverts to normal. In chronic pancreatitis, scar tissue encroaches on to the distal common bile duct and renders it permanently stenosed with resultant bile flow obstruction. Not all patients with chronic pancreatitis and biliary obstruction present with jaundice. A rise in alkaline phosphatase may be found incidentally without unduly raised serum bilirubin. The significance of a chronically raised alkaline phosphatase and its influence on potential liver damage and attacks of cholangitis is not yet clearly established *(3–6,13)*. A recommendation has been made that patients with high alkaline phosphatase levels and pancreatitis should be followed up with liver biopsies twice a year to detect onset of secondary biliary cirrhosis *(4)*. The incidence of biliary stricture in chronic pancreatitis is estimated at 3–62%, depending on the extent of diagnostic endeavour *(1–9)*. The incidence in our study was 9%. Although ethanol is pancreato-, as well as hepato-toxic, there was no documented alcoholic liver damage in any of our patients, although it was suspected in one who died on follow-up. Some patients may well respond primarily with pancreatic, and others with liver disease. Clark *(10)* found cirrhosis at autopsy in 17 (47%) of 36 patients with alcoholic pancreatitis and two other studies found biopsy proven alcoholic liver disease in chronic pancreatitis in 30% and 40%, respectively *(11,12)*. The end result of chronic pancreatitis is exocrine and endocrine insufficiency. Diabetes occurred in 18% of our patients, but the incidence may be as high as 50% *(13)*. Secondary biliary cirrhosis was not unequivocally present in any of our liver biopsies, but various degrees of portal triad fibrosis, with crosslinking around the central lobule in some, was seen frequently. The significance of this is unclear, but it may represent a prephase to cirrhotic change. The incidence of secondary biliary cirrhosis is generally thought to be low, from 0–10% *(1,3–5,7,8,13)*, and our findings are in agreement with this. The duration of biliary obstruction necessary to produce biliary cirrhosis is usually not clearly documented but is probably very important. The long-term effect of continuing bile duct obstruction cannot be assessed, since in 96% of our cases the obstruction was relieved by operation. Cholangitis is another potential complication of bile duct obstruction, manifested by high fever, chills and leucocytosis. Blood cultures are usually positive and liver biopsies show neutrophils in bile ducts and surrounding micro-abscesses. *E. coli* is the most common pathogen; the incidence in our series was 14%, in keeping with other reports of 3–15% *(1,4,7,13)*. In our view, the indications for operation are cholangitis and persistence of obstructive jaundice of 1 month's duration or more. In agreement with others, we would recommend such a period because in other conditions resolution would normally have taken place by then *(13)*. Another reason for operation is the possible development of anergy, reversible after relief of the obstruction *(14)*. Biliary–enteric bypass can be most expeditiously performed by means of a side-to-side choledochoduodenostomy. The anatomical and physiological arrangements make this the procedure of choice. A choledochojejunostomy Roux-en-Y requires an additional suture line and offers no substantial advantage in the absence of duodenal obstruction. Cholecystojejunostomy is a less reliable outflow tract, as the narrow cystic duct with its Heysterian valves is a bottleneck and the gallbladder wall is prone to inflammation and shrinkage, as demonstrated in two of our patients. Furthermore, a low entry of the cystic duct is common. Its use may, therefore, be more appropriate for malignant pancreatic disease with a short life expectancy. The routine removal of the gallbladder during choledochoenteric bypass is supported by the finding of a high incidence of cholecystitis in our series, presumably related to bile stasis and increased intraluminal pressure. A primary biliary bypass operation *per se* is

a low risk procedure. Mortality in our series was related to the need for revisional surgery, concomitant medical disease and exsanguinating pseudocyst-related haemorrhage. This last complication is fairly uncommon and operative exploration is an unrewarding task. An alternative approach by means of transcatheter selective arterial embolisation is worth trying *(15)*. In our series, none of the patients were diagnosed as having carcinoma of the pancreas head, neither at operation nor at available biopsies. During follow-up, no death occurred on the basis of carcinoma. Exclusion of pancreas carcinoma is not easy and diagnosis may be missed despite exploration and biopsy. In the preoperative investigations of patients with pancreatitis and jaundice ERCP plays a central role. It outlines disease in the biliary as well as the pancreatic ducts and helps to identify candidates for dual ductal drainage *(13,16–18)*. Intraoperative cholangiography is mandatory where ERCP has failed and PTC has not been performed, especially when a pseudocyst is present and alleged to be contributing to the obstruction. An underlying stricture of the CBD should be dealt with when bile is not seen to enter the duodenum freely after decompression of the cyst *(17)*.

In conclusion, fixed bile duct obstruction is not an uncommon complication of chronic pancreatitis and should be dealt with surgically if no improvement is noted after a period of observation. Duct-enteric bypass is most effective and choledochoduodenostomy the procedure of choice. ERCP or intraoperative pancreatography provide information as to whether concomitant pancreatic duct drainage may be indicated. Drainage of pseudocysts may relieve bile duct obstruction. If intraoperative cholangiography shows persistent obstruction after cyst drainage, duct-enteric bypass is also required.

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Assessors' comments

> . . . but if the passages which convey the bile to the intestine be obstructed by inflammation of scirrhus, the [gall] bladder gets overdistended, and the bile regurgitates . . . to every point of the body, which acquires the appearance of bile.
>
> *Aretaios* (*c* second century AD)

Although Riedel is considered to have provided the first report of obstructive jaundice in chronic pancreatitis in 1896 *(1)*, Aretaios, the Cappadocian, a prominent physician of the 'late Greek period' must be given some credit *(2)*. While Mayo-Robson in his series of Hunterian Lectures described successful surgical treatment *(3)*, it is