Longmire procedure (hepatojejunostomy) has been tried, but with little success, and many do not recommend it because even in adult cases where carcinoma is the underlying obstructive factor, the result obtained with the Longmire procedure is invariably poor and short-lived. The final cure will ultimately be in the hands of the geneticist, who must prophylactically reduce the number of congenital atresia cases that come before the surgeon. Figures 42 and 50 show the various operative techniques for congenital atretic lesions amenable to surgery.

Liver Transplantation for Biliary Atresia*

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INTRODUCTION

Orthotopic liver transplantation is the treatment of choice for patients with end-stage liver disease. The increasing enthusiasm for hepatic transplantation during the last decade is the result of better immunosuppression, particularly with the introduction of cyclosporine in the early 1980s and of monoclonal antibodies more recently. New improvements in technique have made the operation more practical. For these reasons, liver transplantation is no longer considered an experimental procedure but rather an accepted mode of therapy for patients with hopelessly advanced hepatic disease.

The indications for liver transplantation are changing constantly in order to benefit more patients who otherwise would inevitably die of complications of liver disease, as in fulminant hepatitis. Still, an absolute indication for hepatic transplantation in children is biliary atresia.

CLINICAL TRIALS

The first attempt at hepatic transplantation in a human was in 1963. The patient, a 3-year-old boy with biliary atresia, died on the operating table from hemorrhage. It was not until 1967 that the first long-term survival was obtained. A 1.5-year-old girl with hepatocellular carcinoma survived for 13 months before succumbing to metastatic disease.

Three years later, a 4-year-old girl with biliary atresia and an incidental hepatoma underwent a liver transplant; this patient is alive and attending college more than 16 years later.

During the precyclosporine era from March 1963 to February 1980, 86 children underwent liver replacement, of whom 51 had biliary atresia (Table 1).

Cyclosporine was introduced in March 1980 and since then, there has been a progressive increase in the number of liver transplants performed. The series began at the University of Colorado and continued until 1981, when the program was transferred to the University of Pittsburgh. Five hundred patients received liver transplants from March 1980 to November 1985. There were 203 pediatric recipients, of whom 99 had biliary atresia, the most common indication. Other indications for hepatic transplantation under cyclosporine therapy are listed in Table 2.

Almost all of the children undergoing liver transplantation for biliary atresia had had at least one portoenterostomy procedure (Kasai). Since these patients had failed with a biliary drainage procedure, the decision for transplantation was easy. The children rapidly developed progressive hepatic disease manifested by failure to thrive, increasing jaundice, and complications of portal hypertension.

Table 1. Indications for Liver Transplantation in Pediatric Patients in the Precyclosporine Era

Main Indication	No. of Patients (March 1, 1963–February 29, 1980)	Percent
Biliary atresia	51	59.3
Inborn metabolic errors	13	15.1
Nonalcoholic cirrhosis	13	15.1
Primary liver malignancy	3	3.6
Neonatal hepatitis	2	2.3
Congenital hepatic fibrosis	2	2.3
Secondary biliary cirrhosis*	2	2.3
Total	86	100%

*Trauma or choledochal cyst.

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SURGICAL TECHNIQUES

Donor Operation

The technical aspects of the donor hepatectomy and preservation have been discussed in detail elsewhere. A significant problem in the procurement of organs for children is the limited availability of small pediatric donors. In extreme circumstances, adult livers have been used in children after partial resections at the "back table."

In small donors, it is advisable to leave the celiac axis in continuity with the thoracic or abdominal aorta or both. This is particularly important when the recipient or donor hepatic artery cannot be used for the reconstruction, as in the presence of anomalous vessels. If the donor abdominal aorta cannot be retrieved, the thoracic aorta may be turned down 180° for anastomosis to the recipient's aorta. A useful technique is to transect the thoracic aorta, reanastomose it to the aortic cuff below the celiac axis, and tailor the transected end of the thoracic aorta to form a smooth funnel. This avoids a blind pouch, which could be the source of thrombus formation (Fig. 43). It must be emphasized, however, that in the presence of a recipient hepatic artery of good quality, the best results are obtained when an end-to-end anastomosis is carried out between the recipient hepatic artery and the donor celiac axis.

Recipient Operation

In children, a bilateral subcostal incision, often using the previous incision, will suffice. The dissection is then continued in the hilum of the liver, attempting to identify the Roux-en-Y limb of the portoenterostomy. This is useful in patients with dense adhesions, since dissection of the portoenterostomy will aid in exposing the hilar structures for proper identification. The hepatic artery should be ligated early to minimize bleeding. Then the portal is ligated deep into the hilum in order to obtain a long vessel. It is better to trim a long portal vein during the reconstruction than to come out short, necessitating interposition grafts.

Hepatectomy in children is usually easier than in adults, and this is often the case in patients with biliary atresia and a single portoenterostomy pro-

Table 2. Indications for Liver Transplantation in Pediatric Patients in the Cyclosporine Era

Main Indication	No. of Patients (March 1, 1980–December 1, 1985)	Percent
Biliary atresia	99	48.8
Inborn metabolic errors	45	22.2
Nonalcoholic cirrhosis	21	10.3
Familial cholestasis	14	6.9
Neonatal hepatitis	6	3.0
Acute hepatic necrosis	5	2.5
Congenital hepatic fibrosis	3	1.5
Secondary biliary cirrhosis	3	1.5
Sclerosing cholangitis	2	1.0
Toxic hepatic injury	2	1.0
Trauma	1	0.5
Inflammatory pseudotumor	1	0.5
Budd-Chiari syndrome	1	0.5
Total	203	100%

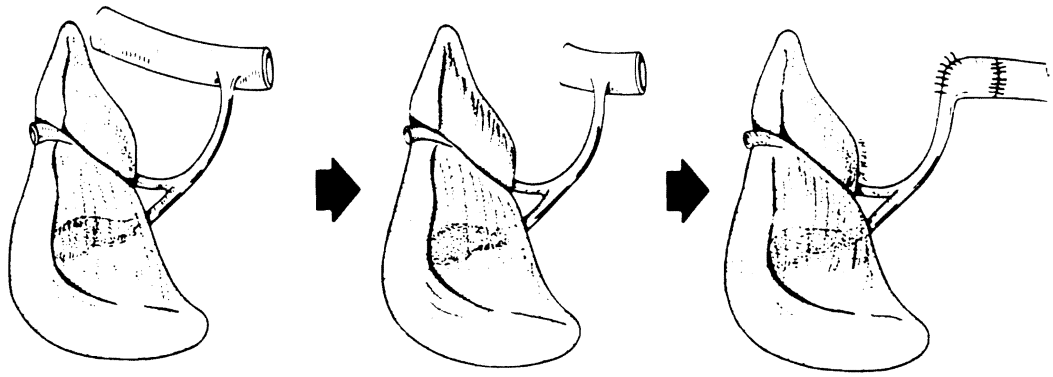


Figure 43. The thoracic aorta is transected above the celiac axis and anastomosed below it. The suraceliac cuff is tailored and closed to form a smooth funnel avoiding a blind pouch that could be the source of thrombus formation.

cedure. However, numerous attempts at biliary drainage, creation of stomas, and infection in the right upper quadrant can make the hepatectomy extremely difficult. Recently, venous bypass has been used more frequently and successfully in children. Decreased blood loss, stable hemodynamic physiology during the anhepatic phase, and less renal insult are some of the advantages of venous bypass. It also facilitates the hepatectomy and allows more time for hemostasis during the anhepatic phase, since the latter is better achieved with venous bypass.

If dissection of the hilar structures is impossible because of dense adhesions, encircling the hepatoduodenal ligament (Pringle's maneuver) will permit en bloc clamping of the portal triad. The ligament is then transected, and the vascular structures are identified so that they may be dissected more safely. Another valuable maneuver employed when adhesions preclude a safe hepatectomy is to clamp the suprahepatic vena cava, divide it, and insert one or two fingers into the intrahepatic cava to minimize blood loss. The liver is then dissected free from above until the infrahepatic cava is encountered. Finally, a clamp is placed on the infrahepatic cava to obtain vascular control.

The sequence and techniques of the vascular anastomoses have been reported elsewhere. Prevention of anastomotic strictures is of the utmost importance. A running suture of monofilament material is used, and excessive traction of the suture should be avoided. The "growth factor" technique is a practical method for eliminating purse string at the anastomosis. Upon termination of the anastomosis, the suture is tied away from the vessel, allowing the anastomosis to expand to its normal diameter. The extra suture will work its way into the suture line as the anastomosis grows (Fig. 44).

The biliary reconstruction is performed last when satisfactory hemostasis has been accomplished. End-to-side anastomosis of the donor common bile duct to a Roux-en-Y loop of jejunum with an internal stent is the technique of choice. This method of biliary reconstruction has provided excellent results even in small bile ducts, as in livers from newborns. As previously mentioned, the majority of these patients have had portoenterostomies with Roux-en-Ys which may be reused if they have not been damaged during the dissection. However, the old Roux-en-Y has had to be resected in most instances because, with previous revisions, the limb has been rendered unsuitable for biliary reconstruction.

IMMUNOSUPPRESSION

Precyclosporine Era

The current immunosuppression therapy for liver transplantation was derived from experience with renal transplantation, since the latter provided a much simpler model with which to work. Combination therapy with azathioprine and prednisone was the first widely used immunosuppressive regimen. However, most of the liver recipients from 1963 to 1980 in our series were treated with azathioprine, prednisone, and antilymphocyte (ALG). Occasionally, cyclophosphamide was substituted for azathioprine. Other additions to the immunosuppressive therapy, such as thoracic duct drainage, had no obvious benefit in hepatic transplantation.

The overall survival with the triple-drug therapy was 32.9% and 20% at 1 and 5 years, respectively.

Cyclosporine Era

Cyclosporine A is derived from two strains of fungi, *Cylindrocarpomlucidum* and *Tolypocladium inflatum* Gams. Cyclosporine was introduced to transplantation based on the experimental work of Borel et al, and the first clinical trials were performed by Calne et al. Better understanding of its mechanism of action has minimized complications such as the development of lymphomas and nephrotoxicity. Patient mortality has been reduced (Fig. 45).

In March 1980, cyclosporine and prednisone were introduced to the liver transplant program. There was a dramatic improvement demonstrated by an overall actuarial survival of 69.7% and 62.8% at 1 and 5 years, respectively. During the last year, a 2-week course with the monoclonal OKT3 (Ortho) was added to the immunosuppression regimen. The first clinical trials with OKT3 showed reversal of steroid-resistant rejection in a high percentage of kidney and liver transplant recipients.

RESULTS (SURVIVAL)

Precyclosporine Era

Eighty-six out of a total of 170 patients underwent liver replacement from 1963 to 1980. Fifty-three of the 86 died within a year after transplantation. The main causes of death are listed in Table 3. There was a high incidence of bacterial, fungal, and viral infections. Technical complications played an important role and, in part, were the cause of the poor results obtained in patients with biliary atresia compared to children with inborn errors of metab-

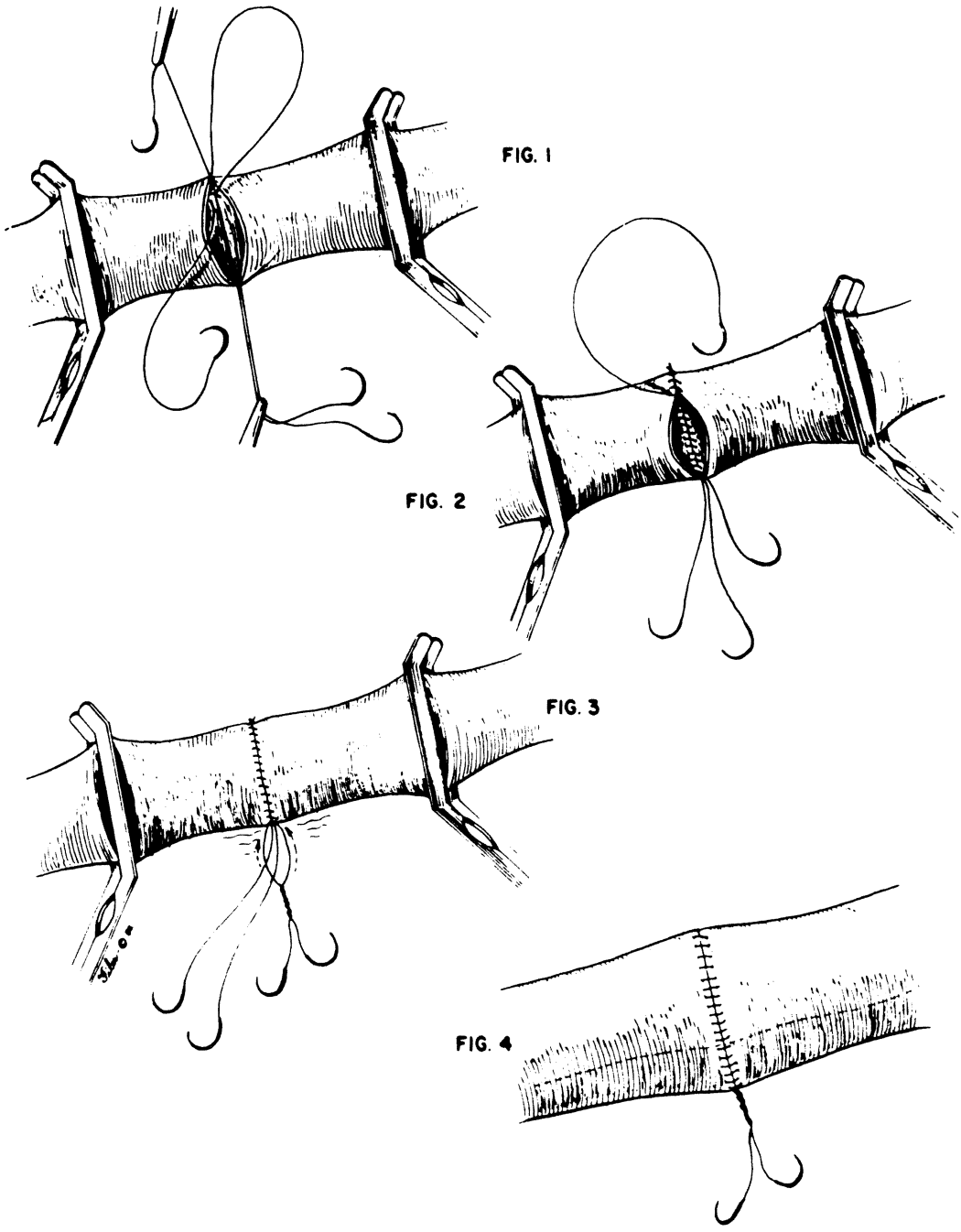
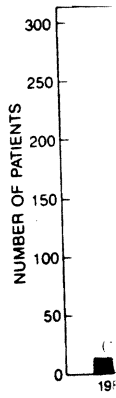


Figure 44. "Growth factor" technique used with continuous Prolene suture of small vessels. Note that anastomosis of half the circumference of the vessels is performed with each half of the original suture. Where the two halves meet, the knot is tied at a considerable distance away from the vessel wall, providing an excess of Prolene that is secondarily drawn into the suture line.



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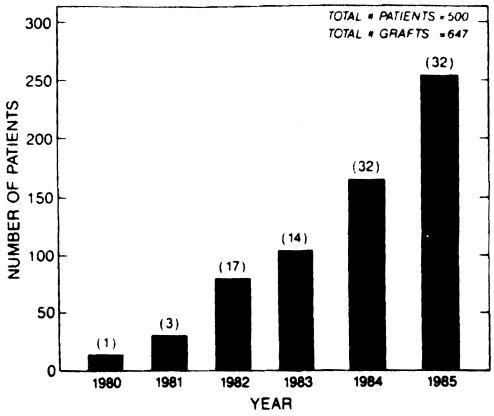

Figure 45. Number of patients receiving orthotopic liver transplants during the cyclosporine era. The number in parentheses represent retransplants per calendar year.

olism (Fig. 46). As mentioned before, previous surgical procedures in the right upper quadrant made the operation more difficult. Additionally, anomalies of the portal vein, including thrombosis, are frequently observed in patients with advanced biliary atresia. The 5-year survival in patients with biliary atresia was 14%.

Cyclosporine Era

The 5-year actuarial survival for the entire series (500 patients) is 60.6%. Of these patients, 203 were children (less than 18 years); the 5-year actuarial survival in this group is 67.7%. The 5-year actuarial survival in patients with biliary atresia is shown in Figure 47. The period of observation in patients less than 2 years of age is only 3 years, and the actuarial survival is slightly better than that of patients older than 2 years (Fig. 48). In contrast to the precyclosporine experience, there was little difference between patients with inborn metabolic errors and those with biliary atresia. The narrowing of the gap between these two groups of patients is explained by the fact that patients on cyclosporine seem to tolerate the perioperative trauma better than those on conventional immunosuppression. Further, there has been more familiarization with the procedure and better understanding of the perioperative metabolic changes as the number of transplants increased during the last

Table 3. Chief Causes of Death Within a Year After Hepatic Transplantation Among 86 Pediatric Patients in the Precyclosporine Era

	No. of Patients	Percent of Total
Infection	20	23.3
Technical complication	15	17.4
Rejection	9	10.5
Intra- and perioperative death	3	3.5
Primary graft dysfunction	3	3.5
Other	3*	3.5
Total	53	61.7%

*One patient died of recurrent malignancy, another from pulmonary embolism, and the third from respiratory failure secondary to an oversized graft.

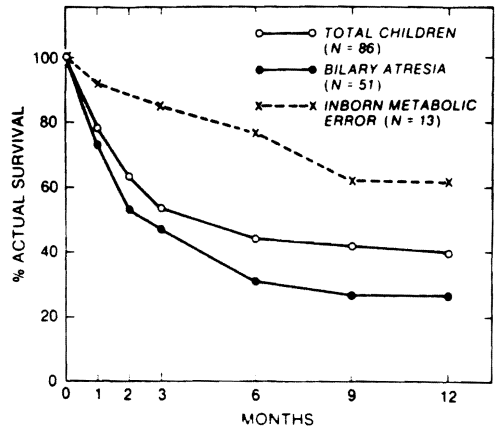

Figure 46. Pediatric liver transplantation: precyclosporin era. Influence of original liver disease on 1-year survival under conventional immunosuppression.

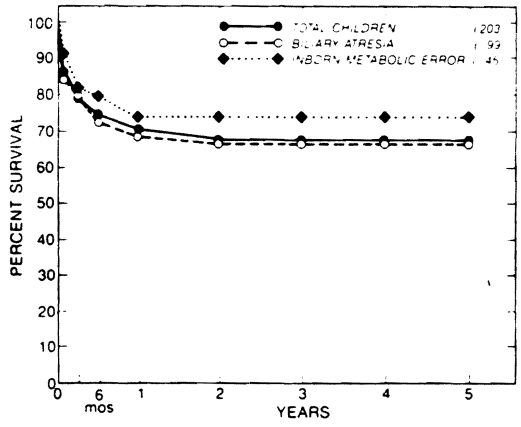

Figure 47. Five-year actuarial survival in pediatric patients receiving orthotopic liver transplants during the cyclosporine era.

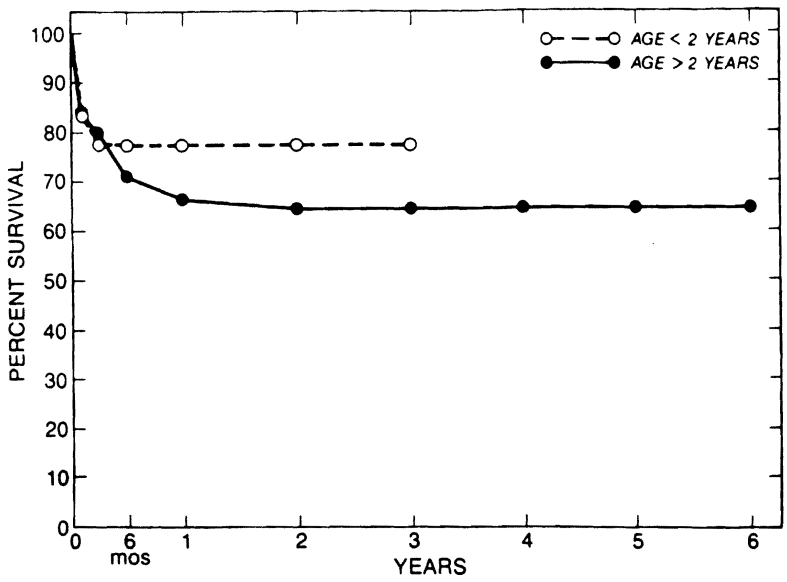

Figure 48. Actuarial survival of liver transplant recipients for biliary atresia under 2 years compared to patients over 2 years of age.

few years. Although there was an immediate improvement in survival when cyclosporine was introduced, there were some early deaths which could have been avoided by more effective dose control of cyclosporine and by aggressive retransplantation. At present, cyclosporine blood levels are monitored daily until the patient is discharged, and then twice a week for several weeks until the best dosage is reached in order to prevent irreversible rejection or overimmunosuppression.

Retransplantation

Retransplantation should be strongly considered when the allograft is failing. Failure of the graft is due to rejection, primary graft dysfunction, or technical complications. The most common problems in the pediatric population are technical, and of these, arterial thrombosis is by far the most frequent reason for retransplantation. The causes of arterial thrombosis are multifactorial: technical errors, small size of the vessels, overcorrection of bleeding with clot-promoting products, infection, and rejection. Rejection with swelling of the liver may create a low-flow state, which in turn could lead to thrombosis.

The 5-year actuarial survival in children who received more than one hepatic transplant is 55.3%. Although this survival is not as good as that of patients with the first graft, it is high enough to justify such efforts when the primary graft has failed or is failing.

Growth

In a recent report, Urbach et al.[1] showed that 76% of 29 children who received liver replacement and were followed for at least 2 years had excellent growth patterns. This response is explained in part by the small doses of steroids needed for immunosuppression when cyclosporine is used in conjunction. Biliary atresia accounted for 13 out of the 29 patients.

Effect of Age on Survival

The influence of age on survival in the pediatric patient population was reviewed by Iwatsuki et al.[2] In the precyclosporine era, 53% of infants and preschool children (less than 6 years), 50% of those between 6 and 12 years, and 76% of those between 12 and 18 years lived for more than 3 months. In the cyclosporine era, 76% of infants and preschool children, 67% of children between 6 and 12 years of age, and 86% of the adolescents lived for more than 3 months. The 3-month survival was not influenced by age either before or after cyclosporine therapy (Fig. 49).

CONCLUSIONS

Biliary atresia is the most common indication for hepatic transplantation in the pediatric population. Liver replacement is the treatment of choice for biliary atresia, and there is no limitation of age or

weight. Transplantation should be performed as soon as the patient begins to show signs of hepatic decompensation.

The scarcity of small pediatric donors is a most important practical factor. Adequate biliary drainage may stabilize the patient and buy valuable time. A single attempt at portoenterostomy may not add any risks to liver transplantation; however, surgical procedures of questionable benefit such as revisions of portoenterostomies and portosystemic shunts should be avoided, since they may jeopardize the final option of a hepatic replacement.

The progress in liver transplantation during the last few years has not been explained by better patient selection. Improvements in surgical techniques in the donor and recipient, aggressive retransplantation, and better immunosuppression have all played a role. Of these factors, cyclosporine has had the greatest impact in improving survival following hepatic transplantation.

A Consensus Development Conference held in 1983 in Maryland concluded that liver transplantation was a service rather than an experimental procedure. Liver transplantation is the most appropriate treatment for biliary atresia. If successfully treated, these patients can grow and function normally.

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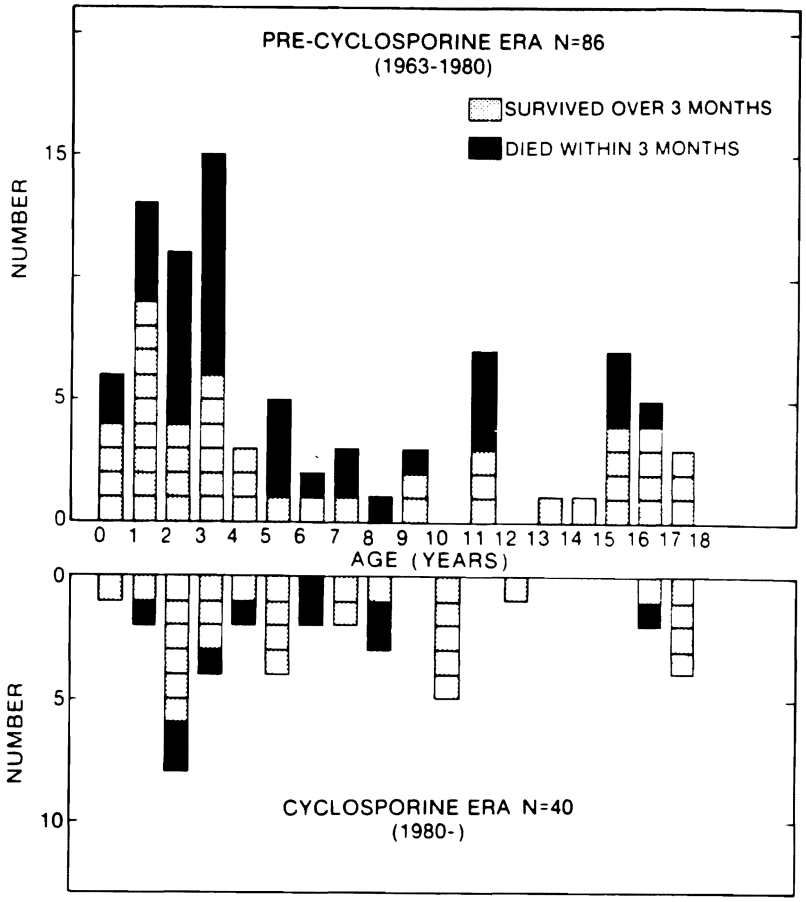

Figure 49. Age distribution of 126 childhood liver recipients. A shaded square represents a child who survived more than 3 months, and a black square represents a child who died within 3 months. All of the surviving patients treated with cyclosporine have follow-ups of at least 15 months.

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Congenital Cyst of the Common Bile Duct (Choledochal Cyst)

Congenital cyst or choledochal cyst is, as the name implies, of congenital origin, idiopathic in nature, and rare. It may be small or large, ovoid or round, and usually presents in the supraduodenal portion of the common bile duct. The cyst may or may not involve the right and left hepatic ducts. The background for this congenital formation has many etiological and theoretical explanations, but none has yet been found universally acceptable. We speak of a choledochal cyst, recognize it, and deal with it as best we can. This condition is more frequent in the female than in the male, and its size may vary from that of a small orange to a grapefruit. No one has established any relationship between the size of the cyst, its duration, and the severity of the symptoms. There is no constant relationship between the size of the cyst and the patient's age. The larger cyst, however, is more often seen in the teenage or adult patient. The wall of the cyst is usually thick and firm, and is almost invariably composed of epithelium; the lining of the cyst may be entirely absent, and on frozen section the wall may contain fibrous tissue. The size of the distal common duct may vary and, more often than not, is narrowed. The gallbladder is usually of normal size. Regardless of the dilatation of the common duct, it is uncommon for stones to be found in the gallbladder or cyst; however, stones in the cyst have been reported (see Fig. 50). As a rule, the intrahepatic ductal system is of normal size, but this too may be dilated on occasion. The

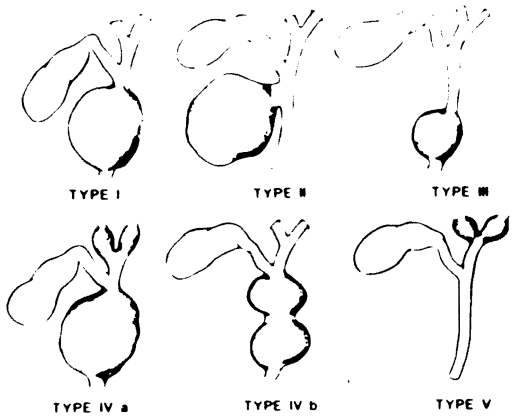

Figure 50. Classification of bile duct cysts. Refer to chapter on Congenital Cysts of the common bile duct. T. Todani describes his classifications of bile duct cysts.