Congenital Biliary Hypoplasia *

WILLIAM P. LONGMIRE, JR., M.D.

From the Department of Surgery, University of California Medical Center, Los Angeles

PERSISTENT obstructive jaundice in the newborn child is most frequently a result of either 1) congenital atresia of a portion, or all of the intra or extrahepatic biliary system; or 2) some form of a clinical syndrome which has been labeled neonatal hepatitis. Norris and Hays have characterized patients with neonatal hepatitis as, "Infants with protracted jaundice, beginning prior to the fourth week of life, who give evidence of hepatic disease of an obstructive type through liver function tests, stool and urine examinations, and in whom patency of the extrahepatic tree is demonstrated by operation, cholangiogram, or clinical recovery." They state further that, "Neonatal hepatitis should be regarded as a useful clinical syndrome, not as a single pathological disease process." [4]

Blockage, either partial or complete, of the biliary ducts by inspissated mucus, or bile was formerly believed to be a common cause of neonatal jaundice. In about three-fourths of these patients normal biliary drainage was reported to result after the ducts were washed out at operation. In more recent reports,[4, 9] it is said to be rare to find inspissated bile as a cause of biliary obstruction. Large series of cases of neonatal jaundice have been reported in which inspissated mucus, or bile was not found in a single patient, and it seems most likely that cases formerly so diagnosed are now generally considered to be some form of neonatal hepatitis.

Brief reference has been made in previous reports to the association of hypoplastic or poorly developed bile ducts and neonatal jaundice,[2, 4, 6, 8, 9] but there have been no detailed reports. Gross [4] stated, "At operation, three of these babies were thought to have obliteration of the extrahepatic ducts, but subsequent to operation had passage of bile and clearance of jaundice. They must have had exceedingly tiny ducts which, subsequent to the regional manipulations, did open up." According to the criteria utilized by others [8] for the diagnosis of neonatal hepatitis such cases might have been included in this category.

Because wide variation in the extent of atresia of the ductal system is found, that is, from complete atresia of the intra and extrahepatic ductal system to isolated atresia of the common duct, it does not seem unusual that hypoplasia or stenosis of the ductal system should occur as well.

Four patients with hypoplasia of the biliary ducts have been seen at the University of California Hospital, Los Angeles, and the author has treated a similar case elsewhere. These five cases are presented to illustrate the anatomical findings and clinical course of patients with a hypoplastic anomaly of the bile ducts.

Case Reports

Case 1. S. H. The patient, a baby girl, was 13 months old when first admitted to the U.C.L.A. Hospital on September 28, 1957 (Fig. 1). Be-

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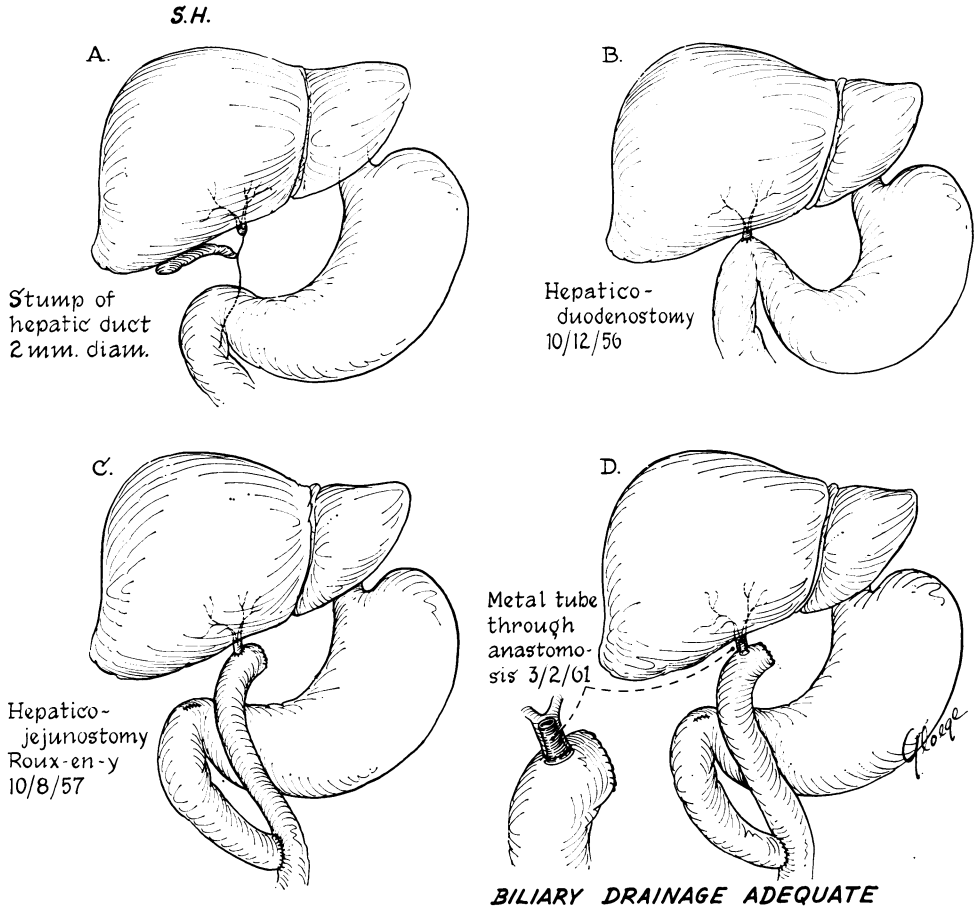

FIG. 1. Sequence of events in Case 1.

cause of persistent jaundice, first noted at the time of birth, the child had been operated upon at six weeks of age. Congenital atresia of the gallbladder and common bile duct were found, with a tiny nubbin of patent hepatic duct 2 mm. in diameter at the hilus of the liver. This hypoplastic hepatic duct was anastomosed to the duodenum. After a brief period during which the icterus cleared and the color of the stool and urine returned to normal, intermittent jaundice with fever returned and over a period of several months became increasingly severe. Before a second operation on October 8, 1957, the serum bilirubin was normal; however, the alkaline phosphatase and cholesterol were markedly elevated.

At this operation the obstructed hepaticoduodenostomy was resected, and a hepaticojejunostomy was performed with a Roux-en-Y jejunal limb. A lacy intrahepatic biliary tree, which seemed hypoplastic, was seen on operative cholangiograms (Fig. 2). Severe cirrhosis of the liver was also observed.

Following the second operation the child did well for several months, when again intermittent attacks of fever and jaundice returned and increased in frequency and severity. A stainless steel tubular prosthesis was inserted through the strictured hepaticojejunal anastomosis by Doctor Donald G. Mulder at a third operation on March 2, 1961. When last seen, five months following this operation, she was free of jaundice. The liver was palpated two fingerbreadths below the costal margin, and it was firm. There were no signs of inadequate hepatic function.

Comment. In this patient there was atresia of the gallbladder and common bile duct with a patent but hypoplastic intrahepatic ductal system. Undoubtedly the

miniature size of the common hepatic duct placed a role in the recurrent stricture at the site of the ductal-alimentary tract anastomosis.

During periods when the anastomotic stricture has been relieved, the serum bilirubin has returned promptly to normal. Tests prior to the last operation, however, indicated an elevation in the alkaline phosphatase and cholesterol, concomitant with a normal bilirubin. Thus, it seems that the intrahepatic ductal system, although hypoplastic, is adequate to provide ample excretion of bilirubin. Elevations of alkaline phosphatase and cholesterol may indicate that bile drainage is not entirely normal.

Case 2. J. S. The patient, a six-year-old boy, was first admitted to the U.C.L.A. Hospital July 8, 1962. Following three bouts of severe hematemesis, he had been admitted to another hospital where a diagnosis of portal vein obstruction of unknown etiology with secondary splenomegaly, had been made.

An enlarged spleen had been noted at 1½ years of age, but the child's general health apparently had been good until six months prior to admission when the hematemesis occurred. Intermittent swelling of the abdomen, clay-colored stools, and dark urine were noted during this period, but there was no mention made of jaundice. The presence of an undiagnosed cardiac murmur had been recorded.

Laboratory Results. Roentgenogram of chest showed possible slight enlargement of heart. No esophageal varices could be demonstrated by radiographic examination. Guaiac test for blood in the stool was one-plus on two occasions. Hematocrit was 34 per cent; total protein, 7.2 Gm. %; albumen, 1.9 Gm. %; globulin, 5.3 Gm. %; SGO transaminase, 132 units/cc.; thymol turbidity, 11.3 units; total bilirubin, 0.86 mg. %; bromsulphalein excretion, 15.9 per cent retention in 45 minutes; alkaline phosphatase, 29.4 King Armstrong units. Radioactive rose bengal uptake was 9.5 per cent indicating significant parenchymal liver damage.

Immediately prior to operation on July 24, 1962, a splenic portagram was performed and a patent portal vein demonstrated. On exploration of the porta hepatis, a normal appearing gallbladder was mobilized. The cystic duct was so small it could be found only with the aid of the binocular loupe magnifying glasses. A very small hypoplastic common bile duct which measured less than 1 mm. in diameter was also identified. A side-to-side anastomosis of the portal vein to the inferior vena cava, liver biopsy, and splenectomy were performed (Fig. 3).

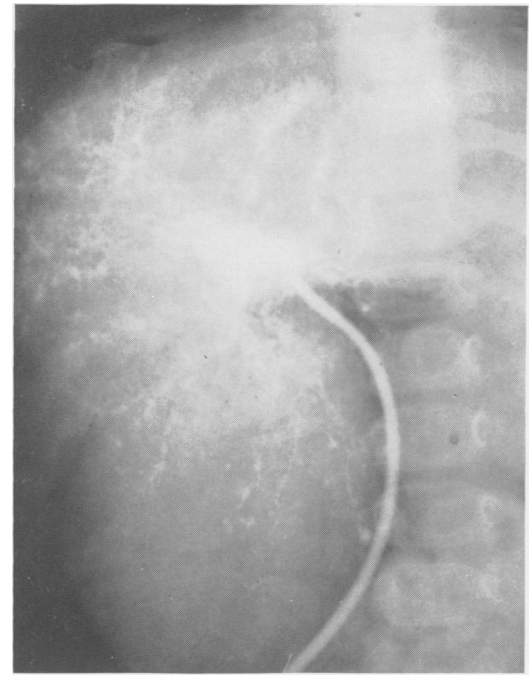

FIG. 2. Operative cholangiogram, Case 1, demonstrating hypoplasia of intrahepatic ducts.

The pathologist's report on the liver tissue was "Liver biopsy showing absence of bile ducts consistent with biliary atresia and portal cirrhosis, severe."

The patient's postoperative course was prolonged, but he was discharged on August 5, 1962 in satisfactory condition. Six weeks later he was readmitted for evaluation of his liver and cardiac function. Hepatic function was not significantly altered. Catheterization of the right side of the heart and cineangiocardiography indicated a markedly enlarged left atrium and ventricle with congenital mitral insufficiency.

In November of 1962 when last seen his progress was unchanged. He was able to return to school and to participate in most of the usual activities for a child of his age.

Comment. The markedly hypoplastic cystic and common duct, and scarcity of intrahepatic ducts, together with the very early development of splenomegaly, suggest that the patient developed advanced

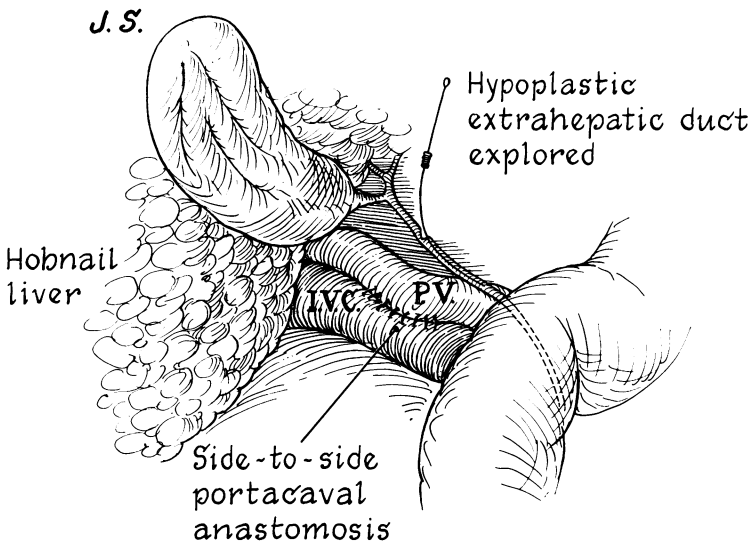

FIG. 3. Operative procedures performed in Case 2.

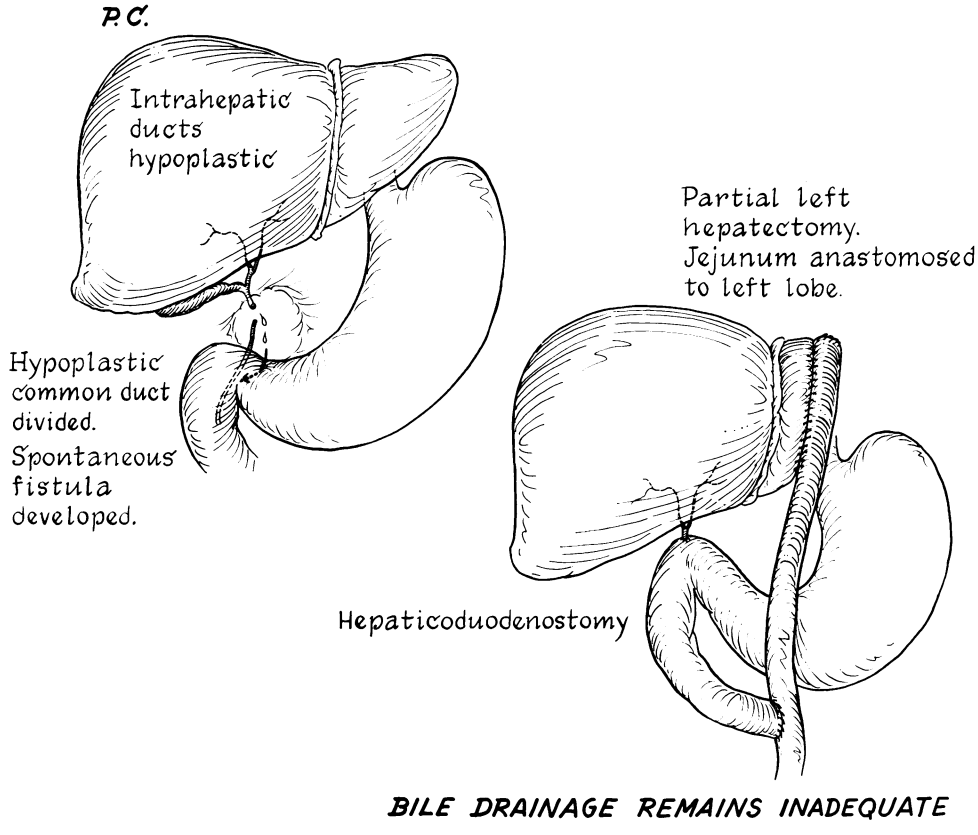

FIG. 4. Procedures carried out at first and second operations in Case 3.

cirrhosis and portal hypertension as a result of a mild chronic impairment of biliary drainage. It is interesting that jaundice was never an important symptom in this child's clinical course.

Case 3. P. C. The patient, a 4½-year-old boy, was first admitted to this hospital on September 12, 1960 with a history of intermittent jaundice since birth. The remarkable history was obtained that, at the time of the child's first operation at six weeks of age, the common duct was found to be replaced by an atretic fibrous cord without a lumen (Fig. 4). This structure was completely divided and the ends returned to the peritoneal cavity without ligature or anastomosis. A liver biopsy performed at this operation showed atresia of the smaller intrahepatic ducts.

There were repeated episodes of nausea and vomiting, with increasing swelling of the abdomen and deepening jaundice, until the child was about four months of age, when over a period of a few days his condition seemed to improve markedly. Following this the intensity of the jaundice waxed and waned, but his general condition was good. He carried on the usual activities of a child his age. His appetite and elimination were normal. From time to time he would develop a *cold* with fever, increasing jaundice and lethargy. These episodes would last for only a few days and then he would improve. At coeliotomy on September 19, 1960 a choledochoduodenal fistula was found. The enlarged cirrhotic liver was biopsied, and this was reported to show fibrosis with rare small bile ducts. The liver parenchymal cells were generally well preserved. There was only minimal evidence of bile stasis with very rare canaliculi thrombi. The hepatic cells were not excessively pigmented. A special note was added by the pathologist as follows: "The lack of extensive evidence of bile stasis is noteworthy and unexplained."

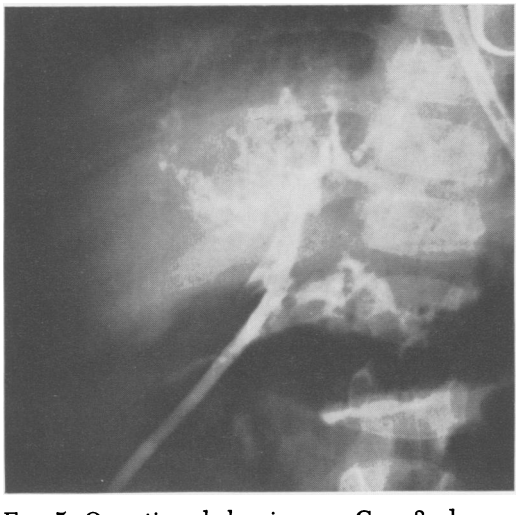

FIG. 5. Operative cholangiogram, Case 3, demonstrating hypoplastic intrahepatic ducts.

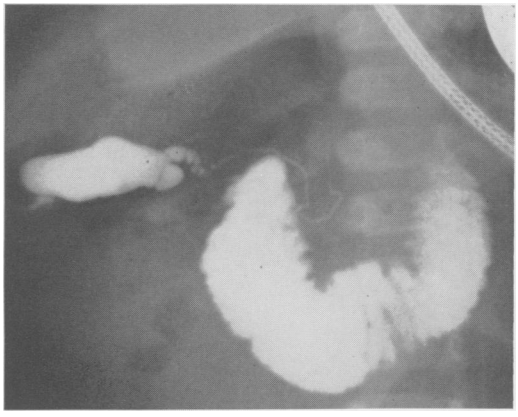

FIG. 6. Operative cholangiogram, Case 4. Dye injected into gallbladder fills minute hepatic, common hepatic, and common duct, and flows into duodenum. Incidental retrograde filling of pancreatic duct is also seen.

An operative cholangiogram demonstrated a lacy, poorly defined intrahepatic ductal system (Fig. 5). In an effort to identify an enlarged intrahepatic duct, approximately two-thirds of the lateral segment of the left hepatic lobe was excised and the opened jejunum sutured to the capsule, despite the absence of any identifiable bile ducts. The very small common duct was reanastomased to the duodenum.

The child's course has not been affected by this operation.

When last seen, the child was six years old. He was going to school and progressing nicely. Appetite was good; bowels moved regularly. Stools were usually light yellow in color. His sclera were yellow, and there were scratch marks in his skin. A loud precordial systolic murmur was present. The liver edge was felt three fingerbreadths below the right costal margin. The spleen was felt four fingerbreadths below the costal left margin. Medially it extended to the umbilicus. His voice was quite deep and hoarse.

Comment. This child probably developed a spontaneous choledochoduodenal fistula when four months old. Biliary drainage has been markedly impaired by the extensive ductal hypoplasia, but the operative findings, cholangiograms, liver biopsy, and

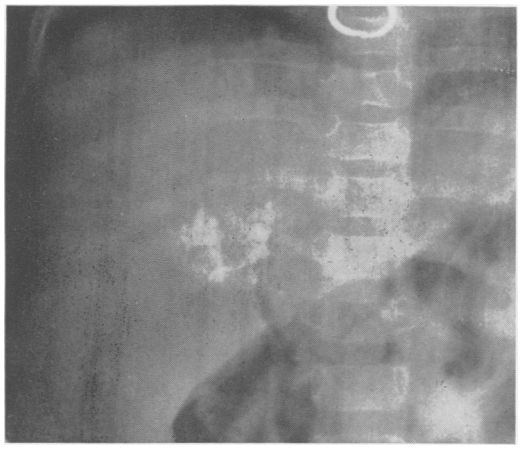

FIG. 7. Operative cholangiogram intrahepatic ducts, Case 4. Marked hypoplasia demonstrated.

the child's clinical course support the contention that there has been some degree of biliary drainage.

Case 4. M. M. The patient, two months old when first admitted to the hospital on January 8, 1961, had been jaundiced from birth. The stools were said to have varied in color from pale yellow to dark brown. The urine had been dark. Exploration of the porta hepatis was performed on January 18, 1961. The gallbladder was of normal size and contained bile. For a cholangiogram, dye was injected into the gallbladder. It flowed into the duodenum demonstrating a patent common duct (Fig. 6). There was very faint filling of the common hepatic duct, and small, poorly developed intrahepatic ducts were visualized (Fig. 7). The liver biopsy showed an absence of intrahepatic biliary ducts with biliary stasis.

As a result of these findings it was decided to observe the child further before attempting any type of corrective operation. However, a second operation was performed on May 3, 1962, as there was no clinical or laboratory evidence of improvement in the biliary obstruction. Because normal appearing bile had been found in the gallbladder and a lumen had been demonstrated by cholangiogram in the common duct, a cholecystoduodenostomy was performed in the hope that a larger biliary enteric anastomosis might promote better biliary drainage. In the four-month interval between the two operations there was no evidence of change in the relative size of any portion of the ductal system (Fig. 8).

When seen recently at 26 months of age, the child was deeply jaundiced. The liver and spleen were markedly enlarged, and there was evidence of total lack of biliary drainage.

Comment. In this patient, patent but hypoplastic hepatic ducts have been demonstrated up to the liver, and normal appearing bile was found in the gallbladder on two occasions. Patency of the intrahepatic ductal system is markedly reduced,

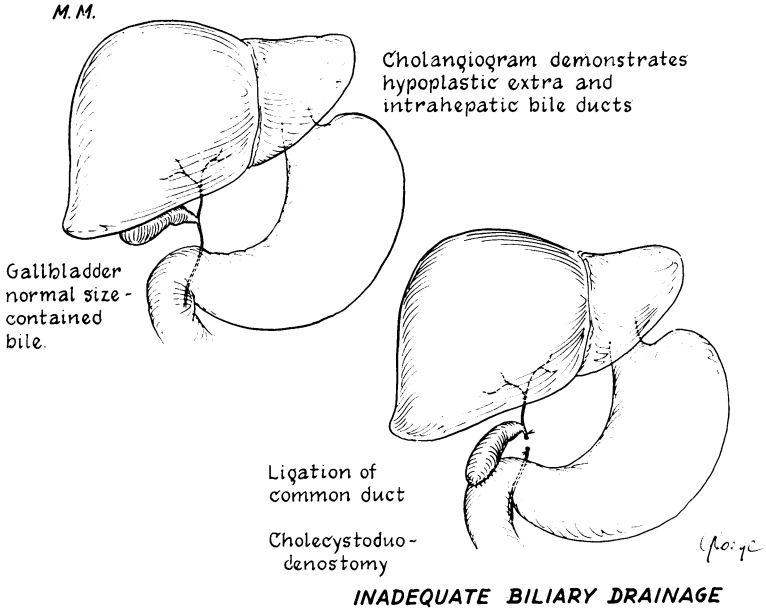

FIG. 8. Marked hypoplasia entire ductal system in Case 4 treated by cholecystoduodenostomy.

and bile drainage is clinically, grossly inadequate.

Case 5. J. H. The patient, who had been jaundiced since birth, was six weeks old at the time of operation. The liver was enlarged and scarred. A small atrophic gallbladder was identified and a minute fibrotic cystic duct traced down to a very small cordlike common duct (Fig. 9). An incision into the duct disclosed no evidence of bile, but a very small lumen was identified with a lacrymal probe. Despite the absence of bile, and lack of dilatation of the duct, a small plastic catheter was threaded into the lumen proximally and brought out through the abdominal wall. At the time the abdomen was closed, the diagnosis was "inoperable atresia of the extrahepatic biliary system." Within a few hours the dressings about the catheter were saturated with normal appearing bile. At early re-exploration an obstructing diaphragm was located at the distal end of the common duct in the region of the papilla of Vater. The diaphragm was disrupted by the repeated passage of probes down the duct into the duodenum, and the duct was repaired over a plastic stent. The child made an uneventful recovery and was free of jaundice when last heard from approximately one year later.

Comment. Certain specific details are missing in the record of this case. However, it is most interesting in view of the marked hypoplasia of the extrahepatic biliary system which existed in association with complete obstruction of the distal end of the common duct. Despite the absence of dilatation of the ducts proximal to the obstruction, a copious flow of bile was obtained within a few hours after relief of the obstruction. Prolonged biliary drainage into the alimentary tract was obtained in adequate quantities by disruption of the obstructing diaphragm and repair of the common duct.

Discussion

The three conditions which are most prominently discussed today [1-3, 6, 8, 10] in relation to obstructive jaundice in the young infant are 1) biliary atresia which accounts for about 75 per cent of the cases; 2) neonatal hepatitis which occurs in approximately 20 per cent of the cases; and 3) a miscellaneous group of about 5 per cent of the cases, which includes intrahepatic atresia, obstruction due to bile pigment associated with hemolytic disease, external pressure, choledochal cyst, and other rare conditions. In several published reports mention has been made of stenosis, or hypoplasia of the extrahepatic ductal system.

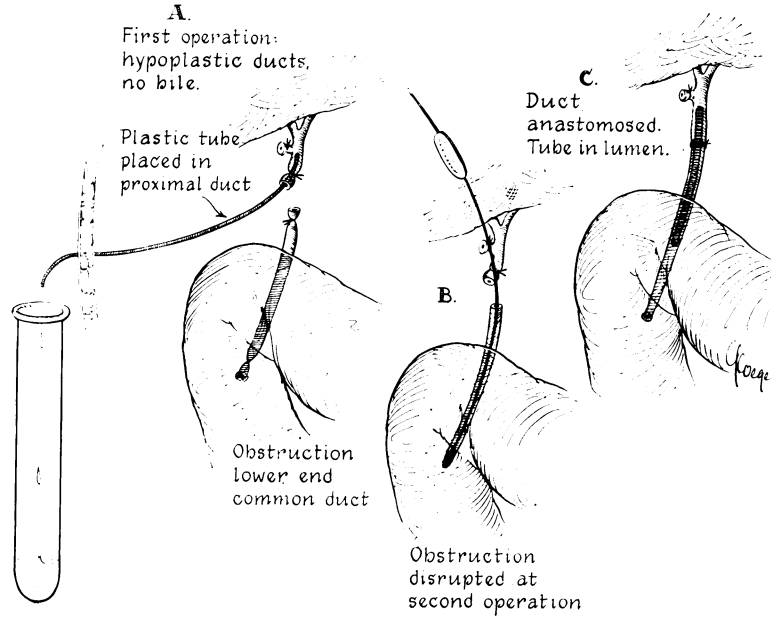

FIG. 9. Marked hypoplasia and atresia of ductal system in Case 5 treated by dilatation of obstructed area.

In the 20 cases of persistent obstructive neonatal jaundice seen in the U.C.L.A. Hospital, four cases of biliary hypoplasia have been identified, and one additional case has been seen elsewhere. The diagnosis of biliary hypoplasia has been established by several criteria, the most important of which have been gross inspection of the duct at operation and the demonstration of marked reduction in the lumen of intra or extrahepatic ducts, or both, by operative cholangiography. Liver biopsy has at times given confirmatory evidence.

It seems likely that cases of biliary hypoplasia may have been classified as atresia or neonatal hepatitis in other series. It also seems quite likely that the patency of these small fibrotic hypoplastic ducts most likely explains the recovery of certain reported cases in which surgical exploration has revealed no evidence of an extrahepatic biliary system, and a fatal outcome has been predicted.

Hypoplasia, with partial but inadequate biliary drainage, may also explain the prolonged survival of certain patients with all of the stigmata of biliary atresia. Case 3 in this report would appear to be of this variety. Hypoplasia may exist in all degrees, and involve various anatomical segments of the biliary system. It may also be associated with areas or segments of biliary atresia. Biliary drainage may be negligible as illustrated by Case 4, or quite adequate once an atretic segment is bypassed as in Cases 1 and 5. Although we have not encountered such a case, it would seem that the minute lumina of these hypoplastic ducts might easily be obstructed by thickened or inspissated bile, which might clear spontaneously or be relieved by incidental regional manipulation during surgical exploration of the area.

In general we would agree with those authors [2, 7, 10] who feel that if the diagnosis of neonatal jaundice is not established by the time the child is seven weeks of age, surgical exploration should be performed. A biopsy of the liver is taken for frozen section, and a cholangiogram is performed if possible. Great care must be exercised in the interpretation of the abnormalities seen in the microscopic examination of the liver section, for the nonspecificity of these changes has been emphasized.[4, 11]

Unless a normal ductal system with filling of the intrahepatic ducts and drainage of the dye into the duodenum is demonstrated, a full-scale exploration of the liver hilus and the hepatoduodenal ligament is carried out. There seems little reason to plan a second delayed operation if a cholangiogram can not be performed, or if it indicates an abnormal extrahepatic ductal system.

Summary

Hypoplasia of the bile ducts is found in patients with neonatal jaundice.

Like atresia, hypoplasia may involve any portion or all of the extra or intrahepatic biliary system, and it may occur with atresia.

Unlike atresia, hypoplasia may vary in degree. It may be associated with normal or near normal biliary drainage or with almost complete absence of biliary drainage, and thereby the clinical course may be similar to that of an irremediable biliary atresia.

Of five patients with hypoplasia of the biliary tract reported here along with their operative findings, cholangiographic picture, and liver biopsy interpretation, two seemed to have normal or near normal bile drainage when last seen. Two patients have suffered the results of prolonged partial biliary obstruction, but are able to carry on many normal activities at six and seven years of age. One patient, 26 months old, has severe biliary obstruction, and is following the general course of a patient with biliary atresia.

Recognition of the condition of biliary hypoplasia may help to explain the unusual clinical course of certain patients with neo-

natal jaundice. For example, it may explain the course of patients who recover spontaneously when a patent ductal system has not been identified at operation, or those with signs of neonatal biliary obstruction who survive in reasonably good general condition for years.

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