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Liver transplantation

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In this account, I will trace the development of liver replacement (orthotopic liver transplantation), tabulate the clinical results obtained so far, and describe the factors leading to success or failure.

Experimental background

The technique of orthotopic liver transplantation in dogs was developed independently in two widely separated laboratories, one in Boston (1) and the other in Chicago (2, 3). These efforts in nonimmunosuppressed animals delineated the typical pattern of acute rejection (1, 3). After operation, the animals often seemed quite normal for several days, even resuming a diet. However, within four or five days, jaundice appeared along with rises in serum transminases denoting massive hepatocyte necrosis. The light and electron microscopic changes in rejecting livers have been well described (1, 3–5) and consist principally of mononuclear invasion of and necrosis in the hepatic homograft.

Chronic survival in canine liver recipients was first achieved in our laboratory, almost a decade and a half ago (6), using azathioprine therapy as the sole immunosuppression. Nineteen animals from that study survived for at least three postoperative months (5), five lived for more than a year, and one dog lived for almost twelve years (Figure 1) before dying of complications of old age plus partial biliary tract obstruction. This animal was given azathioprine only for the first four postoperative months. Seemingly, a change of such magnitude had occurred in the host-graft relationship that a full lifetime survival no longer depended on immunosuppression. The same phenomenon was noted in nine other animals.

The only other agent which has permitted chronic survival in dog liver recipients has been heterologous antilymphocyte serum (ALS) or its globulin derivative which is called ALG (7). In pigs, chronic survival has been possible without immunosuppression (5, 8–10).

Clinical immunosuppression

In spite of these achievements in individual experiments, the consistency with which really long-term survival was obtained was poor. There were at least two obvious reasons. First, complete control of rejection was usually not achieved. Second, it was difficult to prevent or to treat infectious disease complications or to provide other niceties of special care in a standard kennel or piggery environment. It is probably that the animal data would have indefinitely discouraged a clinical trial had it not been for the example of renal homotransplantation. With the latter procedure, the surprising frequency with which long survival was eventually achieved in man could hardly have been predicted from the prior laboratory results which, if anything, were less favorable than those after experimental liver transplantation. In addition, the human experience with the kidney did more than serve as an incentive. It also provided the conditions in which complex and effective immunosuppressive regimens could be evolved in man and applied, in turn, to the transplantation of other organs.

For the treatment of our human liver recipients of both orthotopic and auxiliary homografts two treatment protocols were applied after extensive personal experience had already been acquired in clinical renal transplantation. The first program consisted of double drug therapy with azathioprine and prednisone to which less important or even questionable ancillary measures were sometimes added; in nine trials there were no survivals of more than 34 days. Subsequent liver recipients were given triple agent therapy with azathioprine (which may be replaced with cyclophosphamide), with prednisone and with heterologous antilymphocyte globulin (ALG). The purified immunoglobulin (ALG) was obtained from the serum of horses or rabbits immunized against human lymphocytes. Thus ALG administration was an attempt at lymphoid depletion. The only really dose maneuverable component of the triple drug regimen was the prednisone which was raised or lowered according to the presence or absence of rejection. The way in which these agents were (and are) used is shown in Figures 2 and 3.

Indications for transplantation

Of all the indications for liver replacement, biliary atresia is the most clear. Into these children is made a great social and medical input, from which no conceivable long-term benefit can be expected, since they inevitably die and at a fairly predictable time if a porticoenterostomy is not successful. Thus, one can intervene with a clear conscience before the patients reach a moribund state. In our series, biliary atresia has been the single most common reason for liver transplantation (see Table 3).

When Kasai's porticoenterostomy began to be used extensively for biliary atresia, we feared at first that the extensive dissection required for this operation would jeopardize subsequent transplantation. However, this has not been a problem. There has even been the advantage that the Roux-Y jejunal limb constructed for the Kasai procedure can be reused to drain the homograft biliary tract.

Chronic aggressive hepatitis has been another common indication for liver transplantation both in adults and children. The majority of these patients have been virus free insofar as could be determined, but some have had preexisting Australia antigenemia. The first long survivor who carried the HBsAg marker became Australian antigen negative as judged by agarose gel and complement fixation methods and remained that way for about two months (Figure 2). Although later testing with the more sensitive radioimmunoassay showed that trace quantities of HBsAg were always present, the nearly complete clearing during this time indicated that the major focus of the virus had been in her native liver. About two months postoperatively, at about the time when she would have expected to develop serum hepatitis had she been infected *de novo* at the time of transplantation, she head increases in bilirubin, rises in transaminases, joint pains, and a return positive HBsAg with all the screening tests (Figure 2). Immunosuppression was not increased. She recovered spontaneously, but remained HBsAg positive and slowly recapitulated a variation of her orginal disease, dying after almost two years of nocardial brain abscesses combined with hepatic failure. In spite of this experience, the presence of a virus in these patients does not contraindicate liver transplantation. Now such patients can be treated with specific hyperimmune globulin starting on the day of operation when the titer of the virus is made low by removal of the native liver. We have thereby cleared the virus for many postoperative months, and the same thing has been accomplished by *Calne* et al (11).

Alcoholic cirrhosis is one of the most important potential reasons to consider liver transplantation, but the time of operation may be difficult to decide, particularly if abstinence from alcohol is not achieved in advance. Furthermore, the damage done to the central nervous system by hepatic failure, and the consequences to other organ systems by self abuse as well as for metabolic reasons constitute a severe handicap. Failure of the extrahepatic complications to reverse or come under control have caused the death of a number of these recipients. Only recently have our results with Laennec's cirrhosis provided any encouragement.

An exceptionally interesting group of patients have had liver replacement for inborn errors of metabolism which are known or presumed to be liver based. All hepatic based inborn errors of metabolism are curable by successful hepatic transplantation since the synthetic products and enzyme specificity of the new liver remains that of the donor (5). Even some metabolic disorders in which the exact enzyme defect is not known have

been cured by liver transplantation. An example of the latter is Wilson's disease, victims of which accumulate copper in the liver, brain and elsewhere causing the lesions of Wilson's disease including the typical Kayser-Fleisher rings in the eyes. Wilson's disease is an inherited disorder in which most patient have a reduced or abent serum ceruloplasm. After hepatic transplantation for Wilson's disease, the ceruloplasm increased in one of our patients from essentially zero to normal levels, and it stayed that way for more than seven years post-transplantation (Figure 3). After operation decoppering was evident in a cupruresis for many months (Figure 3). This patient's most severe complication of Wilson's disease was progressive neurologic disability. The nervous system abnormalities reversed over several years and between two and three years postoperatively the Kayser-Fleisher rings disappeared.

Other examples of inborn errors that we have treated include alpha-1-antitrypsin deficiency, congenital tyrosinemia, and Type IV glycogen storage disease. There are many possibilities for further research with other inborn errors.

Initially, we thought that the presence of primary liver tumors that could not be resected with conventional techniques would be an ideal reason for orthotopic liver transplantation. This proved to be a vain hope for the most part since recurrence of tumor has been seen in more than 90 % of such trials with hepatomas, small duct cell carcinomas (Klatskin tumors), and other less common malignancies including hemangioendothelial sarcoma (5, 12). With hepatomas, serial alphafetoprotein determinations have helped follow the evolution of metastases. With all kinds of tumors, a striking tendency has been seen for the recurrences to "home" back to the graft itself.

Tumor recurrence may not be an inevitable complication. An exception in our series is a little girl who had a hepatoma as an incidental finding in a liver that was removed because of biliary atresia. Preoperatively, she had a positive alphafetoprotein examination. The abnormal protein disappeared after the surprisingly long interval of four months. She has remained alphafetoprotein negative and tumor free since that time. She is now 8 1/2 years posttransplantation and the longest surviving liver recipient in the world.

In addition, palliation has been possible in some other cases although eventually there was tumor recurrence. We have had two men with the small duct cell carcinomas (Klatskin tumors) at the confluence of the right and left hepatic ducts. One lived for two years before dying of metastases. The other is surviving but with recurrent tumor and will be four years postoperative in September if he lives that long. We have a female patient who is coming up to two years after surviving liver replacement for a sclerosing cholangiocarcinoma. She has small quiescent pulmonary metastases which have been present since the time of transplantation. Perhaps the door is not entirely closed on hepatic malignancy as an indication for liver transplantation although for the reasons I have stated, the yield in terms of cure will be small.

To summarize indications in more general terms, we think: 1) Ideal recipients should be less than 40 years old. Those who are older cannot stand the rigorous immunosuppression which must be imposed postoperatively. 2) The patient should have a hopeless prognosis, a point to which I will return in a moment. 3) They should not have cancer. 4) They should not have an infection. As I have already implied, we have violated each of these guidelines from time to time. If two adverse conditions are present, the outlook is virtually hopeless.

Now, I would like to focus for the moment on the question of what constitutes a hopeless prognosis. We have treated patients with acute liver disease caused by halothane, isoniazid, and viruses who seemed to have no hope for survival. Yet, they have recovered fully with supportive care including ventilation, exchange transfusion, and renal dialysis. Because of such admittedly uncommon experiences, we are reluctant to proceed with liver replacement for acute disease. Perhaps there could be a role here for auxiliary transplantation whereby a second ectopically placed liver could be used temporarily to tide the patient over the crisis and to allow recovery of the native liver.

In patients with chronic liver disease, it is really important to have a longitudinal view of their course before accepting them for transplantation. Such a view has been made possible by collaboration with profound students of liver disease. We have developed a network of communication with many of the fine hepatology centers in the United States. When referrals come from such sources, we have confidence that the time is ripe

for treatment, even if our own opportunity for observation is limited. When a patient becomes invalided so that he or she cannot function in society and cannot work, we believe further delay is inadvisable. The past practice of taking moribund patients to the operating room for such an extensive procedure will not permit an improvement in results.

A notation is in order here about the inconsequential role of tissue typing in liver transplantation. No correlation has been observed between HL-A typing and the clinical outcome (12). Surprisingly, even a positive cytotoxic crossmatch showing preformed antidonor antibodies in the recipient serum has not led to hyperacute rejection (12) as would be expected after renal transplantation.

Technique of liver replacement

The essential first step in liver transplantation is to obtain a good cadaveric organ from a brain dead donor who still has an effective circulation. The organ can be excised in an orderly way and chilled by infusing cold fluid such as lactated Ringers solution with or without low molecular weight dextran through the portal vein. The cooled liver will tolerate several hours of ischemia.

There has been an important practical breakthrough in the last two or three years in asmuch as cadaveric livers have been infused with special solutions which mimic plasma (13) or alternatively which have an electrolyte composition similar to that in cells (14). The latter fluid which is known as Collins solution has permitted the cold preservation of canine livers safely in our laboratories for 12 to 18 hours. As a clinical extension, it has been possible for us to harvest human livers in California, Minnesota and other distant places, to carry the liver to Denver on commercial airplanes, and to successfully transplant the organs in Colorado. Thus, the possibility of a national liver procurement network has emerged.

In the meanwhile, the recipient operation is usually done through a basic subcostal incision, very often with an extension into the right chest through the seventh intercostal space or with a superior midline extension including excision of the zyphoid process (Figure 4). There usually are formidable technical problems because of the extensive venous collaterals which can render hemostasis almost impossible. The problem is compounded by the fact that clotting factors are never normal. In our early experience, most adult patients with cirrhosis lost 30 to 50 units of blood and the operations were almost always eight to twelve hours or longer. Some technical modifications have improved the situation. Of these, the most important is removal of the liver by transecting the infrahepatic vena cava and the portal triad structures entering it, by removing it from below while pulling on the hilar structures and vena cava, and by ligating all of the tissues that are cut behind. When the upper end of the liver is reached, a clamp can be placed across the suprahepatic vena cava, and a cuff of the vena cava developed for suture by dissecting off the cirrhotic liver (Figure 5).

In concept, liver transplantation is a simple operation which consists of connecting the blood vessels, coming into and going out of the liver in as normal a way as possible and then reconstitution of biliary drainage (Figure 6). There are two vena caval anastomoses, one below and one above the liver. For the last two years, we have continuously infused the homografts through the portal vein during the time of the vena caval anastomoses, allowing air bubbles trapped in the homograft to come out as the suture lines were completed (Figure 7). Omission of this precaution in early cases resulted in air embolus, particularly in adult recipients (15). The air floated to the right heart and because of the extensive venous anastomoses from right to left in patients with liver disease, these emboli passed straight to the left heart and up to the brain causing grave neurologic damage.

For biliary reconstruction in most of our early cases, cholecystoduodenostomy (Figure 6 A) was used because it was the simplest and fastest way to complete a long and tiring operation. The patients had an extraordinary incidence of symptomatic or asymptomatic bacteremia (5). It seemed as if the liver itself was the focus of and the entry for bacteria that passed into the general circulation and then caused infections elsewhere. Ultimately, it became obvious that the contamination with gastrointestinal contents was causing cholangitis.

Consequently, we now believe that the ideal way of reconstructing the biliary tract is simple end-to-end common duct anastomosis (Figure 6 D). Of course in many patients (children with biliary atresia for example) this option is not available. Then, we perform cholecystojejunostomy (Figure 6 B) or choledochojejunostomy (Figure 6 C) anastomosing gall bladder or the common duct to a Roux limb of jejunum. For nonsurgeons it is worth pointing out that the Roux principle defunctionalizes a loop of the intestine, theoretically allowing the gastrointestinal stream to pass distally to the liver without seriously contaminating it.

Calne and his associates (11) at Cambridge have described an alternative and somewhat more complicated technique in which the common duct is anastomosed to the gallbladder, and the resulting cloaca connected to the distal common duct. We have not had experience with this method.

Postoperative complications and causes of failure

Because of the high mortality after liver transplantation, this procedure has not had wide clinical application. In an effort to improve the situation, I reviewed the first 93 consecutive Colorado cases during a sabbatical leave in London in the summer of 1975. The survey was done in collaboration with Professor *K. A. Porter* who is a world authority on transplantation pathology. We tried in each case to determine the reasons for success or failure. The details of this work have been published (12). The central findings of that study changed our attitudes about management for all subsequent cases, and led to a number of improvements.

One expected cause of failure was uncontrolled acute rejection. However, it was surprising how relatively infrequently (about 10 %) this was the primary reason for death. Similarly, chronic rejection, with its typical occlusive vascular lesions and parenchymal fibrosis only accounted for a few failures.

What were the main reasons for the exorbitant mortality up to that time? The majority of deaths were found to result from technical or mechanical problems. These included thrombosis of the hepatic artery or portal vein, the use of graft damaged by ischemia, the development of cerebral air embolus as discussed earlier, and hemorrhage to mention just four examples.

However, by far the greatest single cause of technically based mortality was failure of the biliary tract reconstruction. In the 93 consecutive cases analyzed in London, almost 35 % of the patients had either obstruction of or fistula formation from their biliary tracts (16). Many of these patients were not treated with re-operation, and the complication was discovered at autopsy. One excuse was that the reconstructions usually had been with cholecysto- or choledochoenterostomy. It was not possibly to make the diagnosis by means which are now standard such as percutaneous transhepatic cholangiaography, using the so-called skinny (Chiba) needle. It was obvious that patients who became jaundiced in the postoperative period were not necessarily having rejection, but that there was a good possibility of obstruction.

Using cholangiography frequently, the kinds of obstructive lesions seen in Figure 8 were discovered with increasing frequency and ducts were reconstructed secondarily. Re-operation and secondary repair of these dilated duct systems was shown to be safe (16).

Clinical results

I will conclude with some statistics and follow-ups which were brought up to date as of a few days ago. The material can be split into two phases.

To June, 1976

The first phase was prior to the clinical-pathologic correlations which I mentioned that were started in the summer of 1975 and were completed in early 1976. There were 111 consecutive patients who were treated between 1963 and June, 1976. Only 31 (28 %) lived for as long as one year (Table 1). Of the 31 patients that lived for a year, 15 are still surviving after 2 1/3 to 8 1/2 years.

Amongst the 111 orginal patients, there were 50 adults (Table 2) including 13 with malignancies. Several of these 13 died of recurrent malignancy as described earlier before or after one year. Chronic aggressive hepatitis and alcoholic cirrhosis were the

other common diseases treated. With all of the major diagnostic categories, extended survival was uncommon. There were only ten (20 %) of the 50 adult patients who lived for as long as a year, and five are still surviving with follow-ups as short as 28 months and as long as about four years. The woman with the Budd-Chiari syndrome (Table 2) has had a baby. The patients who died late had survival of 13 1/2 to 25 months (Table 2). In the first 111 patients there were 61 who were 18 years or younger. In this pediatric subdivision there were 42 examples of biliary atresia with a one year survival of only 12 (29 %) (Table 3). In the assortment of other diagnoses were included the inborn errors of metabolism, hepatomas, and chronic aggressive hepatitis. Twenty-one (34 %) of the total pediatric series of 61 lived for a year. Ten are still alive with follow-up of 3 1/2 to 8 1/3 years (Table 4). The 12 late deaths were after one to six years. The most remote death was a particularly tragic one caused by a biliary duct complication six years following liver replacement for Wilson's disease. Thus, the overall survival in the pediatric series was better than with the adults but still poor.

After June, 1976

Improvements in technical and diagnostic care were instituted after the case reviews which took place in 1975 and early 1976. These included the use of microvascular techniques for vascular anastomoses, cholangiography, and liberal use of liver biopsies after operation. Since then and with a cut off of December, 1977, we accumulated 30 more cases (Table 5). The survival in the latest group is now 50 %. Fourteen of the 15 survivors are more than six months and nine are more than a year. All of these patients are out of the hospital and from past experience, it seems clear to us that the one year mortality overall with liver transplantation is now in the order of 50 %*,

A breakdown of the recipients in the adult and pediatric subgroups is given in Table 6. The survival in both categories is about double that in the original series. Perhaps a new era in liver transplantation is at hand.

* In the month since the lecture, no further deaths have occurred.

Summary

The development of liver transplantation has been difficult. However, substantial advances have been made mostly because of better surgical techniques and because of better postoperative management. It has been necessary for surgeons to be more inquisitive about the reasons for post-transplantation liver dysfunction rather than to ascribe hepatic perturbations to rejection. With these nonspecific improvements, there has been movement of liver transplantation into the area of actual service. Before the next great step will be made, there must be an improvement in immunosuppression. The nature of such improvement is not yet clear.

Lebertransplantation

Zusammenfassung

Die Entwicklung der Lebertransplantation war schwierig, dennoch wurden wesentliche Fortschritte durch bessere chirurgische Technik und besseres postoperatives Management erzielt. Es war für Chirurgen notwendig gewesen, intensiver nach den Ursachen der Leberdysfunktion nach der Lebertransplantation zu forschen, als die Leberstörungen einer Abstoßungsreaktion zuzuschreiben. Mit unspezifischen Verbesserungen bewegt sich die Transplantation auf das Gebiet einer wirksamen Dienstleistung. Bevor der nächste Schritt getan wird, muß eine Verbesserung der Immunsuppression erfolgen. Die Art und Weise dieser Verbesserung ist nicht klar.

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Table 1: Total number of patients
March, 1963, through July, 1976
(Follow-up to May 1, 1978)

Total	111
Lived > 1 year	31 (28 %)
Alive now	15 (after 2 1/3–8 1/3 years)

Table 2: 50 adult patients
March, 1963, through July, 1976
(Follow-up to May 1, 1978)

Diagnosis	Number of examples	Survival 1 year	Alive now**
Malignant tumor*	13	2 (15 %)	1 (44 months)
Chronic aggressive hepatitis	17	5 (30 %)	1 (32 months)
Alcoholic cirrhosis	11	1 (9 %)	1 (49 months)
Primary biliary cirrhosis	4	0 (0 %)	0
Secondary biliary cirrhosis	1	0 (0 %)	0
Sclerosing cholangitis with ulcerative colitis	1	0 (0 %)	0
Massive hepatic necrosis due to hepatitis B virus	1	0 (0 %)	0
Budd-Chiari syndrome	1	1 (100 %)	1 (43 months)
Congenital biliary hypoplasia	1	1 (100 %)	1 (28 months)

* 7 hepatomas, 4 duct cell carcinomas, 1 cholangiocarcinoma, and 1 hemangioendothelial sarcoma. The patient who is still alive had a small obstructing duct cell carcinoma.

** The 5 deaths after 1 year occurred after 13 1/2, 15 1/2, 19, 20 1/2, and 25 months.

Table 3: 61 pediatric patients
March, 1963, through Juli, 1976
(Follow-up to May, 1, 1978)

Diagnosis	Number of examples	Survival 1 year
Congenital biliary atresia	42	12 (29 %)
Chronic aggressive hepatitis	10	3 (30 %)
Hepatoma	3	2 (67 %)
Wilson's disease	2	2 (100 %)
Congenital biliary cirrhosis	1	1 (100 %)
Alpha$_1$-antitriypsin-deficiency	1	1 (100 %)
Tyrosinemia	1	0 (0 %)
Giant cell hepatitis	1	0 (0 %)
Total	61	21 (34 %)

Table 4: 61 pediatric patients
March, 1963, through July, 1976
(Follow-up to May 1, 1978)

Diagnosis	Alive now	Follow-up Present survivors (months)
Congenital biliary atresia	6 / 42	43, 56, 63, 75, 82, 100
Chronic aggressive hepatitis	2 / 10	42, 51
Hepatoma	0 / 3	
Wilson's disease	1 / 2	86
Congenital biliary cirrhosis	1 / 1	72
Alpha$_1$-antitrypsin deficiency	0 / 1	
Total	10 / 61	

11 other patients died late after 12½, 13, 13½, 14, 17, 20, 26, 28, 30, 41 and 72 months.

Table 5: Liver transplantation
August, 1976, through December, 1977
(Follow-up to May 1, 1978)

Total cases	30
Alive	15*
Dead	15

* $\geq$ 6 months = 14
$\geq$ 1 year = 9

Table 6: Adult/pediatric division of 30 cases
August, 1976, through December, 1977
(Follow-up to May 1, 1978)

	Number of examples	Alive	Follow-up
Adults	18	8 (44 %)	6–20 months
Pediatric (18 years)	12	7 (58 %)	4–20 months

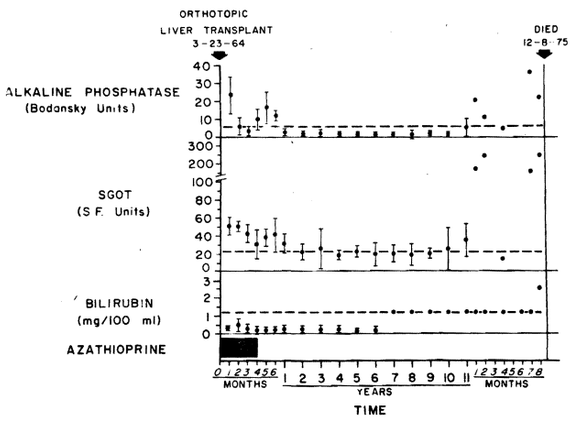

Fig. 1: Serum biochemistries during the 11 years and 8½ months of survival of a mongrel dog following orthotopic liver transplantation from a mongrel recipient on March 23, 1964. The values recorded during the last 8 months of life represent individual determinations. All other points on the graph are mean values for each time period; the brackets indicate 1 SD above and below the mean. Beginning with the 7th year of follow-up, bilirubin concentrations, if normal, were reported as < 1.2 mg%. The upper limit of normal in our laboratory for each test is marked by the horizontal broken line. (By permission of Transplantation *23* [1977] 168–171)

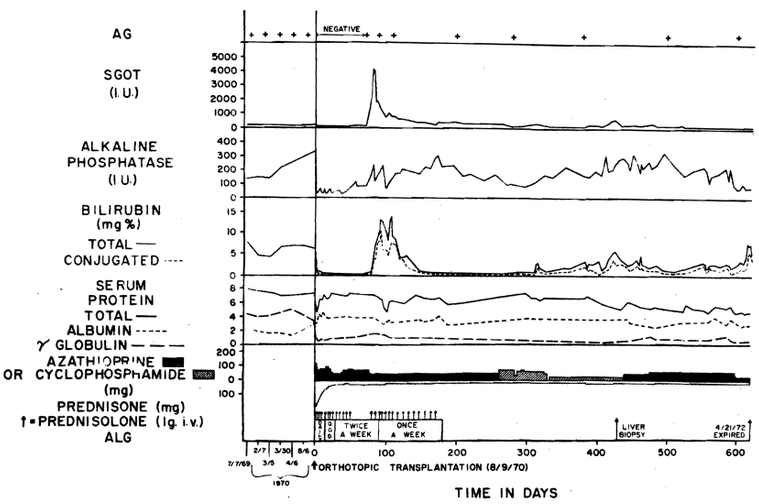

Fig. 2: Course of the patient before and after liver replacement. AG: agarose gel immunodiffusion test for HBsAg. (By permission of Arch. Surg., in press, 1978)

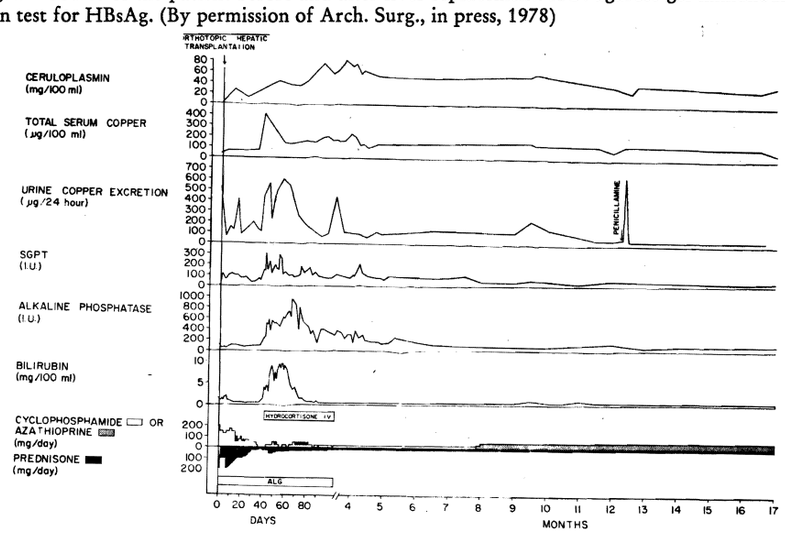

Fig. 3: The course of a patient with Wilson's disease who received an orthotopic liver homograft more than 7 years ago. Note that the cerulo-plasmin rose from undetectable to normal levels and that there was a heightened urinary copper excretion for almost a year. In this patient cyclophosphamide and azathioprine were used interchangeably. The deterioration in liver function starting just after a month was caused by serum hepatitis (HBsAg). (By permission of Transplantation Proc. *5* (1) [1973] 829–833)

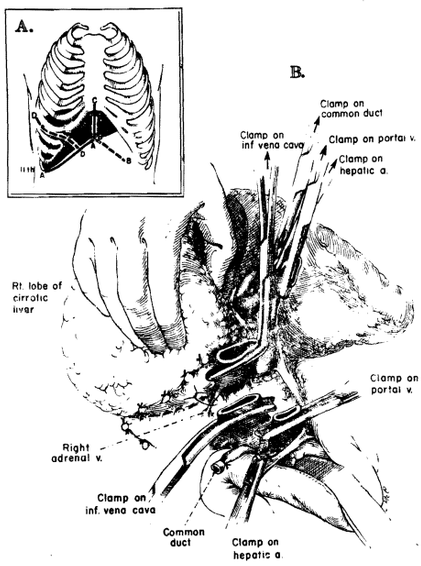

Fig. 4: Technique of retrograde removal of liver. A, Incisions. AA, Subcostal incision used for all orthotopic liver transplantations. BB, CC and DD, Frequently used extensions from the AA incision. B, Beginning retrograde removal after transection of inferior vena cava and hilar structures. All posterior tissue that is cut should be ligated, although the named vessels encountered, such as the right adrenal vein, are few in number. (By permission of Surg. Gynecol. Obstet. *142* [1976] 487–505)

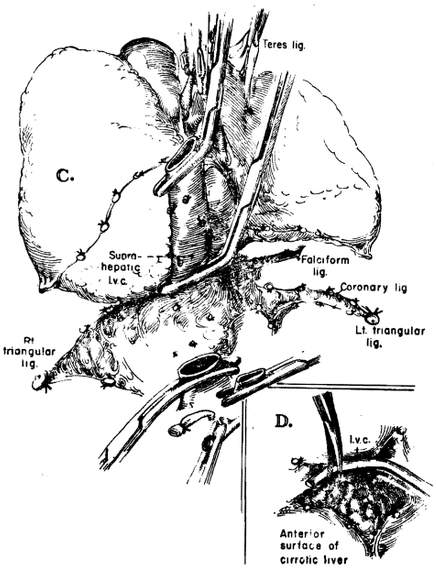

Fig. 5: A, Operative field after retrograde liver mobilization. The last remaining structure, the suprahepatic inferior vena cava, has been clamped above the liver. B, Technique for mobilizing a suitable length of suprahepatic vena cava after placement of clamp. In adults, this usually involves cutting away cirrhotic liver tissue over the frequently distorted and foreshortened right and left hepatic veins. (By permission of Surg. Gynecol. Obstet. *142* [1976] 487–505)

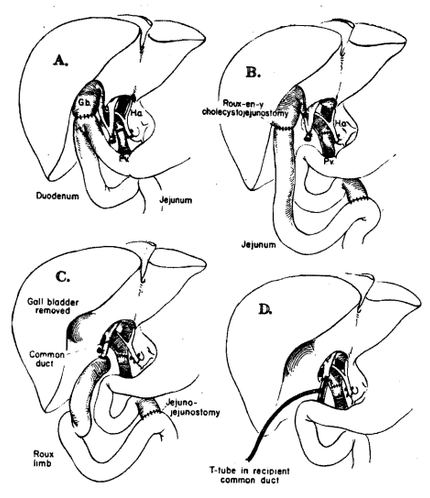

Fig. 6: Techniques of biliary duct reconstruction used for most of the transplantation recipients. A, Cholecystoduodenostomy. B, Cholecystojejunostomy. C, Choledochojejunostomy after removal of gallbladder. D, Choledochocholedochostomy. Note that the T-tube is placed, if possible, in recipient common duct. (By permission of Surg. Gynecol. Obstet. *142* [1976] 487–505)

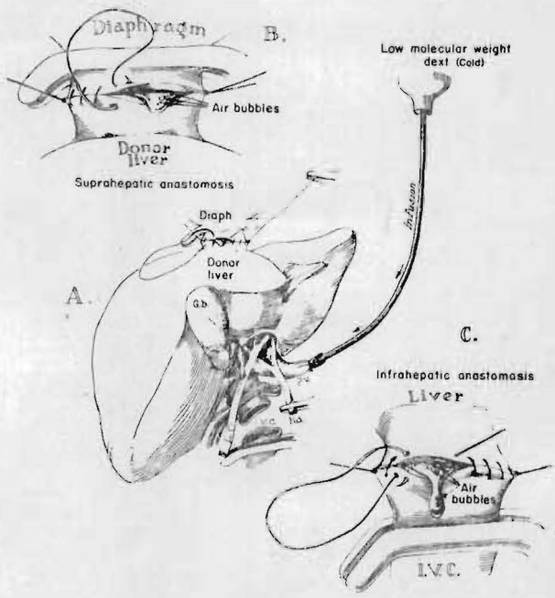

Fig. 7: Technique to prevent air embolism from orthotopic liver homografts. A, Continuous perfusion of solution through portal vein as vena caval anastomoses are constructed. B, C, Escape of air bubbles as the anastomoses are completed. (By permission of Ann. Surg. *187* [1978] 236–240)

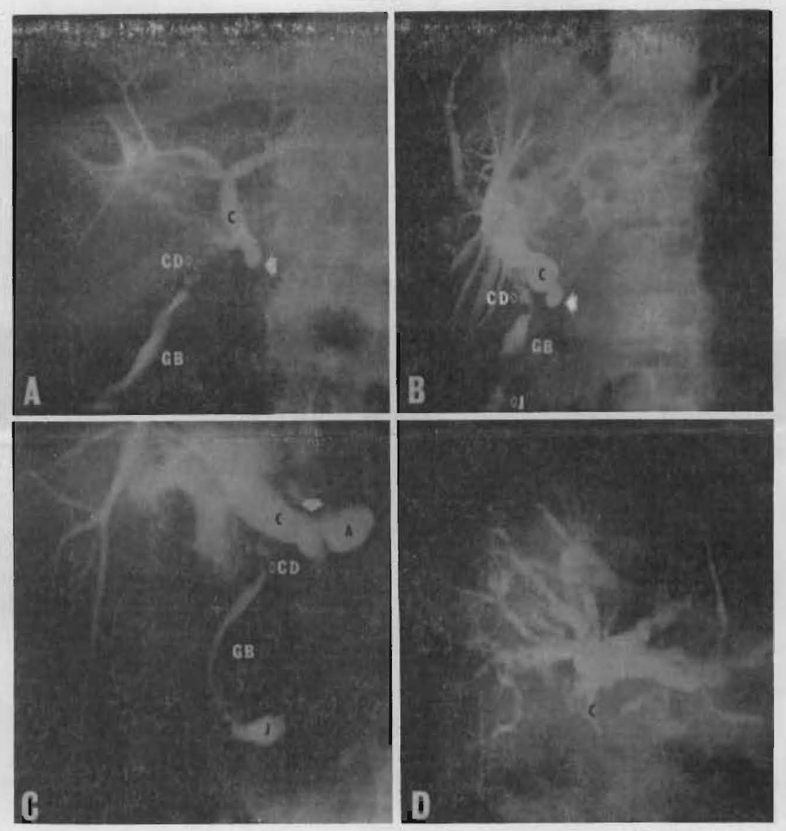

Fig. 8: Transhepatic cholangiograms in four patients whose original biliary reconstructions were with Roux-en-Y cholecystojejunostomy, as depicted in Fig. 6 B. A, minimal obstruction. B, Moderate obstruction. C, Severe obstruction with leak and abscess formation (A) near site or common duct ligation. D, Very severe obstruction. At reoperation the common duct was necrotic. (C) = cystic duct; (GB) = gallbladder; (J) = jejunum; large arrow = site of common duct ligation. (By permission of Surgery *81* [1977] 222–227)