Hypothesis: Excision of the extrahepatic portion of congenital choledochal cysts (CCs) avoids the risk of cancer. The standard classification scheme is out of date.

Design: Retrospective case series and literature review.

Setting: Tertiary care university hospital.

Patients: Thirty-eight adult patients diagnosed as having CC from 1990 to 2004.

Main Outcome Measures: Clinical and radiographic imaging findings, operative treatment, pathologic features, and clinical outcome.

Results: Thirty-nine adult patients were treated for CCs (mean [SD] age at diagnosis, 31 [17] years, and mean [SD] age at surgery 37 [14] years). The primary report was abdominal pain (36 of 39 patients). Eight patients had cholangitis, 5 had jaundice, and 6 had pancreatitis. Radiographic imaging studies and operative findings showed that the abnormality predominantly involved the extrahepatic bile duct in 30 patients, the intrahepatic and extrahepatic bile ducts in 7 patients; and 2 were diverticula attached to the common bile duct. Surgical treatment in 29 (90%) of 31 patients with benign cysts (regardless of intrahepatic changes) consisted of resection of the enlarged extrahepatic bile duct and gallbladder and Roux-en-Y hepaticojejunostomy. Eight patients (21%) were initially seen with associated cancer (cholangiocarcinoma of the extrahepatic duct in 6; gallbladder cancer in 2). Seven of 8 patients had a prior diagnosis of CC but had undergone a drainage operation (3 patients), expectant treatment (3 patients), or incomplete excision (1 patient). In none of the patients with cancer was surgery not curative. Nine patients had previously undergone a cystoduodenostomy and/or cystojejunostomy as children. Four of them had cancer on presentation as adults. There were no postoperative deaths. Cancer subsequently developed in no patient whose benign extrahepatic cyst was excised, regardless of the extent of enlargement of the intrahepatic bile duct.

Conclusions: Congenital CCs consist principally of congenital dilation of the extrahepatic bile duct with a variable amount of intrahepatic involvement. We believe that the standard classification scheme is confusing, unsupported by evidence, misleading, and serves no purpose. The distinction between type I and type IV CCs has to be arbitrary, for the intrahepatic ducts were never completely normal. Although Caroli disease may resemble CCs morphologically, with respect to cause and clinical course, the 2 are unrelated. The other rare anomalies (gallbladderlike diverticula; choledochocele) are also unrelated to CC. Therefore, the term “congenital choledochal cyst” should be exclusively reserved for congenital dilation of the extrahepatic and intrahepatic bile ducts apart from Caroli disease, and the other conditions should be referred to by their names, for example, choledochocele, and should no longer be thought of as subtypes of CC. Our data demonstrate once again a persistent tendency to recommend expectant treatment in patients without symptoms and the extreme risk of nonexcisional treatment. The entire extrahepatic biliary tree should be removed when CC is diagnosed whether or not symptoms are present. The outcome of that approach was excellent.

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Described initially in 1852, congenital choledochal cysts (CCs) were separated into 3 types by Alonso-Lej et al.2 in 1959. Todani and colleagues3 modified this classification in 1977 adding types IV and V, and more recently Todani4 revised it further to reflect the presence of pancreaticobiliary maljunction. The Todani classification system, which has been widely adopted, includes no less than 8 separate alphanumeric subtypes (Figure 1).3

Though the diagnosis of CC is most often made in childhood, 25% of patients are initially seen as adults.6,7 In the past, CCs were often treated using drainage procedures (cystoduodenostomy or cystojejunostomy),6,10 but it has since become clear that these operations have not only an unac-
The clinical and laboratory findings of 39 adult patients who were treated for CCs at the University of California, San Francisco, from 1990 to 2004 were analyzed for demographic and clinical information. The preoperative data included the patient’s age at diagnosis, manifesting symptoms, and the results of diagnostic tests. Preoperative radiographic imaging findings were reviewed to verify the morphologic condition of the biliary abnormalities. Ten patients had previously undergone 1 or more operations on the biliary tree (ie, cystoduodenostomy or cystojejunostomy) at other hospitals. Among the 31 patients with benign disease, 28 patients (90%) were treated by excision of the extrahepatic bile duct and gallbladder and reconstruction with a Roux-en-Y hepaticojejunostomy. One patient had excision of the duct and end-to-side hepatocoduodenostomy, 1 underwent a Whipple pancreaticoduodenectomy, and 1 underwent excision of a large distal remnant of a cyst that remained after partial resection and hepaticojejunostomy at another hospital. No patient underwent liver resection for intrahepatic involvement.

Eight patients (21%), whose mean age was 52 (15) years, presented with an invasive cancer. Six had cholangiocarcinoma and 2 had gallbladder cancer. The presence of the CC had been known for many years in 7 of 8 patients (90%) had lesions consisting of a polypoid diverticulum (similar in appearance to a gallbladder) attached to an otherwise normal bile duct (Todani type II). Deciding whether to call the disease type I or type IVA was arbitrary, because the intrahepatic ducts were never entirely normal in any patient with congenital dilation of the extrahepatic bile duct. The presence or absence of pancreaticobiliary maljunction was poorly documented in the patients who had undergone endoscopic retrograde cholangiopancreatography.
to revise a stricture at the hepaticojejunostomy anastomosis. One patient died of gastrointestinal hemorrhage from an arteriobiliary fistula after percutaneous transhepatic dilation of an anastomotic stricture.

### COMMENT

As now used, the term choledochal cyst is unfaithful to the usual meaning of these words. Choledoch, a word that refers to the common bile duct, comes from the Greek words chole (bile) and dechomai (to receive). The word cyst, from the Greek kystis (sac, bladder), is conventionally defined as a closed cavity or sac lined by epithelium. Choledochal cyst, however, has escaped from this etymology and is used to cover the entire spectrum of congenital dilation throughout the biliary tree. Furthermore, the lesions are not really cysts

The cause of CCs is uncertain. Most patients with types I and IV lesions also have an anomalous pancreaticobiliary junction, in which the pancreatic duct joins the bile duct 1 to 2 cm proximal to the sphincter of Oddi.15,17,18 This results in a common channel of 15 mm or more, which has been thought to allow reflux of pancreatic enzymes into the bile duct, increasing ductal pressure, and causing it to dilate.19 Experimental diversion of pancreatic juice into the bile duct produces progressive dilation in dogs.20 Nevertheless, a high junction is seen in about 90% of endoscopic retrograde cholangiopancreatograms performed in patients without congenital choledochal cysts.18 Others have postulated that partial distal obstruction, whether due to a stricture, web, or sphincter of Oddi dysfunction, might have a causative role.15,21,22 These theories are interesting but supported by sparse evidence. At most, they could only partially explain the pathogenesis since CCs occur without an anomalous biliary-pancreatic junction, anomalous junction is common in the absence of biliary disease, and pancreatic enzymes are not universally found within congenital CCs.

The first classification system for CCs was proposed by Alonso-Lej et al,2 but the most widely used one, authored by Todani and colleagues,3,4 includes 8 separate alphanumeric subtypes (Figure 1). Types I and IVa, which are variations of a single disease, account for more than 90% of the patients.6,21,24 Type III cysts are better known as choledochoceles, and type V refers to Caroli disease. The type II lesions appear as a diverticulum of the common bile duct. Some such cases closely resemble gallbladder duplication while others are more rudimentary diverticular structures. There is no reason to believe that these choledochoceles are related to the more common congenital ductal dilation. In choledochoceles, the duct terminates in a small intramural cystic lesion lined by duodenal mucosa. Choledochocele has no clinical, pathologic, or etiologic relationship to CC, and most observers consider it to be a variant of duodenal duplication. Caroli disease is thought to arise from ductal plate malformation and is often associated with congenital hepatic fibrosis (with cirrhosis and portal hypertension).25 It is an au-

### Table 1. Patients Presenting With Cancer

<table>
<thead>
<tr>
<th>Patient No./ Age at Initial Diagnosis, y</th>
<th>Prior Operation</th>
<th>Age at Diagnosis of Cancer, y</th>
<th>Manifestation</th>
<th>Choledochal Cyst Type*</th>
<th>Operation at UCSF</th>
<th>Pathologic Features</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/5</td>
<td>Cystojejunostomy and cystojejunostomy</td>
<td>40</td>
<td>Pain</td>
<td>I</td>
<td>Excision of cyst and hepaticojejunostomy</td>
<td>T3 cholangiocarcinoma at prior anastomosis in cyst</td>
</tr>
<tr>
<td>2/15</td>
<td>Cystojejunostomy</td>
<td>35</td>
<td>Pain</td>
<td>I</td>
<td>Excision of cyst and hepaticojejunostomy</td>
<td>T4 cholangiocarcinoma in cyst</td>
</tr>
<tr>
<td>3/62</td>
<td>None</td>
<td>62</td>
<td>Jaundice and weight loss</td>
<td>IVa</td>
<td>Excision of extrahepatic BD and R-sided trisegmentectomy</td>
<td>T3 cholangiocarcinoma from R hepatic duct</td>
</tr>
<tr>
<td>4/5</td>
<td>Cystojejunostomy</td>
<td>33</td>
<td>Pain, jaundice, and weight loss</td>
<td>I</td>
<td>None; CT revealed tumor in choledochal cyst and liver metastasis; underwent PTBD</td>
<td>FNA of liver metastasis: cholangiocarcinoma</td>
</tr>
<tr>
<td>5/52</td>
<td>None (‘observed’ after diagnosis because symptoms improved)</td>
<td>58</td>
<td>Pain</td>
<td>I</td>
<td>Excision of cyst, radical choledystectomy, and hepaticojejunostomy</td>
<td>T3N1 gallbladder cancer</td>
</tr>
<tr>
<td>6/68</td>
<td>None (planned excision but preoperative workup revealed CAD required CABG; then lost to follow-up)</td>
<td>73</td>
<td>Pain, jaundice, and weight loss</td>
<td>I</td>
<td>Palliative choledystectomy and choledochoduodenostomy</td>
<td>T2N2 gallbladder cancer</td>
</tr>
<tr>
<td>7/50</td>
<td>None (‘observed’ after diagnosis because symptoms improved)</td>
<td>53</td>
<td>Pain and weight loss</td>
<td>I</td>
<td>Excision of cyst and hepaticojejunostomy</td>
<td>T3 cholangiocarcinoma in cyst</td>
</tr>
<tr>
<td>8/23</td>
<td>Cholecystectomy; partial excision and choledochocystoplasty; choledochocystoplasty</td>
<td>45</td>
<td>Pain</td>
<td>I</td>
<td>Whipple operation</td>
<td>T2 cholangiocarcinoma in cyst remnant</td>
</tr>
</tbody>
</table>

Abbreviations: BD, bile duct; CAD, coronary artery disease; CABG, coronary artery bypass graft; CT, computed tomography; FNA, fine-needle aspiration; PTBD, percutaneous transhepatic biliary drain; UCSF, University of California, San Francisco.

* Todani choledochal cyst classification type I indicates dilation of the extrahepatic bile duct with less prominent dilation of the intrahepatic ducts; type IVa, dilation of the extrahepatic ducts with accompanying equally prominent dilation of the intrahepatic ducts.
tosomal recessive inherited condition with specific chromosomal abnormalities\textsuperscript{26,27} and clinically is associated with intrahepatic gallstone formation and a high incidence of renal disease. Although the radiologic findings in Caroli disease may resemble a CC, the other features show it to be a distinct, unrelated entity.

In the current series as well as in other reports\textsuperscript{7,28,29} many patients with CC presented with concomitant cancer. In the Japanese registry of 1353 patients, 16\% overall had coincident cancer, increasing with each age of life decade from 2\% for patients in their 20s, to 43\% for those in their 60s.\textsuperscript{30} Type I and IV cysts have the highest risk of cancer,\textsuperscript{31} while cancer is rare in choledochoceles and gallbladder duplications.\textsuperscript{32,33} Caroli disease carries a small (about 7\%) risk of cholangiocarcinoma,\textsuperscript{34,35} but most patients with Caroli disease require treatment for cholangitis or compromised liver function well before cancer appears.\textsuperscript{36} While most of the reported cases of cancer arising in CCs are cholangiocarcinoma within dilated extrahepatic bile ducts, 10\% are gallbladder cancers.\textsuperscript{29} The overall survival following the diagnosis of cancer is poor, regardless of treatment. Few patients survive beyond 2 years.\textsuperscript{7,28,37,38}

Thus, the pathogenesis, risk of malignancy, natural history, and treatment of CCs vary with each of the Todani subtypes except I and IV, which are the same condition. We believe the current classification system is a cause of confusion and has no discernible purpose. First, it incorporates 4 distinct diseases, and by grouping them together incorrectly suggests that they are related. Second, by separating types I and IV into different subtypes, a distinction is made that is artificial or at least greatly exaggerated. The intrahepatic ducts are almost always abnormal; just the magnitude varies (Figure 2).

Furthermore, the intrahepatic dilation could either reflect congenital ectasia or stasis from the extrahepatic disease, and the contribution of each may be impossible to judge. We think discussions of these anomalies would be simplified and made more understandable by aban-

Table 2. Patients Who Had Prior Operations

<table>
<thead>
<tr>
<th>Patient No./Age at Diagnosis, y</th>
<th>Prior Operation</th>
<th>Symptoms at Second Presentation</th>
<th>Age at UCSF Operation, y</th>
<th>Operation at UCSF</th>
<th>Cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/21</td>
<td>Laparoscopic exploratory surgery (planned cholecystectomy but aborted when found cyst)</td>
<td>Pain</td>
<td>21</td>
<td>Excision, Roux-en-Y hepaticojejunostomy</td>
<td>No</td>
</tr>
<tr>
<td>2/5</td>
<td>Cholecystectomy, cystoduodenostomy, and cystojejunostomy</td>
<td>Pain</td>
<td>40</td>
<td>Excision, Roux-en-Y hepaticojejunostomy</td>
<td>Cholangiocarcinoma</td>
</tr>
<tr>
<td>3/Child</td>
<td>Cystoduodenostomy and cystojejunostomy</td>
<td>Pain and weight loss</td>
<td>66</td>
<td>Excision, Roux-en-Y hepaticojejunostomy</td>
<td>No</td>
</tr>
<tr>
<td>4/57</td>
<td>Cystojejunostomy</td>
<td>Cholangitis (intrahepatic stones)</td>
<td>60</td>
<td>Excision, Roux-en-Y hepaticojejunostomy, and gastrojejunostomy</td>
<td>No</td>
</tr>
<tr>
<td>5/3</td>
<td>Cystojejunostomy and excision with hepaticojejunostomy</td>
<td>Pain</td>
<td>29</td>
<td>Excision of cyst remnant</td>
<td>No</td>
</tr>
<tr>
<td>6/5</td>
<td>Cystoduodenostomy</td>
<td>Pain, jaundice, and weight loss</td>
<td>33</td>
<td>None, unresectable cholangiocarcinoma required PTBD</td>
<td>Cholangiocarcinoma</td>
</tr>
<tr>
<td>7/2</td>
<td>Cystoduodenostomy</td>
<td>Pain</td>
<td>35</td>
<td>Excision, Roux-en-Y hepaticojejunostomy</td>
<td>No</td>
</tr>
<tr>
<td>8/15</td>
<td>Cystojejunostomy</td>
<td>Pain</td>
<td>35</td>
<td>Excision, Roux-en-Y hepaticojejunostomy</td>
<td>Cholangiocarcinoma</td>
</tr>
<tr>
<td>9/15</td>
<td>Cystoduodenostomy</td>
<td>Pain and cholangitis</td>
<td>37</td>
<td>Excision, Roux-en-Y hepaticojejunostomy</td>
<td>No</td>
</tr>
<tr>
<td>10/23</td>
<td>Cholecystectomy and partial excision with choledochojejunostomy</td>
<td>Pain</td>
<td>43</td>
<td>Whipple operation</td>
<td>Cholangiocarcinoma</td>
</tr>
</tbody>
</table>

Abbreviation: PTBD, percutaneous transhepatic biliary drain.

Figure 2. Endoscopic retrograde cholangiopancreaticogram showing Todani type I choledochal cyst (arrowhead), although the intrahepatic biliary tree is also abnormally dilated (arrows).
doning the numerical designations altogether and just re-
ferring to them according to the descriptive terms al-
ready in common use: CC, choledochal diverticulum, cho-
ledochocele, and Caroli disease (Figure 3). The term
congenital CC should be reserved for the single condi-
tion made up of Todani types la through lc and IVa. It
would then be unnecessary to include cases of the un-
related anomalies in articles on congenital CCs.

It has been suggested that cystenterostomy, by ex-
posing the mucosa of the abnormal duct to pancreatic juice,
may hasten the development of cancer in a choledochal
cyst.34 But as mentioned earlier, time seems to be the domi-
nant factor. Thus, the principal risk of a drainage pro-
cedure may be to render the patient asymptomatic until can-
cer appears many years later. Although for 30 years the
literature on the surgical treatment of congenital CCs has
stressed the superiority of cyst excision over a drainage
procedure, drainage procedures may still be required un-
der circumstances in which a more aggressive operation
is too risky for technical or clinical reasons. What needs
emphasis at this point is the importance of electively ex-
cising the abnormal bile duct later after the patient has re-
covered from the palliative bypass. Even some recent au-
thors have equivocated on the indications for surgery in
patients who have had a bypass. Two people in our series
who had cystoduodenostomies in childhood had been told
that they might some day need another operation but that
they could wait until symptoms developed. The first symp-
toms, several decades later turned out to be from incur-
able cancer in the cyst. Three (30%) of 10 patients in the
current series who had previously undergone cystentero-
tomy were found to have cancer on presentation at our
institution. We recommend that any patient with a con-
genital CC who had had a bypass operation in childhood
have the cyst excised before the age of 30 years whether
or not symptoms are present.

Despite near universal recognition of the impor-
tance of excision, the specific surgical technique remains
controversial, particularly with regard to the proximal and
distal extent of resection.6,39,40 and the conduit for recon-
struction (ie, hepaticojjunostomy7,41 vs hepaticojejunodu-
odenostomy42,43 vs appendicoduodenostomy44). The ap-
propriate treatment for most patients with benign types I
and IV cysts (regardless of any intrahepatic changes) is re-
section of the extrahepatic biliary tree and Roux-en-Y he-
paticojejunostomy. This procedure, performed in 28 (90%)
of our 31 patients with benign disease, eliminates the mu-
cosa at highest risk for malignant degeneration. The re-
section should extend from the bifurcation of the lobar he-
patic ducts into the parenchyma of the pancreas to a point
just short of where the duct abruptly narrows to a 1- to
3-mm diameter. For the rare patient with extensive intra-
hepatic biliary dilation complicated by gallstone forma-
tion, cholangitis, or biliary cirrhosis, liver resection (for
unilobar disease)35 or transplantation (for bilobar dis-
ease)46 may be indicated. But we did not see such a case.

Several recent reports have described cases of cho-
langiocarcinoma that developed after excision of CCs.35-49
Cancer after excision is rare (<1%),30 with fewer than
30 cases reported to date. In most such cases the previ-
ous excision has been found to be incomplete.30,47 After
complete cyst removal, the risk of cholangiocarcinoma
developing in the remaining ductal system is small. In
fact, malignant degeneration in the intrahepatic ducts may
be related to the enteric anastomosis itself rather than to
any intrinsic quality of the biliary epithelium associated
with CC disease.30 Therefore, more radical procedures—
hepatic resection and transplantation—are unwar-
ranted as prophylaxis against cancer, regardless of
the extent of dilation of the intrahepatic ducts.

This series, one of the largest in North America, dem-
onstrated the extreme risk of nonexcisional treatment of
CCs. The standard classification scheme for CCs is con-
fusing and inaccurate. The distinction between Todani
type I and type IV is arbitrary because the intrahe-
patic ducts are never completely normal. We believe that
the numbered system of types should be abandoned, the
term congenital CC should be reserved for the anomaly
consisting of extrahepatic and variable degrees of intra-
hepatic dilation, and the other conditions should be called
choledochocele, choledochal diverticulum, and Caroli dis-
ease. Patients whose cyst was bypassed in childhood
should have the lesion excised before the age of 30 years.
Patients diagnosed as having CCs as adults, regardless
of symptoms, should undergo complete excision of the
extrahepatic duct, cholecystectomy, and Roux-en-Y hep-
taticojejunostomy. The outcome of that approach was
excellent.

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manuscript.

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.ucsf.edu).

Figure 3. Proposed new nomenclature of biliary lesions formerly all termed
"choledochal cysts." The choledolchal cysts depicted are not meant to
represent distinct subtypes, but merely to depict the spectrum of intrahepatic
involvement.

CONCLUSIONS


DISCUSSION

Clifford W. Devaney, MD, Portland, Ore: The authors have described their experience with CCs and make the point that the cysts of choice of the types I and IV of the 1959 Classification of Alonso-Lej as modified by Todani and colleagues in the 1970s. The authors correctly point out that types II, III, and V are different entities with different treatments and that they should not be called CCs. The authors advocate abandoning the Alonso-Lej classification and simply calling these biliary abnormalities by what they are (ie, types I and IV CCs, type II choledochal diverticulum, type III choledochocele, and type V Caroli disease). This would certainly make things simpler. Because of the risk of cancer developing in the CCs (types I and IV), the authors recommend excision of the entire extrahepatic biliary tree and Roux-en-Y hepaticojejunostomy for resection of the diver- ticular?
Cancer developed in the cyst in several of your patients, but 2 of your patients had gallbladder cancer. Is gallbladder cancer associated with types I and IV CCs?

Some technical questions. Do you ever have any difficulty distinguishing where the duct becomes normal as it goes into the pancreas for your distal margin?

Do you ever use hepatic stents? For example, in patients with intrahepatic ductal dilation who have had a preoperative percutaneous transhepatic cholangiogram and there is a stricture. What do you think the risk of cancer is in those patients with intrahepatic ductal dilation? Is there an increased risk of cancer in any of the remaining ducts (ie, in the pancreas)? You have addressed this somewhat in your paper. Your follow-up on your patients is rather short to really determine if you have avoided the development of cancer, but you might comment on that from the literature.

I would commend the authors, Drs Visser, Suh, Way, and Kang, for simplifying a confusing classification of biliary ductal abnormalities and for reemphasizing the need for excision of all extrahepatic bile ducts when CCs (type I and IV) are present.

Susan Orloff, MD, Portland: That was a very nice and important series. I am wondering what you suggest based on your study as to the follow-up of patients in whom you perform excision and hepaticojejunostomy, especially those patients who have intrahepatic or suspected intrahepatic ductal involvement in terms of the risk for cancer. What do you suggest is the best screening imaging and how often should these patients be followed up given that you had a 16-year interval as a mean for recurrence of cancer or development of cancer?

Eric W. Fonkalsrud, MD, Los Angeles, Calif: I congratulate Dr Visser and his colleagues on using their data with this large number of adult patients with CCs to revise the classification and to emphasize the high frequency of virulent carcinoma when less than complete cyst excision is performed, even in children. In fact, one wonders since the average age of your patients was 50 years, are these truly congenital CCs or are they occasionally developmental? I wonder if the authors could speculate why there is such a great propensity to develop carcinoma in the common bile duct wall even when the cyst is drained adequately into the jejunum. In other types of biliary surgery, this rarely occurs. How many of your patients having carcinoma were actually diagnosed preoperatively, or was this a finding that you made at operation? Should we consider all of those patients who have had drainage procedures in previous years for callback—to have total cyst excision now even though they are asymptomatic?

There are several patients we see in the pediatric age group that have a fusiform dilation of only 1 to 2 cm in diameter. Do these patients have the same risk of developing carcinoma as those large giant CCs that you have shown so nicely? Or should these patients with fusiform dilations not even be considered as CCs in your new proposed classification?

Since patients with Caroli disease have an increased risk of developing carcinoma, and we are unsure if drainage actually lowers the risk in these patients, what should we do with all of those patients that have intrahepatic ductal dilation with CC? Do they have a lower risk of developing carcinoma than those with Caroli disease?

Lastly, I wonder if the authors could speculate on the relationship between sclerosing cholangitis and the frequency and type of ductal carcinoma compared with the CC and the carcinoma, which develops there?

Theodore X. O’Connell, MD, Los Angeles: I certainly agree that CCs should be completely excised and patients who had them drained in the past should be called back to have them excised because when they develop carcinoma it is really devastating. Once CCs have been previously drained, you do not know that they have developed a carcinoma because the drainage is already there so they do not get early obstruction and, thus, early treatment.

But one of the questions that I had was the large amount of Asian patients that were presented. That certainly is not most people’s experience unless you are operating in China or Japan, but certainly not in the United States, although this may be the experience in San Francisco. Especially the ones that were not diagnosed previously, did not have a previous drainage procedure, and were diagnosed in their 50s and 60s—how many of those patients were Asian? Do they have rather than a congenital CC, the biliary dilation that you see in Asians, cholangiogtitis type, an acquired biliary dilation, secondary to parasites or other unknown reasons?

The second question is to echo what Dr Deveney said. As far as I know, there is no real association between gallbladder cancers and CCs. Which were the patients in whom gallbladder cancer developed in this series and was it in patients who were older, with biliary dilation rather than a strict congenital CC?

The third question is that the authors come out strongly recommending a Roux-en-Y hepaticojejunostomy, and although I think that is acceptable, have they considered doing a hepaticoduodenostomy? That is much more physiologic, surveil the duct that remains, and in case stenosis develops, you have access to your anastomosis to dilate it. In fact, in one case they actually did an excision with a choledochoduodenostomy. What was the occasion that they did that type of operation? Why did they choose that operation that one time?

Yeu-Tsu M. Lee, MD, Honolulu, Hawaii: I had a chance to go to China and Taiwan and just like Dr Ted O’Connell said, the Asians have a much higher rate of CCs. They also have a higher rate of CC with associated cancer too. So I have 2 questions. (1) Since you are reporting the largest series in America, I like to see a racial breakdown, specifically how many were Asians and maybe their associated age distributions. (2) Now with all the human genetic research in patients with cancer, whether the authors know of any genetic studies because I do know there are a few cases with positive family histories in Chinese.

Kimberly S. Kirkwood, MD, San Francisco, Calif: I want the authors to speculate on the pathogenesis of the development of cancer in these patients. You implied that excision of the extrahepatic duct was adequate and that you had not seen development of cancer within the intrahepatic ducts. Dr Fonkalsrud’s question implied that biliary stasis might not be the cause since even patients who had adequate drainage of choledochal cysts were still at risk for development of carcinoma. So what is the hypothesis that explains the lack of development of carcinoma in the residual dilated intrahepatic ducts and what is known about the genetics of this disease?

Bruce E. Stabile, MD, Torrance, Calif: An observation that has been made is that there is an anomaly of the pancreaticobiliary system associated with CC and that is a long common channel or a more proximal than normal insertion of the pancreatic duct into the bile duct. This has been thought to perhaps cause abnormal reflux of pancreatic juice into the biliary system. This particular anomaly has been observed in cases of both CC, at least of the type I and IV varieties, and has also been observed in cases of gallbladder cancer. Do the authors have any information on this large patient experience as to any anatomical information related to the long common channel in the patients with CC and gallbladder cancer?

Dr Way: I want to thank all of the discussants. It is rewarding to see that your paper has titillated a lot of interest like that. I will try to answer the questions. Some of the questions I do not have answers to. I think Dr Deveney and others asked whether the gallbladder cancer is associated with congenital CC and, in fact, that has been reported from all of the series.
The gallbladder is abnormal just as the rest of the extrahepatic biliary tree. The reason why cancer develops in this lesion is really unknown. There is a variety of things that have been pointed out as being associated with the condition, and Dr Stable just mentioned one of them and that is a high junction of the pancreatic duct and the bile duct that people have said is probably pancreatic juice reflux and maybe that causes the cyst in the first place and in the second place gives rise to cancer. But we have a lot of situations in which there is reflux of pancreatic juice and it does not cause much trouble and there are a lot of abnormal junctions that have been shown on endoscopic retrograde cholangiopancreatograms performed in people who do not have CCs and in addition to that pancreatic enzymes are not universally found within these cysts. So I think that is an interesting and enticing observation, that there is such a high incidence of this malfunction but whether you can just have a full-blown satisfying theory on the causation from that alone I think is not yet there. But it is an important observation that still needs to be considered.

As far as the development of cancer, one thing not brought out in the presentation and really not discussed much in the paper is the fact that the biliary epithelium tends to be abnormal when you see it. Whether this is owing to reflux or stasis or whatever, there is quite a bit of abnormality within the epithelium, signs of chronic inflammation, and this gives rise, probably is a steppingstone on the way to the development of cancer, and it also is responsible for the many times anastomoses to this abnormal dilated bile duct tends to stricture down. I recall a case about 5 or 6 years ago of a young woman who several years previously underwent a choledochoejunojunoamy with a nice big anastomosis and when we reoperated on her, it had completed healed over so there is something peculiar about this epithelium in general and the risk does seem to be concentrated in the extrahepatic biliary tree because not only in our series which is a short-term follow-up but throughout the literature the appearance of cancer within the liver, in the abnormal bile ducts there, is really uncommon. So that is why we think a good thorough job in the extrahepatic biliary tree is important in this respect. It is important to get all of that lower into the bile duct because there are quite a few cases of cancer developing in an incompletely resected lower end, and that is the result of surgeons being a little bit timid about taking that lower end because the lower end really is inside the pancreas. Surgeons are a little bit frightened about getting that high junction of the pancreatic duct and the bile duct. So there are a couple of reasons why you might, if you are new to this, be a little shy of a thorough operation at that level. If you stay right on the surface of that bile duct, cut it across right at the surface of the pancreas, stick your thumb or your finger down, and then stay right on the external surface using little clips. You can take that out, stop short about a centimeter of where that duct comes to an abrupt halt, and you can remove just about all of it.

So Dr Orloff, I do not know the answer to your question about the follow-up of these patients because the risk of developing cancer is so low and the period would be so great. I just do not know the answer. It is sort of a statistical question on whether you would be doing repeated studies on these people over the years. You think of all of the morbidity involved with these follow-up studies, frightening people periodically, so I do not know the answer to that.

Dr Fonkalsrud, the diagnosis of cancer was suspected preoperatively in many of these patients because they had weight loss and the pain was more unremitting and boring and they had something other than just cholangitis in an otherwise healthy person and so we were quite concerned in a many of these patients although we might not have had complete proof preoperatively.

About the risk of the patients and the drainage procedure, you see in this study and in many studies that these people are returning in their 30s, 40s, and 50s with cancer. As somebody mentioned, the drainage procedure takes away early the development of the early symptoms of obstruction and then the cancer is incurable. So I recall a young woman in her late 30s who was a nurse in the surgical unit and she had had a drainage procedure as a child and was told, well, as long as you are asymptomatic, you might need that out some day but as long as you are asymptomatic you might as well wait. Our conclusion from our observations is that all of these cancers appeared in patients in their 30s. None appeared in patients in their 20s, and if it were me, I would want to have the thing out of there while I was in my 20s and then you know that the risk really is as low as possible. The patients are adults. The operation is not particularly difficult at that time, so that is our proposal. We put it out there. We do not know all of the answers, but it certainly would have saved a few of these patients if that had been done.

Dr Fonkalsrud, I do not know about all of the experiences of pediatric surgeons and the fusiform dilation and what the natural history of this disease is. Certainly, there is not much in the way of observations of the untreated patient so I cannot answer your question in that regard.

Carol’s disease—we are pretty sure that is a separate entity. Cancer develops in some of these patients but they have congenital hepatic fibrosis. They have intrahepatic gallstone disease that is pretty uncommon except in patients who have had a lot of cholangitis in the ordinary form of congenital CC, so most of these people have serious liver disease before cancer ever has the chance to develop in them. I do not think there is any relationship in my mind between sclerosing cholangitis and CC on the one hand and the development of cancer on the other, but I think that we would have to admit that we do not know the steps leading to cancer in either condition.

Dr O’Connell, what about the large number of Asians? Well, we had 9 Asians and for San Francisco that might not be an inappropriate balance. That may very well represent the demography of our community. This disease is not easily confused with the recurrent pyogenic cholangitis or what used to be called “Oriental cholangiohepatitis” which begins as a primary gallstone formation in the bile ducts, not in the gallbladder but in the bile ducts, and is very early associated with a lot of intrahepatic gallstone formation. Those patients do not undergo a high junction of the pancreatic duct and the bile duct and they can generally in the early stages be treated by an endoscopic sphincterotomy which I believe is the most common treatment in Hong Kong. It is only the more advanced cases that require complex things like hepatic lobectomy. But I do not think there is any relationship between these 2 conditions, nor do I think we have any patients in this series who have cholangiohepatitis. We know what that is because we have seen quite a bit of it.

I think I answered your questions about cancer and you asked me, well, why not hook the bile duct up to the duodenum. Well, I do not know. I suppose that could be done. There is some concern about reflux of duodenal juices and in some cases it will be something of a stretch. But I do not otherwise have any objections to that.