Pancreaticobiliary ductal union

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Abstract

The main pancreatic duct and the common bile duct open into the second part of the duodenum alone or after joining as a common channel. A common channel of >15 mm (an anomalous pancreaticobiliary duct) is associated with congenital cystic dilatation of the common bile duct and carcinoma of the gall bladder. Even a long common channel (≥8 mm) is associated with a higher frequency of carcinoma of the gall bladder. Gall stones smaller than the common channel and a long common channel predispose to gall stone induced acute pancreatitis. Separate openings for the two ductal systems predisposes to development of gall stones and alcohol induced chronic pancreatitis. The role of ductal union has also been investigated in primary sclerosing cholangitis and biliary atresia.

The anatomy of the distal ends of the common bile duct and the main pancreatic duct has received attention because of its importance in pancreaticobiliary diseases (Table I). The two ducts open in the duodenum either separately or via a common channel. In the pre-endoscope era, a common channel was noted in 20–90% of the general population at necropsy and in 7–50% by cholangiography.[1] In a later study a common channel was found in 74% of specimens, 7% of which had interposed septum and 19% separate openings for the two ducts.[2] Another necropsy study noted separate ducts (separate openings plus one opening without a common channel) in 16·9% subjects while 83·1% had a common channel.[3] Our own data, based on a retrospective analysis of 259 selected endoscopic retrograde cholangiopancreaticograms (ERCPs), in which the pancreaticobiliary ductal union could be clearly seen, showed a common channel in 63%.[4]

The length of the common channel in normal people ranges from 1–12 mm, with a mean of about 4·5 mm[4 5] (Table II). Jona *et al*[7] noted that the length of the common channel was <5 mm in normal people. A common channel of 4 mm in infants and 6 mm in adults was considered abnormal.[8] In Di Magno's series 25% of patients had a well defined ampulla, 31% had a common

TABLE II *Length of the common channel in normal subjects in various series*

Authors	Mean (mm)	Range (mm)
Misra *et al*[4]	4·7	1·6–18·4
Kimura *et al*[5]	4.6	2–10
Dowdy *et al*[6]	4·4	1–12

channel of <3 mm, and 18% had a common channel of >3 mm. The mean length was not mentioned.[2] In a necropsy study of 35 infants, Miyano *et al*[9] noted that the average length of the common channel was 1·3 mm.

Kimura *et al*,[5] using cineradiography during ERCP, have shown contractile motility of the ductal wall extending well beyond the common channel, towards the liver. The mean (SD) length of the contractile segment was 20·5 (4·6) mm (range 14–31 mm).

Anomalous pancreaticobiliary ductal union (APBD)

In APBD the connection between the common bile duct and the main pancreatic duct is located outside the duodenal wall and is therefore not under the influence of the sphincter of Boyden (Table III).[11] The frequency of APBD varies from 1·5–3·2%.[4 5 10–15] The highest incidence of 3·2% was reported by Kimura *et al*[5] and Unozawa *et al*.[11] If it appears that the pancreatic duct is joining the common bile duct it is denoted as P-B type and if the common bile duct appears to join the main pancreatic duct it is denoted as B-P type (Fig 1).

Kimura *et al*[5] have shown that the contractile segment of the common channel, in APBD, ended well below the common channel. The mean (SD) length of the contractile segment was 14·8 (4·6) mm (range 11–22 mm) in subjects with APBD compared to 20·5 (4·6) mm (range 14–31 mm) in those without APBD. The difference between the two groups was significant (p<0·001).

MECHANISM OF APBD

It may be that APBD is a result of uneven proliferation of bile duct epithelium during fetal life.[17] The union of the common bile duct and the main pancreatic duct is located lateral to the duodenum up to the eighth week of gestation and then it shifts medially to lie finally within the

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TABLE I *Diseases associated with disorders of the pancreaticobiliary ductal union*

Anomalous pancreaticobiliary ductal union:
  Congenital cystic dilatation
  Carcinoma of the gall bladder
Long common channel:
  Carcinoma of the gall bladder
  Gall stone induced acute pancreatitis
Separate openings of the common bile duct and the main pancreatic duct:
  Gall stones
  Alcohol induced chronic pancreatitis

**TABLE III** *Definition of anomalous pancreaticobiliary ductal union used by various workers*

Common channel >15 mm[4 5 10–14]
Common channel >20 mm or ducts joining perpendicular to each other, or both[15]
Common channel >15 mm plus amylase activity in bile >10 000 IU[13]
Common channel >6 mm outside duodenum[16]

Figure 1: Two types of
union. In the BP type the
common bile duct appears to
join the main pancreatic
duct, while in the PB type
the main pancreatic duct
appears to join the common
bile duct.

PB   BP
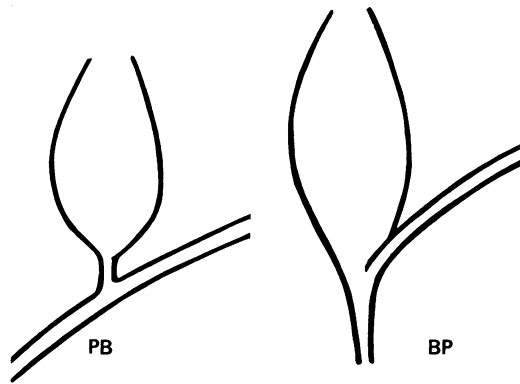
duodenal wall. Failure of this movement could result in APBD.[18]

APBD and congenital cystic dilatation of the common bile duct

In 1906 Arnolds noted an association between APBD and congenital dilatation of the common bile duct.[19] Since then many workers have reported this association.[5 7 10 14–17 20–27] The incidence of this association in various studies is shown in Table IV.

Ono et al[16] found APBD in 15 (68%) of 22 patients with congenital cystic dilatation, while Sameshima et al[26] found APBD in 47·5% of patients with congenital cystic dilatation. In two other studies APBD was noted in 33%[24] and 100%[7] of patients with congenital cystic dilatation.

TYPE OF UNION

Kimura[10] and Komi et al[24] noted that B-P type of union is usually associated with congenital cystic dilatation, while another study from Japan noted the P-B union in nine of 15 (60%) cases.[16] In a recent series 28 (56%) of 50 cases were of the P-B type and 22 (44%) of the B-P type.[5] Arima and Akita noted the B-P type in 66% and P-B type in 34% of patients.[25]

MECHANISM OF CONGENITAL CYSTIC DILATATION

The exact cause of congenital cystic dilatation is not known. Babbitt et al[20] proposed that because of the abnormally long common channel maldevelopment of the sphincter of Oddi occurs, which results in a reversed pressure gradient between the common bile duct and the main pancreatic duct. This leads to regurgitation of the pancreatic juice into the common bile duct and repeated attacks of cholangitis. This results in thickening of the common bile duct wall, stenosis, and finally dilatation. Komi showed that bile from patients with dilatation contained

TABLE IV   Incidence of congenital cystic dilatation of the
common bile duct in patients with anomalous
pancreaticobiliary ductal union

Author	Incidence (%)
Kimura et al[5]	77
Kato et al[15]	33
Yamauchi et al[14]	75
Sameshima et al[26]	82·8

amylase,[22] but he failed to produce localised dilatation by regurgitating pancreatic juice experimentally into the common bile duct.[24] Cylindrical dilatation of varying degrees has been produced by injecting pancreatic juice through the bile duct in mongrel dogs.[27]

Oguchi et al[27] found epithelial hyperplasia with round cell infiltration and thickening of the wall with fibrosis in all of their patients with cystic dilatation (n=40). They divided their patients into two groups. One group presented with abdominal pain; 86·4% showed predominant epithelial hyperplasia and round cell infiltration (glandular type). The amylase activity in bile was increased. The other group presented with obstructive jaundice; 73·7% of these patients showed predominant thickening of the wall with fibrosis (fibrotic type). Amylase activity, in bile of these patients, was significantly less than in the other group. 14 of 31 patients with cystic dilatation had glandular type while the other 17 had fibrotic type but all nine patients with cylindrical cystic dilatation had glandular type. In their animal model, where a pancreatico-cholecystostomy was done, they observed only cylindrical dilatation. They concluded that cylindrical congenital cystic dilatation may be accounted for by an APBD union, with resultant reflux of pancreatic juice into the common bile duct. But for cystic dilatation both an APBD union and an obstructive element in the lower part of the cyst play a part.

APBD and carcinoma of the gall bladder

Several Japanese workers have reported an association between APBD and carcinoma of the gall bladder.[11 13–15 28–35] Kato et al[15] reported that four of nine (44·4%) patients with APBD had carcinoma of the gall bladder. Only four of 291 (1·3%) patients without APBD had carcinoma of the gall bladder.

Kimura et al[5] noted APBD in 16·7% of patients with carcinoma of the gall bladder compared to only 2·8% of patients with other hepatobiliary and pancreatic diseases. They also found that of the 65 cases of APBD, carcinoma of the gall bladder was present in 24·6% compared to 1·9% in those without APBD. Of these 65 patients with APBD, 50 had congenital cystic dilatation of the common bile duct. Of the remaining 15 (who did not have congenital cystic dilatation), 11 (73·3%) had gall bladder cancer compared to only five (10%) of the 50 patients. Ours is the only group, outside Japan, to find an association between APBD and carcinoma of the gall bladder.[4]

The prevalence of carcinoma of the gall bladder in APBD varies from 57% to 77% in Japanese series.[5 9 12 13 28–30] Two of four (50%) patients in our series had carcinoma of the gall bladder[4] (Fig 2b and c).

Patients with APBD develop carcinoma of the gall bladder earlier than those without APBD. The median age was lower by about a decade in those with APBD.[14] In another report from Japan the mean (SD) age of patients with carcinoma of the gall bladder associated with APBD was 49·8 (9·8) years compared to 61·7
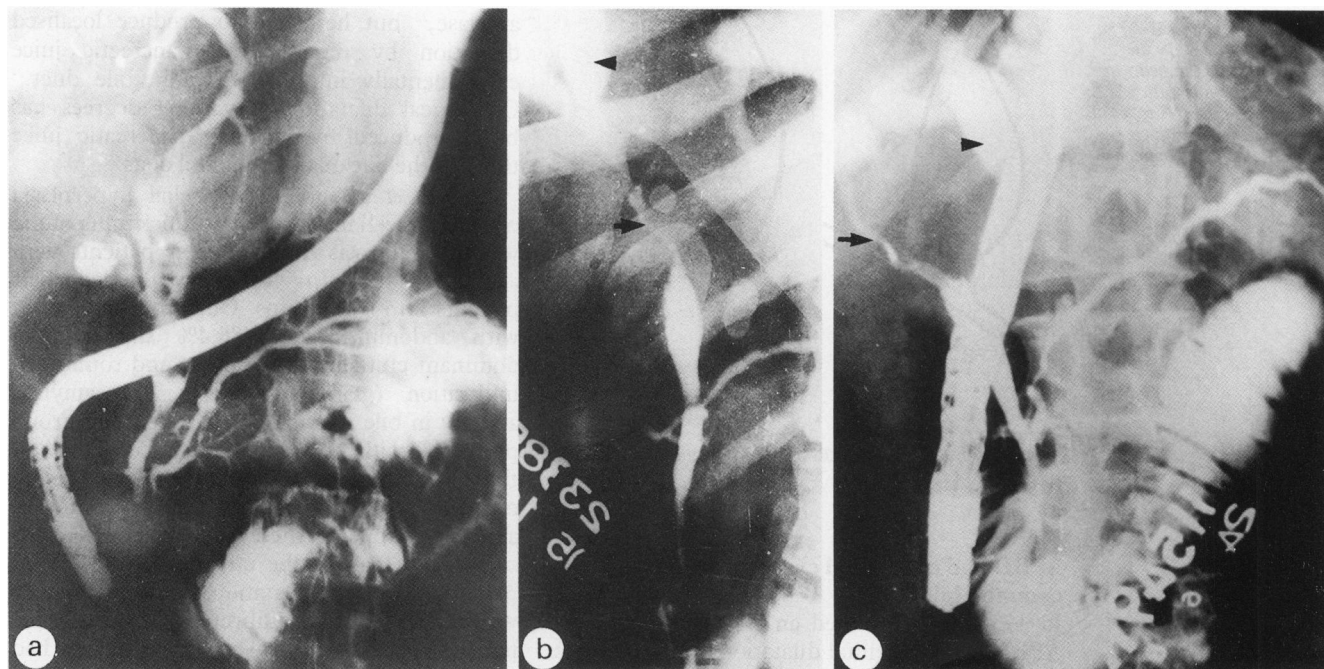
Figure 2: (a) Separate openings of the common bile duct and the main pancreatic duct in a patient with choledocholithiasis.
(b) Anomalous pancreaticobiliary ductal union in a patient with carcinoma of the gall bladder. The common hepatic duct shows narrowing (arrow) with dilatation of proximal ducts (arrow head).
(c) Endoscopic retrograde cholangiopancreatogram of a patient with carcinoma of the gall bladder and a long common channel. The common bile duct is narrowed (arrow) with dilation of the intrahepatic biliary radicles (arrow head).

(10·3) years for those without APBD (p<0·05).[5]

TYPE OF UNION IN CARCINOMA OF THE GALL BLADDER ASSOCIATED WITH APBD

In a review of all 47 reported cases of carcinoma of the gall bladder associated with APBD, Yamauchi *et al*[14] observed that in 39 of 42 (92·9%) cases the union was of the P-B type. In the remaining five patients the type of union was not mentioned. In another study 13 of 42 (31%) patients with a P-B union had carcinoma of the gall bladder compared to only three of 23 (13%) with a B-P union.[5]

MECHANISM OF GALL BLADDER CARCINOMA IN APBD

A review of all 47 reported cases of carcinoma of the gall bladder associated with APBD up to 1985 showed that gall stones were present in only 17·5% of patients[14] compared to 74% found by Piehler and Crichlow in patients with gall bladder cancer[36] and 57% in a Japanese study.[37] Kimura *et al*[5] found gall stones in only 12·5% of patients with APBD associated carcinoma of the gall bladder compared to 66·9% in those with carcinoma of the gall bladder without APBD. Gall stones are probably not an important aetiological factor in patients with carcinoma of the gall bladder with APBD.

It has been postulated that in APBD pancreatic juice refluxes freely into the biliary tree, leading to chronic inflammation and metaplasia.[5 14] When pancreatic juice is mixed with bile, lysolecithin and phospholipase A2 are produced, which may also be irritants.[14] The gall bladder acts as a reservoir in patients with APBD without congenital cystic dilatation and thus carcinoma of the gall bladder occurs more frequently in such patients. In patients with congenital cystic dilatation irritation occurs in the cyst rather than in the gall bladder, and it is well known that there is a high incidence of carcinomatous change.[38-43] The amylase content in bile was high in 10 of 11 such patients.[14] The highest activity recorded was 567000 IU by Kinoshita *et al*.[13] Sphincteric action stopped short of pancreaticobiliary ductal union in patients with APBD and thus the normal control mechanism preventing regurgitation of pancreatic juice into the biliary tree is absent in these patients.[5] In an experimental study on mongrel dogs, development of mucosal and intestinal metaplasia was observed in the gall bladder after the creation of a cholecystopancreatic communication.[35] Thus APBD is a predisposing factor for carcinoma of the gall bladder and may be a premalignant condition, especially in patients without congenital cystic dilatation of the common bile duct. One worker even goes as far as to recommend prophylactic cholecystectomy in these patients.[14]

Long common channel

We have defined a long common channel as a common channel of ≥8 mm.[4] In our study 12 (5%) of 259 ERCPs examined showed a long common channel. Eight (67%) of these patients had carcinoma of the gall bladder (Fig 2c), one patient had gall stones, and three were in the control group. The prevalence of a long common channel in the control group was three (3%) of 102 and one (1%) of 95 patients with gall stone disease compared to eight (38%) of 21 with carcinoma of the gall bladder. If only those with a common channel were considered, three (5%) of 64 control subjects, one (3·5%) of 28 patients with gall stone disease, and eight (57%) of 14 patients with carcinoma had a long common channel. The mechanism of carcinoma of the gall

bladder may be the same as that for APBD associated carcinoma.

Pancreaticobiliary ductal union in gall stone disease

In a retrospective analysis a total of 95 patients with gall stone disease of whom 59 patients had stones seen at ERCP, either in the common bile duct or the gall bladder, and 36 patients who had undergone cholecystectomy in the past for gall stone disease were evaluated by ERCP for post-cholecystectomy symptoms.[4] Sixty seven of 95 (70%) had separate openings of the common bile duct and the main pancreatic duct (Fig 2a). When compared to the control group (separate opening for the two ducts in 37%) this difference was highly significant ($p<0.001$), but the mean (SD) length of the common channel in gall stone disease (4·6 (2·6) mm) was similar to that in the control group (4·7 (2·5) mm).

MECHANISM

Two hypotheses might explain the higher incidence of gall stone disease in those who have separate openings for the two ducts. Firstly, the sphincteric mechanism at the distal end of the common bile duct may behave differently in these patients, leading to prolonged stasis of bile in the common bile duct and gall bladder, thus causing stone formation. Sphincterotomy inhibits gall stone formation in prairie dogs,[44] and this effect is reversed by giving atropine.[45] The alternative hypothesis is that a common channel may prevent gall stone formation because of reflux of pancreatic juice in the common bile duct where the glyco and proteolytic properties of the pancreatic juice dissolve the mucin nidus of gall stones, which is found at the core of most cholesterol gallstones.[46-48] An in vitro study has shown that trypsin enhances the dissolution of gall stones.[49] Furthermore, studies from Japan have shown a much lower incidence of gall stones in patients with carcinoma of the gall bladder and APBD compared to those without APBD.[5 14] Amylase levels in the bile of patients with carcinoma of the gall bladder with APBD were also high in 10 of 11 patients.[14]

Pancreaticobiliary ductal union in acute gall stone pancreatitis

Opie[50] noted impacted gall stones at the ampulla of Vater in a patient with pancreatitis, and it was suggested that reflux of bile into the pancreatic duct causes pancreatitis in patients with cholelithiasis.[51] This led to the common channel theory.[52] Since then many workers have shown that common bile duct stones are involved in the pathogenesis of gall stone pancreatitis[53-62] and are found in 20–30% of patients with gall stone pancreatitis at necropsy.[53 55 59 60] When surgery was performed early, stones were found causing ampullary obstruction in 63–72% of patients.[55 61] Stones can be recovered from the stools of most patients with gall stone pancreatitis.[55 57 63]

A common pancreaticobiliary channel occurs in 67–80% of patients with gall stone pancreatitis.[57 58 64–66] Jones *et al*[66] noted a common

pancreaticobiliary channel in 67% of 37 patients with gall stone pancreatitis compared to 32% of 109 patients with other biliary tract diseases.

Most of the stones found in patients with gall stone pancreatitis are small.[66-68] Even microliths (stones <3 mm) have been implicated in the pathogenesis.[69]

Jones *et al*[66] correlated the size of the gall stone to the length of the common channel. The length of the common channel was greater than the diameter of the smallest stone in nine of 27 (33%) patients with gall stone pancreatitis compared to 13 of 109 (12%) with other biliary tract disease. Thus, a common channel occurs more frequently in patients with gall stone pancreatitis, and the size of the stone and the common channel have important implications in the pathogenesis of gall stone induced acute pancreatitis.

Pancreaticobiliary angle (angle of reflux)

Even the width of the pancreatic duct and the angle at which the common bile duct and the main pancreatic duct meet are important in the pathogenesis of gall stone pancreatitis. In a study of 53 patients who had had attacks of acute gall stone pancreatitis and 561 patients without such a history (controls), it was noted that pancreatic duct reflux occurred in 33 (62·5%) patients with a previous history of acute gall stone pancreatitis compared to only 82 (14·6%) of the controls. Among all patients with pancreatic reflux, those with a past history of acute gall stone pancreatitis had wider cystic, common bile, and pancreatic ducts and the angle of reflux was greater (mean (SD) 40 (12)°) compared to those with no history of acute gall stone pancreatitis (angle of reflux 21 (15)°). The length of the common channel was greater in patients with a history of gall stone pancreatitis compared to controls (8 mm *v* 4 mm). Furthermore, 72% of patients had a common channel of 5 mm or more compared to only 20% in the control group. Apart from the frequency of pancreatic duct reflux, similar results were found in another study.[71]

Pancreaticobiliary ductal union in chronic pancreatitis

Yatto and Siegel[72] reported separate openings of the common bile duct and the main pancreatic duct in 24 (86%) of 28 patients with alcoholic pancreatitis compared to only six (20%) of 30 alcoholics without chronic pancreatitis. The difference was significant ($p<0.001$). We evaluated ERCP films of 49 patients with chronic pancreatitis: 18 (37%) had alcoholic pancreatitis and 31 (63%) had non-alcoholic pancreatitis. Thirteen (72%) of the 18 patients with alcoholic pancreatitis had separate openings for the two ducts, and 14 (45%) of 31 patients with non-alcoholic pancreatitis had separate openings. The difference between the two groups just failed to reach statistical significance. When compared to our earlier study in a control population[4] separate openings in alcoholic pancreatitis patients were much more common (72% *v* 37%). If the entire series of 49 patients is considered, separate openings were noted in 27

(55%), which, when compared to the control group, was significantly higher. The length of the common channel was, however, similar (4·5 (1·2) v 4·7 (2·5) mm) (unpublished observations).

Mechanism of chronic pancreatitis

Di Magno et al[2] observed that separate openings for the common bile duct and the main pancreatic duct were associated with hyperplasia of the pancreatic ductular epithelium. This might lead to obstructed flow of pancreatic secretions. An association between pancreatic ductular epithelial changes, obstruction of pancreatic secretion, and chronic pancreatitis has been observed.[73] Chronic alcohol intake results in hyperplasia of the pancreatic ductular epithelium and increased secretion of pancreatic juice.[74] It may be that separate openings for the two ducts lead to hyperplasia of the pancreatic ductular epithelium which is enhanced by chronic alcohol intake, resulting in obstruction of the flow of pancreatic juice and later precipitation of protein plugs and chronic pancreatitis. Protein plugs form in the initial stages in most patients with chronic pancreatitis.[75]

APBD and abnormal pancreatograms

Kato et al[15] in a study of nine cases of APBD noted abnormality of the pancreatogram in eight (77·8%). An abnormal pancreatogram was found in only 24 (36·9%) of 65 patients with some type of biliary disease without APBD. There is no mention of an abnormal pancreatogram in most series of APBD. In our study[4] we found no abnormality of the pancreatogram in our four patients with APBD.[4]

Pancreaticobiliary ductal union in primary sclerosing cholangitis

Muller et al[76] studied the role of pancreaticobiliary ductal union in primary sclerosing cholangitis. In 20 of the 46 patients, in whom the pancreaticobiliary ductal union could be clearly seen, anomalous union was noted in only two (10%) cases. Fourteen (70%) patients had a common channel of 1 or 2 mm, three patients had a common channel of 3 to 10 mm, and one patient had separate openings for the two ducts. Pancreatic duct abnormalities were found in half of these patients. It was concluded that the variations in the pancreaticobiliary ductal union were rare in patients with primary sclerosing cholangitis.

Pancreaticobiliary ductal union in other diseases

Abnormally long pancreaticobiliary ductal union was found in two (12%) of 17 children with infantile hepatitis, three (5%) of 57 with biliary atresia, and one patient with chronic pancreatitis.[25]

In another study of 28 cases with biliary atresia, the junction of the common bile duct and the main pancreatic duct was situated below the propria muscularis of the duodenum in 17

(60·7%). The common channel was longer (>6 mm) in these patients than in the control subjects. The angle at which the two ducts joined was less acute than in the control subjects. The common channel in patients with choledochal cyst was longer than in patients with biliary atresia. An APBD was noted in all patients with choledochal cyst compared to 60% of patients with biliary atresia.[9]

Two cases of anomalous drainage of the common bile duct into the fourth portion of the duodenum have been described.[8] Both were in young children who had recurrent attacks of abdominal pain and vomiting and, on investigation, hyperbilirubinaemia and hyperamylasemia. The common channels measured 1·0 and 2·7 cm.

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