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Surgical Approaches for Primary and Metastatic Liver Neoplasms, Including Total Hepatectomy with Orthotopic Liver Transplantation

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During the last 15 years, very important advances have been made in two areas of hepatic surgery. First, techniques have been perfected that permit the relatively safe removal of as much as 85 to 90 percent of the liver.[1] Second, it has become feasible to carry out total removal of a diseased liver and to replace it with a hepatic homograft.[2] This chapter will consider the limitations and possible benefits of these approaches in the field of oncology.

DIAGNOSTIC PITFALLS

In the absence of contraindications such as proven metastases, abdominal exploration should usually be carried out without delay to obtain a tissue diagnosis and with a view to curative resection, if feasible. From the biopsy tissue, the accurate and rapid histopathologic classification of liver masses is essential. A potentially serious error is failure to recognize for what it is a lesion known as focal nodular hyperplasia. These masses, which are not true neoplasms, do not ordinarily require major resection and should usually be left alone except for biopsy. There are exceptions to this generalization, since rupture and massive bleeding have been reported,[3] particularly with large areas of involvement that may, in addition, cause pressure symptoms. We have performed extended right hepatic lobectomy (trisegmentectomy) for a patient with such extensive disease. Histopathologically, the nodules, which have a cobblestone appearance, are composed of uniformly normal-appearing liver cells in cords or sheets, usually without orientation to central veins or portal triads which are sparse. There may be areas of fibrosis, infarction, or hemorrhage.

Among solid hepatic neoplasms, one tumor has a special place by virtue of its occasional huge size, slow natural history, and failure to metastasize. These characteristics, which were particularly well recognized by Edmondson,[4] have caused this tumor to be called benign hepatoma, minimum deviation hepatoma, or hepatic adenoma. Another designation has been "pill tumor" because of the frequent association of these neoplasms in young women with the use of oral contraceptive drugs. Alpha-fetoprotein determinations are negative (see chapter by Drs. Christopherson and Mays.

The tendency of hepatic adenomas to rupture has made their presence similar to that of a time bomb. Two women with hepatic adenomas treated early in our experience presented with massive bleeding. After emergency hepatic lobectomy, the women carried the diagnosis of hepatoma and were treated with 5-fluorouracil for more than 2 years before the pathologic specimens were reviewed and reclassified. Of the 7 women with hepatic adenomas treated by us, all are well with follow-ups of from 1 to almost 8 years after hepatic resection.

Hepatic cell carcinoma (hepatoma) accounts for 80 to 90 percent of the malignant primary hepatic neoplasms. Cholangiocar-

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cinoma is next in frequency. Both tumors may be multifocal. The list of unusual or rare malignancies is a long one, including hemangioendothelial sarcoma, squamous cell carcinoma in an intrahepatic cyst, and carcinoma of the larger intrahepatic ducts. Patients with the last type of neoplasm may be candidates for liver transplantation (see below).

PARTIAL HEPATECTOMY

The Limits of Safe Removal

The human liver consists of four segments. The segmental combinations that lend themselves to excision (Fig. 1) include the right and left true lobes (each consisting of two segments), the true right lobe plus the medial segment of the left lobe (trisegmentectomy or extended right lobectomy), and the lateral segment of the left lobe. In planning the appropriate operation, the dissection may be facilitated by information from preoperative arteriography (Fig. 2). Consequently, this study is performed in many candidates for partial hepatectomy.

The historically high risk of hepatic resection has been reduced drastically. Since 1963, more than 35 patients have been operated upon by the senior author (T.E.S.) at the University of Colorado (Table 1), and no patient has died after partial hepatectomy. The numbers of hepatic resections have increased steadily, so that the majority of these partial hepatectomies have been since 1970. Twenty of the 37 patients have had trisegmentectomy, and the rest had removal of conventional lobes or of the lateral segment (Table 1).

Operative Evaluation

At exploration, if the lesion in question is thought to be other than focal nodular hyperplasia and if it is resectable and localized to the liver, enough liver is removed by one of the formal resections shown in Fig. 1 to excise the mass with as full a margin as possible. We believe that the piecemeal re-

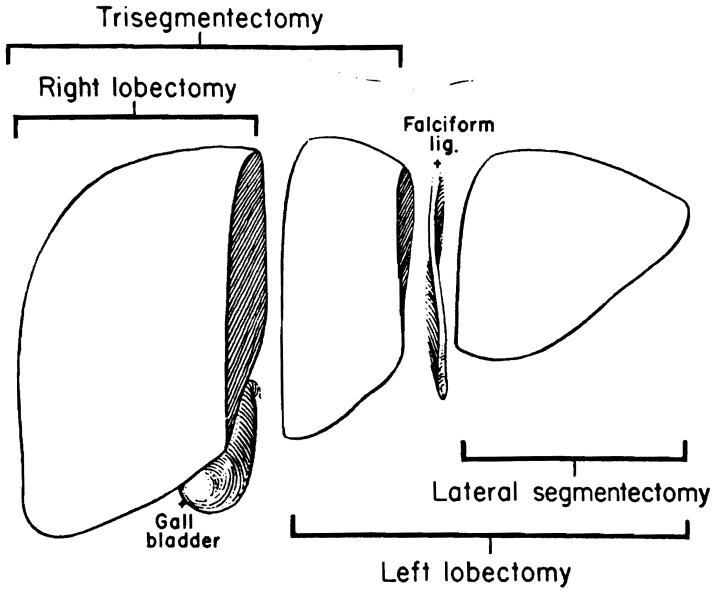

Fig. 1. The common hepatic resections, of which there are only four. The most radical procedure, trisegmentectomy, involves removal of the true right lobe plus the medial segment of the left lobe. The least radical procedure, lateral segmentectomy, was incorrectly termed left lobectomy in the older literature.

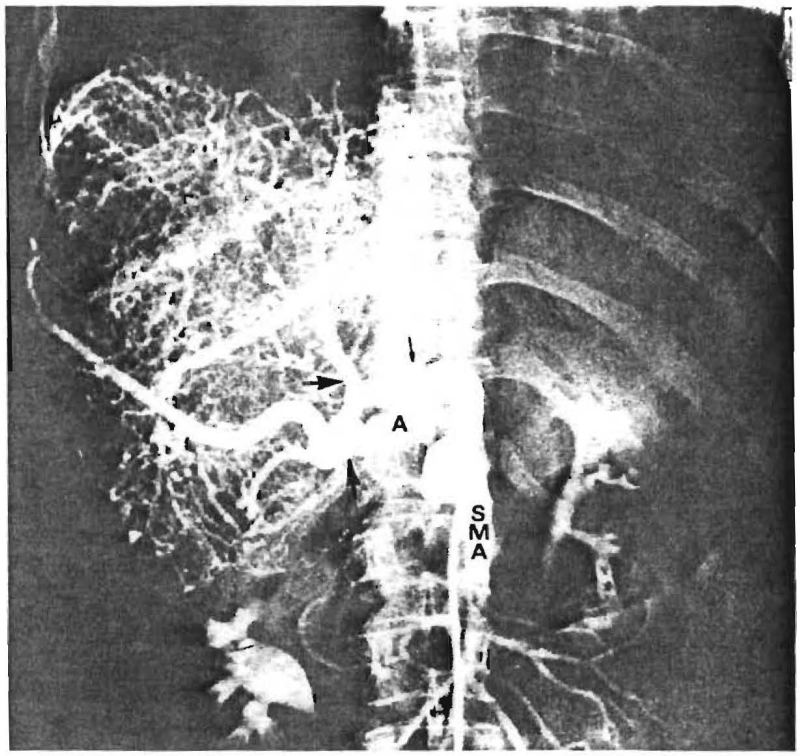

Fig. 2. Arteriogram performed prior to trisegmentectomy for hepatic adenoma in a 16-year-old girl. The entire liver was supplied by an anomalous artery (A) arising from the superior mesenteric artery (SMA). Branches to the right lobe and to the medial segment of the left lobe were ligated (*large arrows*), preserving the main trunk and its tiny branch to the left lateral segment (*small arrow*).

moval of hepatic masses, even those thought to be benign, is rarely justifiable from a technical point of view if the amount of excised tissue is to be more than 100 or 200 gm.

The assessment of operability varies from case to case. Two criteria must be fulfilled. First, the operator must be sure that the liver fraction left behind has an intact blood supply and adequate biliary drainage. Second, it must be determined that tumor spread has not already made the operation futile.

The Special Question of Liver Metastases

The expectations after resection for hepatic metastases are unclear. With the exception of carcinoid tumors, there is surprisingly little actual experience with partial hepatectomy for metastatic disease. Flanagan and Foster[5] in 1967 surveyed the world literature and found 32 reports involving 72 patients who had survived liver resection. The primary malignancy was colonic in 45 instances. The overall 5-year survival rate for the 72 patients was 24 percent.

Later, Foster, and Berman,[6] in a liver tumor survey of 98 U.S. hospitals, made a critical review of surgical resections for metastatic cancer to the liver. They found that 176 patients had undergone surgical resection for embolic metastases to the liver of which 126 patients (72%) had primaries in the colon or rectum. Eight of 126 patients with liver resection for metastatic colon and rectal cancer died immediately after the operation. Follow-up data were not available in

TABLE 1
Hepatic Resections (1963–July 1977)*

	Number	Late Deaths†
Trisegmentectomy	20	6
Right lobectomy	8	0
Left lobectomy	5	3
Lateral segmentectomy	4	1
Total	37	10

* Thirteen of these resections were for benign disease (7 hepatic adenomas, 2 focal nodular hyperplasia, 2 traumatic injuries, 1 hemangioma, and 1 single simple cyst). The other 24 patients had primary or metastatic liver disease.

† All 10 patients had recurrent tumor, which in 9 cases was directly responsible for death after 4½ months to 5 years. One patient with recurrence died of hepatic insufficiency 2 months after trisegmentectomy.

5 of the remaining 118 patients, and 25 patients were followed for less than 5 years. Of the 88 patients available for the 5-year evaluation, 16 patients (18 percent) were alive 60 months after liver resection. Six of these patients developed recurrences, and 4 of the 6 had died. Thus, 10 of the 88 determinate cases seem "cured."

Since the lure of describing successes exceeds the temptation to report failures, the reported series may be an overstatement of the therapeutic expectations. Yet the report by Wilson and Adson[7] from the Mayo Clinic of 60 hepatic resections for metastatic colon disease was also optimistic. When resection was performed for multiple metastases, there were no 5-year survivors. But when the metastases were single, 42 percent of 36 patients lived for 5 years or more and 8 were alive without recurrence 10 years or more after hepatectomy.

In the last 13 years, we have performed hepatectomy for metastatic cancer upon only 9 patients (Table 2); 3 had primary colon or rectal carcinoma, and 1 each had carcinoid, Wilm's tumor, carcinoma of gallbladder, neuroblastoma, glucagonoma, and

TABLE 2
Liver Resections for Metastatic Tumor at University of Colorado*

Patient Number	Age	Date of Operation; Type of Hepatectomy	Primary Tumor	Follow-up (to September 19, 1977)	Survival (Months)
1	2	12/8/74 Trisegmentectomy	Neuroblastoma, right adrenal	No evidence of tumor	33
2	71	7/12/76 Left lateral segmentectomy	CA colon	No evidence of tumor	33
3	43	2/12/75 Trisegmentectomy	CA colon	Died 8/12/76; metastases to brain and lung	18
4	41	4/29/75 Trisegmentectomy	CA gallbladder	Died 10/8/76; widespread metastases	14
5	12	5/30/75 Left lobectomy	Wilm's tumor of kidney	Died 3/17/76; Wilm's tumor, left flank	9½
6	48	10/27/75 Trisegmentectomy	CA rectum	Positive CEA but no demonstrable tumor	23†
7	50	4/29/76 Trisegmentectomy	Glucagonoma of ? pancreas	Died 5/15/77; widespread metastases	13
8	50	7/12/76 Left lateral segmentectomy	Metastatic carcinoid of ileum	Small tumor nodules in remnant, not obviously changed	14
9	34	7/18/77 Right lobectomy	Melanoma of eye	Small residual tumor nodules left in remnant	2

* Except in case 1, the primary tumors were resected from 1 month to 14 years earlier. The 14-year interval was in patient 9.

† Right lower lobectomy for metastatic tumor of lung on 6/1/76.

melanoma. The results with these cases have been encouraging, although the follow-ups are still relatively short. Five of the 9 patients are still alive, and 2 are free of tumor as far as can be determined.

The paucity of our experience and that elsewhere undoubtedly reflects the tendency of liver metastases to be widespread once they occur. However, a further factor could be a bias against using secondary partial hepatectomy because of its reputed high mortality. The reduction in operative risk in recent times should encourage an aggressive approach.

Postoperative Therapy

The tacit assumption is usually made that neither irradiation nor chemotherapy is safe or effective following subtotal hepatectomy, but such negative attitudes may eventually prove to be completely unjustifiable. Several of our recent patients with hepatomas have been treated with the triple drug regimen of cyclophosphamide, 5-fluorouracil, and vincristine sulfate with or without adriamycin. Therapy was not started for several weeks after operation until regeneration had a chance to begin and good wound healing was evident. A number of these patients who had massive tumors, including some with blood vessel invasion, are clinically free of tumor after several years.

TOTAL HEPATECTOMY AND TRANSPLANTATION

The appeal of liver replacement for the treatment of hepatic cancers is that the boundaries of permissible resection could be considerably expanded. Some liver tumors that cannot be completely excised by standard techniques of subtotal hepatectomy would become removable if the whole organ could be extirpated.

A Potentially Self-Defeating Aspect

Of course, the extension by this means of surgical procedure would not ensure against metastases. Indeed, there is the possibility that the growth of residual tumor could actually be accelerated as a consequence of the immunosuppressive therapy that is necessary for prevention of homograft rejection. This would be expected if the concept is valid that the immunologic system provides a surveillance function by which mutant neoplastic cells are identified and either eliminated or restricted in their growth potential. The individuality of such cells, which allows their recognition as foreign, has been thought to be due to tumor-specific antigens.

It has been thoroughly documented[2,8] that immunosuppression leads to a striking incidence of new tumors and that it permits the transplantation of malignant tumors in humans which may become autonomous and, therefore, deadly even if immunosuppression is stopped. It has not been proven that metastases are enhanced by immunosuppressive therapy, but this strong possibility has been raised from observations with patients treated with hepatic replacement for primary malignancies of the liver.[2,8]

Liver replacement with a homograft was first attempted in a human on March 1, 1963.[9] Between then and November 28 1974, 92 more patients were similarly treated at our center. As was reviewed in December 1975 and published the following April,[10] 27 of the 93 recipients achieved survival of at least 1 year after transplantation, with a maximum then of 6 years. Many of these patients had been able to return to a full and useful life. Sixteen were still alive in December 1975, with follow-ups of 13 to 71 months.

The following discussion will update the results in that original series, with further follow-ups of another 22 months. At the same time, attention will be focused upon the causes for the heavy mortality that had retarded the acceptance of liver transplantation and upon means by which the record has been improved subsequently.

Case Material

Pediatric patients

Fifty-six of the first 93 recipients were 18 years or younger at the time of the operation (Table 3). Forty of these 56 pediatric recipients had biliary atresia. In the 36 youngest of the 40 patients with atresia, the mean age at the time of operation was 31.3 ± 15.7 (S.D.) months, range 3 to 67. The 4 oldest children in the atresia group were 7, 11, 11, and 15 years. Because of their long survival, they were thought on clinical grounds to have intrahepatic biliary atresia, and this diagnosis was compatible with the histopathologic findings of micronodular biliary cirrhosis in their native livers. Two of these latter four livers contained incidental liver cell carcinomas. Only one such malignancy was found in the diseased livers of the other 36 patients with extrahepatic biliary atresia whose transplantations were carried out at a younger age.

The 16 pediatric recipients with diagnoses other than biliary atresia (Table 3) had a mean age of 12.9 ± 4.6 (S.D.) years, range 1 to 18. Nine had some variant of chronic aggressive hepatitis without HB_sAg antigenemia. Three had hepatomas that could not be removed with conventional partial hepatectomy. Two had Wilson's disease. There was one example each of congenital biliary cirrhosis and cirrhosis associated with $alpha_1$-antitrypsin deficiency.

Adult patients

The 37 adult patients treated during the same time averaged 39.0 ± 11.1 (S.D.) years, range 21 to 68. Their most frequent diagnoses were primary hepatic malignancy, chronic aggressive hepatitis, and alcoholic cirrhosis (Table 4). All the patients with nonneoplastic disease were profoundly ill before they were considered for transplantation. Five had the diagnosis of the hepatorenal syndrome, several were unconscious, and almost all were wasted from their chronic disease.

Management

The operative and postoperative care of patients with liver transplantation has been described before,[2,10] but some details deserve emphasis. Since 1968, when the concept of brain death became widely accepted in the United States, cadavers usually have not been considered for liver donation unless there is still effective circulation and unless aortography can be performed to delineate the hepatic arterial supply in advance. Complicated preservation devices

TABLE 3
Pediatric Patients

Diagnosis	Number of Examples	Survival >1 Year	Alive* Now	Follow-up Present Survivors (Months)
Congenital biliary atresia	40	11 (27.5)	7	35, 48, 56, 66, 68, 75, 93
Chronic aggressive hepatitis	9	3 (33)	2	35, 44
Hepatoma, liver cell carcinoma	3	2 (67)	0	
Wilson's disease	2	2 (100)	1	79
Congenital biliary cirrhosis†	1	1 (100)	0	
$Alpha_1$-antitrypsin deficiency	1	1 (100)	0	
Total	56	20	10	

Figures in parentheses indicate percentages.
None of the 56 pediatric patients were HB_sAG positive preoperatively.
* The 10 late deaths were after 12½, 13, 13½, 14, 20, 26, 28, 30, 41, and 72 months.
† Associated with congenital deafness.

TABLE 4
Adult Patients

Diagnosis	Number of Examples	Survival >1 Year	Alive† Now	Follow-up Present Survivors (Months)
Malignant tumor*	12	2 (17)	1	36
Chronic aggressive hepatitis	9	3 (33)	0	
Alcoholic cirrhosis	9	1 (11)	1	42
Primary biliary cirrhosis	3	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	35
Total	37	7 (19)	3	

Figures in parenthesis represent percentages.

The patient with massive hepatic necrosis and 2 of the patients with chronic aggressive hepatitis had HB_sAG positive tests preoperatively.

* Included 7 liver cell carcinomas (3 with cirrhosis), 3 duct cell carcinomas at the confluence of the right and left hepatic ducts which caused complete bile obstruction, 1 cholangiocarcinoma, and 1 hemangioendothelial sarcoma. The patient who is still alive had a small obstructing duct cell carcinoma.

† The 4 deaths after 1 year occurred after 13½, 19, 20½, and 25 months.

are no longer used. Infant and child livers are usually perfused with 1 to 3 liters of a chilled electrolyte solution through the portal vein just before and after organ removal. Longer preservation, for up to 18 hours, is feasible with infusion of intracellular electrolyte solutions.[11]

The quality of HL-A matching has not seemed to influence the outcome, and for this reason the HL-A match has not been used as a criterion of donor selection for a number of years.

Preformed anti-red cell isoagglutinins that react against donor tissues and cytotoxins that can be detected by their lysis of donor lymphocytes immediately destroy many renal homografts that are transplanted in violation of such positive crossmatches. The liver is very resistant to this so-called hyperacute rejection. In our first 93 cases, three liver transplantations were carried out in spite of red blood group incompatibility, and three more were performed in confrontation of cytotoxic antibodies.[10] There were no unequivocal hyperacute rejections.

Host hepatectomy is usually still performed by individually dissecting the hilar structures and the vena cava above and below the liver and then by cross-clamping and dividing the vessels just as the liver is removed.[2] In some adults, however, a safer way[10] has been first to transect the hilar structures and subsequently the infrahepatic inferior vena cava when all else is in readiness (Fig. 3); then, by pulling on clamps, which are placed on the hepatic side of these structures, the liver is dissected free from below to above, ligating all cut tissues on the way (Fig. 3). The suprahepatic inferior vena cava remains intact as the stalk of the specimen until it is clamped just before the liver is removed. This variation in operation has been particularly useful in developing a reasonably long suprahepatic cuff of the inferior vena cava in adults. The vena cava or main hepatic veins may be dissected free from within the cirrhotic liver in a bloodless field (Fig. 4B).

In several of our first recipients who did not have biliary atresia, bile duct reconstruction was with choledochocholedochostomy over a T-tube stent (Fig. 4D). The method lost favor because of a high inci-

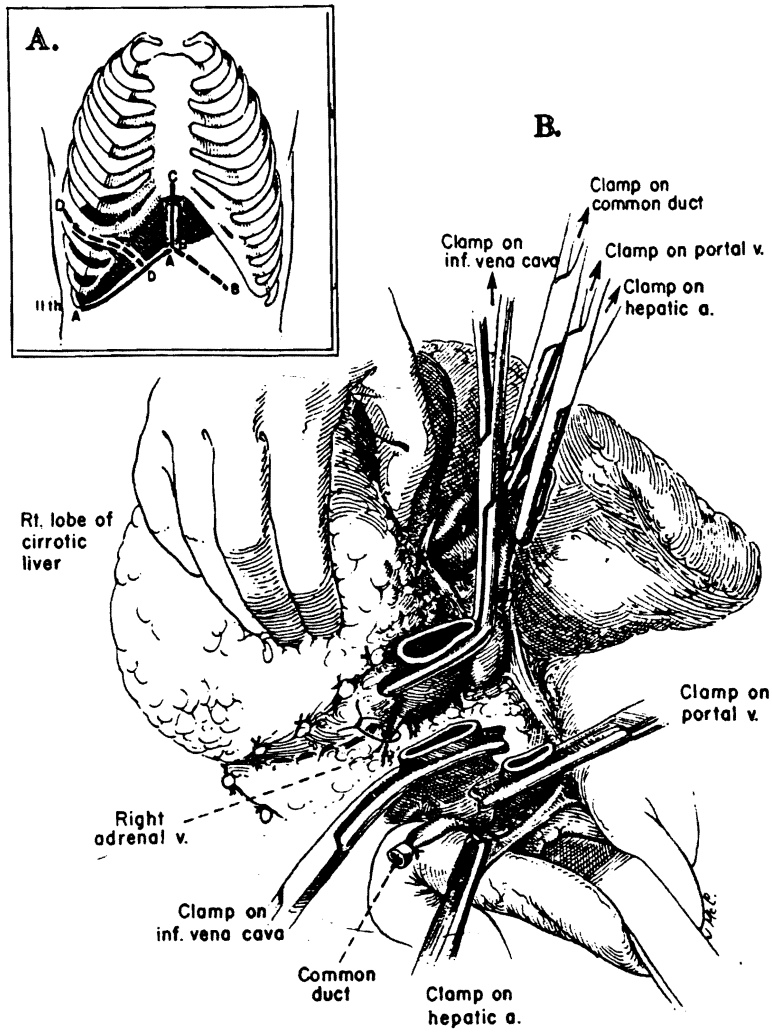

Fig. 3. Technique of rectrograde removal of liver. (A) Incisions. (AA) Subcostal incision used for all orthotopic liver transplantations. (BB, CC, DD) Frequently used extensions from the AA incision. (B) Beginning retrograde removal after transection of inferior vena cava and hilar structures. All posterior 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 *Surgery Gynecology and Obstetrics* 142:487–505, 1976.)

dence of bile fistula, and cholecystoduodenostomy after ligation of the common duct (Fig. 4A) became our first choice for a number of years. Recently, the preferred techniques have been choledochocholedochostomy (Fig. 4D) or, alternatively, cholecystojejunostomy with a Roux-en-Y loop (Fig. 4B), thus removing the homograft from the mainstream of the gastrointestinal tract and draining it through a defunctionalized jejunal limb. Alternatively, Roux-en-Y choledochojejunostomy (Fig. 4C) has been used for recently treated patients. In a number of cases it has been necessary to convert from cholecystojejunostomy to choledochojejunostomy (Figs. 4B and 4C) because of obstruction at the cystic duct.[12]

The first 5 patients were treated with

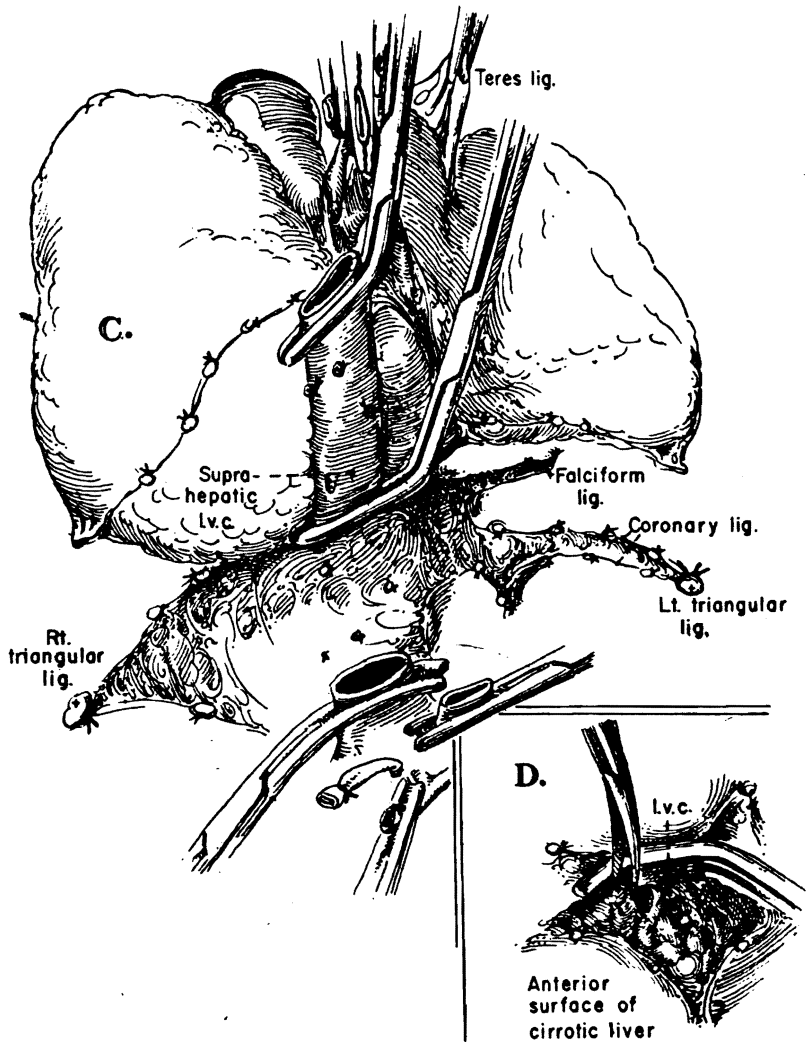

Fig. 3(C,D). (C) Operative field after retrograde liver mobilization. The last remaining structure, the suprahepatic inferior vena cava, has been clamped above the liver. (D) Technique for mobilizing a suitable length of suprahepatic vena cava after placement of clamp. In adults, this usually involves cutting away cirrhotic liver tissue over the frequently distorted and foreshortened right and left hepatic veins. (By permission of *Surgery, Gynecology and Obstetrics* 142:487–505, 1976.)

azathioprine and prednisone. The next 88 recipients were given triple drug immunosuppression, which usually consisted of azathioprine and prednisone to which a 2-week to 4-month course of horse antilymphocyte or antithymocyte globulin was added. If hepatotoxicity of azathioprine was suspected, cyclophosphamide was substituted, since it has an immunosuppressive effect comparable to that of azathioprine.

Results in Pediatric Patients

Other than biliary atresia

Nine (56 percent) of the 16 patients lived for at least 1 year after transplantation. The 7 others who received a total of eight grafts died after 1 to 188 days but from only one example each of acute rejection and late chronic rejection. The nonimmunologic factors of biliary obstruction, tumor recur-

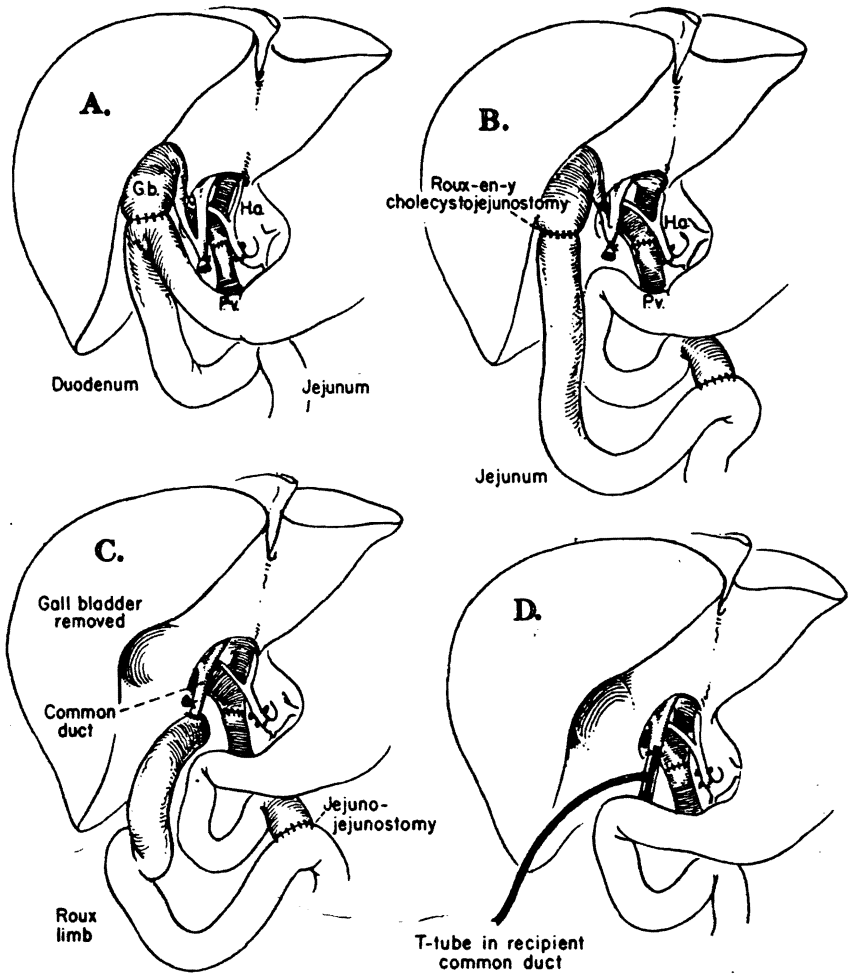

Fig. 4. Techniques of biliary duct reconstruction used for most of the transplantation recipients. (A) Cholecystoduodenostomy. (B) Cholecystojejunostomy. (C) Choledochojejunostomy after removal of gallbladder. (D) Choledochocholedochostomy. Note that the T-tube is placed, if possible, in recipient common duct. (By permission of *Surgery, Gynecology and Obstetrics* 142:487–505, 1976.)

rence, perforation of a colon diverticulum, and ischemic liver necrosis were responsible for all the other fatalities within the first year. The tumor recurrence led to death 143 days postoperatively.

Shortly after 1 year, 2 more patients died with recurrences from the hepatomas for which the transplantations had been performed. The three other late deaths (Table 2) were from chronic rejection or unrecognized biliary obstruction.

Four of the 16 recipients in this nonatresia pediatric subgroup are still alive after 3 to more than 6½ years (Table 3). They all have normal or nearly normal liver function, with serum bilirubin concentrations ranging from 0.5 to 1.5 mg/100 ml.

Biliary Atresia

The 40 recipients were given a total of 45 livers. This group (Table 3) will not be discussed in this paper dealing with oncology. It is presented in detail elsewhere.[10]

It should be recorded, however, that 6 of these recipients are still alive after 35 to 93 months (Table 3). The longest survivor is a child whose liver contained a 2-cm incidental hepatoma. After operation, previously positive alpha-fetoprotein determinations became negative.

Results in Adult Patients

Only 7 (19 percent) of the first 37 adult recipients lived for as long as 1 year postoperatively. The results were not satisfactory after transplantation for any of the main indications for liver transplantation (Table 4). Only 1 of 9 alcoholics survived for as long as a year. Three of 9 patients with chronic aggressive hepatitis lived for this long, as well as 2 of 12 patients with primary hepatic tumors. The 2 patients in the malignant category who lived for more than a year after liver replacement had been treated for the small intrahepatic duct cell carcinomas, described by Klatskin,[13] that obstruct the confluence of the right and left hepatic ducts and cause early jaundice. One of these recipients died of multiple recurrences in the new liver 25 months after transplantation. The second patient is well without evidence of recurrence after 3 years. Two adult patients with nonneoplastic disease are also still alive after 35 and 42 months (Table 4).

Causes for Failure

In reviewing these 93 consecutive (56 pediatric and 37 adult) cases, it became obvious that rejection of the liver as judged by classical histopathologic criteria played a suprisingly small role in the heavy overall mortality, accounting for less than 10 percent of the deaths. Technical or mechanical problems, especially those of biliary duct reconstruction, were a far greater cause of failure, as were systemic infections. For example, 6 of the 37 adult recipients had lethal cerebrovascular accidents during or just after operation that were probably due to air embolism introduced from the homograft.[14] When abnormalities of liver function developed in the postoperative period, the nearly automatic diagnosis of homograft rejection, in retrospect, proved to have been wrong in most instances.

It was concluded that further development of liver transplantation depended upon two kinds of progress. The first was reduction of operative and early postoperative accidents and complications by more discriminating patient selection, purely technical improvement, and better standardization of biliary duct reconstruction. The second area was in sharpening the criteria for the differential diagnosis of postoperative hepatic malfunction, including the liberal use of transhepatic cholangiography and needle biopsy. Better decisions could then be made about changes in medication or about the need for secondary corrective surgical procedures.

Institution of these reforms has markedly changed the outlook after liver replacement. For example, 29 liver transplantations were carried out from August 1976 to September 1977. Twenty-one of these 29 recipients are still alive. With such improvement, the question of liver transplantation for malignant disease inevitably will be raised again.

Transplantation and Cancer

In a positive sense, the most important conclusion that emerged from this early experience of 93 liver replacements was that prolonged survival repeatedly was possible. A total of 27 patients lived for at least a year following operation. Sixteen of this group were still alive in December 1975, after more than 1 to almost 6 years, and after an additional 22 months, 14 survivors remain. The outlook slowly improved as the 93 cases were compiled, although not to a satisfactory state. The first 25 recipients included only 5 one-year survivors. The next group of 25 contained 6, and the group after that had 8. There were 8 one-year survivors among the 18 patients beginning with number 76. The chronic survivors, particularly those in

recent times, have had remarkably stable liver function, and they have usually achieved complete social rehabilitation.

The treatment of hepatic malignancies with liver replacement remains a controversial issue. One of our patients is cured of a hepatoma after almost 8 years, but that neoplasm was small and was an incidental finding in a liver that had biliary atresia. Among the first 93 recipients, 5 other patients with hepatomas who lived long enough for us to make observations developed recurrences, as did a sixth patient whose native liver and later whose liver graft were destroyed by a hemangioendothelial sarcoma. Two of 3 patients with intrahepatic duct cell carcinomas lived for more than 2 years, but unfortunately, 1 of these patients had massive and lethal recurrences that were predominantly in the homograft. The other is still alive without recurrence often more than 3 years.

Although details have varied, the overall message from Williams and his associates[15] has been the same, although somewhat more optimistically expressed. In their series of transplantations for four hepatomas, five duct cell carcinomas, two metastatic malignancies, and one cholangiocarcinoma, 8 of the 12 patients were afflicted with recurrent neoplasm. Four of their 5 patients with duct cell carcinoma developed obvious metastases, the exception being a recipient who died after 3 weeks. On the other hand, hepatoma recurred once in 4 cases, but only 1 of these recipients lived for as long as a year. That exceptional patient, who died of biliary obstruction after more than 5 years, was free of metastases at autopsy. Her original tumor was apparently slow growing, however, since she had been aware of an abdominal mass for more than 6 years preceding transplantation.

Recurrences after liver transplantation for primary hepatic malignancy have also been recorded by Hume[16] and Fortner[17] and their associates. It is axiomatic that the outcome in any given case will depend on the extent of the neoplasm at the time of transplantation. In this connection, a precautionary note about what constitutes genuine candidacy for liver replacement may be introduced on the basis of our unusually large experience with hepatic trisegmentectomy alluded to at the beginning of this chapter. A number of those patients (see Table 1) who, as it turned out, could be treated by conventional means had been referred to us for consideration of liver transplantation after an erroneous decision of nonresectability had been made at earlier operations.

In spite of the foregoing reservations, we have not absolutely precluded liver transplantation for malignant disease as the following recent case demonstrates. A 27-year-old woman from Iowa was first diagnosed in 1971 as having a sclerosing cholangiocarcinoma after tissue evaluation by Dr. Kamal G. Ishak of the Armed Forces Institute of Pathology, Washington. The slowly growing tumor eventually caused complete biliary obstruction and extensively invaded the central part of the diaphragm. Liver replacement was performed on September 19, 1976. In order to perform total hepatectomy, it was necessary to resect a large portion of both hemidiaphragms in continuity with the liver. Multiple, small pulmonary metastases were found.

The resected diaphragm was replaced with a plastic mesh (Marlex). After a very stormy postoperative course, the patient recovered completely and has normal liver function more than 1 year later. Postoperatively, she gained almost 80 pounds in weight. The hepatic specimen was subsequently reviewed by Dr. Hugh Edmondson of Los Angeles, who made the diagnosis of primary myxosarcoma of the liver. Drs. Paul Blaustein and R. H. Fennell of our own Pathology Department diagnosed the hepatic and pulmonary lesions as sclerosing angiosarcoma. The full story in this patient can obviously be told only with longer follow-up, but it is already clear that very significant palliation has been achieved.

SUMMARY

In recent years, partial hepatic resection for the treatment of liver tumors has become well standardized and safe, even with removal of 80 to 90 percent of the liver. At the University of Colorado Medical Center, 37 consecutive hepatic resections have been performed without an operative mortality in spite of the fact that 20 of the 37 extirpations were of 80 to 90 percent of the liver. The resections have been for primary as well as metastatic malignancies.

Total hepatectomy in association with transplantation increases the field of resectability, but the extent to which extensive hepatic tumors can be cured remains controversial. In our experience, and in that of other observers, the incidence of recurrence after liver replacement for tumors has ranged from 66 to more than 90 percent. Nevertheless, "cures" after liver replacement for cancer have been recorded.

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