PAPERS AND ORIGINALS

Orthotopic liver transplantation: the first 60 patients

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Summary

Between May 1968 and 31 December 1976 60 orthotopic liver allografts were transplanted by the Cambridge-King's College Hospital team. During this period there were changes in the selection of patients and their management. Initially some patients were operated on when they were too ill, often because of a prolonged wait for a donor. There was a high incidence of fatal complications of biliary drainage in patients who survived longer than the first week after operation. Improved results have been due to the development of a simple method of preserving the liver, thereby increasing the pool of potential donors, and by a new technique of biliary drainage, which allows well-vascularised anastomoses without tension, retains the sphincter of Oddi, and leaves access for radiological examination of the biliary tree.

Uncontrollable rejection of the liver has occurred in less than 10% of cases. This contrasts strongly with the incidence of rejection among kidney transplants. Six patients have lived for over a year, the longest surviving for more than five years, and 13 patients were still alive at the beginning of 1977.

Introduction

There have been many changes both in the management of patients and in the selection of cases for orthotopic liver graft since we began transplantation in May 1968. Initially, patients often underwent operation when they were too ill for the procedure, because of the prolonged period of waiting for a suitable donor liver. There was also a high incidence of fatal

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complications relating to the biliary tract.[1] During the past 18 months our results have steadily improved. This has been due mainly to the development of a better technique for biliary drainage. Greater confidence in the simple, short-term, hypothermic technique of liver preservation has also allowed more transplants to be carried out. Since 1973 19 livers have been preserved in this way and transported to Cambridge or King's College Hospital from hospitals 35 to 480 miles away. Ischaemia times have ranged from 2 hours and 42 minutes to 8 hours and 10 minutes, and in all cases the grafts have functioned well after transplantation.[2]

The last detailed analysis of our results was based on the 26 patients operated on up to 12 December 1971,[1] and in the five years since then a further 34 patients have been treated. We describe here our experience gained from these 60 patients and compare our results with those obtained by Starzl in patients with different conditions.

Overall results and long-term survivors

Malignant disease of the liver and cirrhosis constituted the two major groups of conditions (table I). Of the 25 patients with a primary liver tumour, five had an underlying cirrhosis and in one of these the indication for transplantation was encephalopathy rather than tumour, which was not detected until the liver was sectioned after

TABLE I—*Indications for orthotopic transplantation in first 60 patients treated (2 May 1968-31 December 1976)*

Diagnosis	No of cases
Primary hepatoma:	25
Hepatocellular carcinoma	19
Intrahepatic cholangiocarcinoma	4
Kupffer cell sarcoma	1
Haemangioendothelioma	1
Carcinoma of hepatic ducts	8
Hepatic metastases	4
Cirrhosis:	19
Cryptogenic	6
Primary biliary cirrhosis	4
Alcoholic	3
Cirrhosis after serum hepatitis	2
Subacute hepatic necrosis	1
Sclerosing cholangitis	1
Haemochromatosis	1
Galactosaemia	1
Budd-Chiari syndrome	2
Extrahepatic biliary atresia	2
Total	60

removal. The median age of the 60 patients was 43 years and the oldest patient was 65 years. Only five patients were aged 17 or under, and only one was aged under 11 years—an infant of 10 months with biliary atresia.

EARLY POST-TRANSPLANT PERIOD

Of the 35 patients operated on before 1975 12 died within the first week after operation, but there were no deaths within this period in the 25 patients operated on in 1975 and 1976.

In most cases the function of the transplanted liver has been strikingly good.[3] Liver function test results in deeply jaundiced patients have returned to normal over the first 10 days, and other signs of liver failure, particularly hepatic encephalopathy, have been rapidly reversed. This occurred even in patients with chronic encephalopathy of several years' duration in whom the brain might have been considered to be irreversibly damaged.[4] A striking example of this occurred early in the series in a patient (case 10) who had developed severe chronic encephalopathy after a portacaval anastomosis. After the transplant all clinical and electrocencephalographic (EEG) signs of encephalopathy receded and he could undertake normal daily activities again, and even built a greenhouse. Another instance was in a woman of 55 with cirrhosis (case 22) who had been in and out of coma for some months and was areflexic at the time of transplantation. Yet by the second day after operation she was fully conscious and her subsequent clinical improvement was remarkable, with a return of mentality and EEG tracing to normal. Similar improvement occurred in a 37-year-old man with cirrhosis (case 45) who had had two admissions for hepatic encephalopathy in 1975, during the last of which he was in coma for seven days.

Various hormonal manifestations of primary hepatic tumours disappeared even more rapidly. The blood sugar concentrations of a patient with hypoglycaemia, massive secondary hepatic deposits, and an insulinoma-like state, were normal from the time the anastomosis was completed. In another patient, hypercalcaemia was found to be due to secretion of a parathyroid hormone-like substance by the primary hepatic tumour,[5] and both serum calcium and raised parathyroid hormone concentrations fell to normal over 36 hours.

SURVIVAL FIGURES AND CASE HISTORIES

Fourteen of the 60 patients survived for over six months, and six of these lived beyond a year. Of the 13 patients still alive at the time of writing, one has survived nearly three years after operation. The longest survivor in the series lived for 5 years and 3 months after transplantation (table II).

The clinical course of four of the six patients who survived for more than one year is described to give some indication of the quality of life that can be enjoyed after a liver allograft.

Case 9—This patient was 45 years old in 1969, when transplantation was carried out for a primary hepatocellular carcinoma without underlying cirrhosis. The removed tumour weighed 4 kg. Apart from one minor episode of rejection during the second week and an episode of cholangitis during the third month, she remained well for over five years. She could work as supervisor of domestic cleaners at a town hall and travel overseas. Liver function test results were virtually normal until 10 days before her final illness. She died in 1974 from cholangitis and septicaemia. Necropsy showed inspissated sludge throughout the biliary tract with secondary infective changes in the liver parenchyma, but there was no evidence of tumour recurrence or rejection.

Case 29—This 44-year-old housewife underwent transplantation in March 1973 for a hepatocellular carcinoma arising in a non-cirrhotic liver. She remained well, with only occasional episodes of cholangitis, until August 1974, when evidence of recurrent growth in the lungs and liver was detected during a routine check-up. She was treated with cytotoxic drugs and remained clinically well until February 1975. She died at home on 1 April 1975, 24 months after the transplant.

Case 34—In 1971, when she was 31, this patient underwent a hemi-hepatectomy for a primary hepatocellular carcinoma apparently confined to the left lobe of the liver. She remained well until early 1974, when evidence of tumour recurrence in the remaining right lobe was observed. Transplantation was carried out shortly afterwards (February), and during the three years since transplantation she has led an active life, and regularly cycles up Denmark Hill (fig 1). The biliary tract anastomosis had to be reconstructed in June 1975 because of calculi within the biliary tract.

Case 40—This university lecturer presented in April 1975 at the age of 39 with a short history of obstructive jaundice, which was due to a small carcinoma arising in the porta hepatis. Transplantation was carried out on 17 June 1975. Biliary obstruction and fistulae developed in July and continuity was re-established using the new technique of anastomosis described below. He then remained well, lectured round the country, and led an active life until his condition deteriorated quite suddenly and he died on 10 July 1976. Necropsy showed recurrent growth blocking the hepatic artery and portal vein.

FIG 1—Case 34. Patient cycling 2 years and 6 months after transplantation.

TABLE II—*Analysis of survival results in the 60 patients according to year of operation. Case numbers are given in parentheses*

Survival:	1st Week	1-4 Weeks	1-6 Months	6 Months-1 year	≥1 Year	Alive at 31 Dec 1976	Date of transplant in survivors	Totals
1968	3 (cases 2, 6, 7)	1 (case 4)	3 (cases 1, 3, 5)					7
1969	4 (cases 11, 12, 14, 15)	1 (case 13)	1 (case 8)	2 (cases 10, 16)	1 (case 9) (lived 5 yr 3 months)			9
1970			7 (case 17, 18, 19, 20, 21, 22, 23)					7
1971	2 (cases 24, 25)	1 (case 26)	1 (case 27)					4
1972		1 (case 28)						1
1973	1 (case 32)	2 (cases 30, 31)	1 (case 33)		1 (case 29) (lived 2 yr 2 weeks)			5
1974	1 (case 35)					1 (case 34)	19 Feb 74	2
1975		1 (case 38)	2 (cases 39, 41)	2 (cases 36, 37)	1 (case 40) (lived 1 yr 1 month)	2 (cases 42 43)	24 Dec 75 30 Dec 75	8
1976		1 (case 53)	4 (cases 46, 47, 50, 51)	2 (cases 44, 45)		10 (cases 48 49 52 54 55 56 57 58 59 60)	12 April 76 20 April 76 3 Oct 76 8 Nov 76 10 Nov 76 19 Nov 76 21 Nov 76 17 Dec 76 24 Dec 76 29 Dec 76	17
Totals	11	8	19	6	3	13		60

Recent improvements

FIRST WEEK AFTER TRANSPLANT

The sharp reduction in mortality in the first week after operation since 1974 was due to less ischaemic damage to the donor livers, better initial assessment of the recipient, greater anaesthetic and surgical experience, and an appreciation of the potential hazards during the operation.

Better donor organs—Removing a liver from a "heart-beating cadaver" provides the most perfectly preserved organ for transplantation. This technique has been standard practice for years in Denver. Until recently in the United Kingdom, where the concept of "brain death" has not yet been fully accepted, organ removal was not started until after circulatory arrest following cessation of mechanical ventilation.[6] While the heart beat continued, the liver almost certainly suffered ischaemic damage as a result of being perfused with deoxygenated acidic blood. In the past year, however, it has been possible to start liver removal either immediately after cessation of mechanical ventilation or while ventilation continued.

Hazards during operation—Great care has to be taken when the vena cava is clamped above the liver and more than half the blood return to the heart is cut off. Some hypotension is inevitable at this stage and cardiac arrest may occur. Another danger period is when the vena cava is unclamped, probably because cold acidic blood containing a high concentration of potassium ions is released from the donor liver and floods suddenly into the right side of the heart. To minimise this, the liver is flushed with 400 ml of plasma protein fraction without additives at room temperature before the portal venous anastomosis is completed. Cardiac arrests may, however, occur at all stages of the operation.[7] Even if the arrest is rapidly reversed the postoperative course may be complicated by heart failure. One patient (case 46) who suffered arrest during the operation continued to have an arrhythmia after operation and died from left ventricular failure and pneumonia after six weeks.

BILIARY TRACT COMPLICATIONS AND NEW TECHNIQUE OF ANASTOMOSIS

Until recently biliary tract complications were distressingly frequent. A detailed analysis of the first 33 patients[8] showed that 14 of the 22 who survived the immediate operation developed biliary fistulae, and masses of inspissated bile were found in the biliary tract in 12 of these at laparatomy or necropsy. The next seven cases (cases 34 to 40) had as the primary procedure a choledochodochostomy over a T-tube, which was left in place as a permanent stent. Of the five who survived
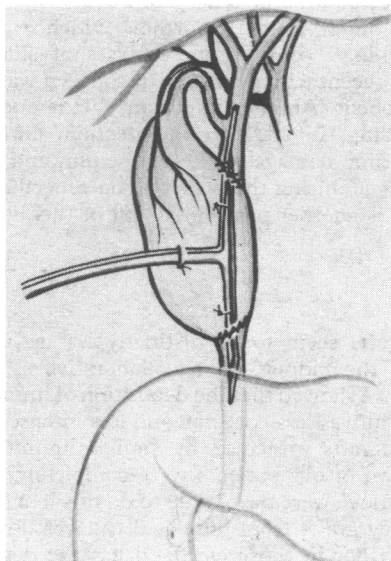
FIG 2—Pedicle graft conduit with donor gall bladder. Hartmann's pouch is anastomosed to donor common duct and fundus anastomosed to recipient common duct. Irrigating T-tube is inserted with irrigating arm through upper anastomosis. Blood supply to gall bladder is carefully preserved.

the immediate postoperative period three had some leakage at the site of anastomosis but died of other causes—two of tumour recurrence and the third of a massive cardiac infarction. Another (case 34) was still alive at the time of writing, and the fifth (case 40) developed an obstruction at the site of the anastomosis with leakage of bile above (see above). At reoperation biliary tract continuity was established using a new technique in which the gall bladder of the donor serves as a biliary conduit.[9] This has been used in all subsequent cases (cases 41 onwards) as the primary procedure (fig 2).

FIG 3—T-tube cholangiogram of patient with orthotopic allograft with gall bladder used as pedicle graft conduit.

Anastomosis—The gall bladder of the donor is mobilised, leaving its blood supply intact, and the common duct is trimmed back and cut obliquely so that the subsequent anastomosis carried out can be a wide one with a good blood supply. At transplantation Hartmann's pouch of the donor gall bladder is anastomosed to the donor common duct, and the fundus of the gall bladder is anastomosed to the obliquely cut recipient common duct. The anastomoses are splinted with a specially constructed T-tube with a narrow gauge irrigating arm, threaded through the proximal anastomosis. Two litres of heparinised normal saline are infused by a drip set through the irrigating tube each day for the first two weeks after operation.

If cholangiography (fig 3) is satisfactory further flushing is stopped and the T-tube is spigotted. The latter is then left in place without disturbance provided there are no complications. One tube has been in place for more than a year, but in two patients the tube fell out after a few months. In each patient biliary drainage has been initially satisfactory and the incidence of biliary leakage and anastomotic stenosis has been considerably reduced, although formation of biliary sludge can still be a problem. In one patient whose common duct could not be used (case 55) the technique was modified by anastomosing the fundus of the gall bladder conduit to a long Roux loop of jejunum.

Rejection

In many patients serum bilirubin concentrations rose at the fifth to 10th day after the operation. In most cases no other evidence of rejection was obtained, and the jaundice subsided without change in immunosuppressive treatment. Although this early rise in serum bilirubin might have been related to ischaemic damage, it did not seem to become more severe or frequent after we began to use livers removed at other hospitals and transported over longer distances. There was no evidence either that these episodes were related to azathioprine toxicity. For the past two years we have routinely used cyclophosphamide instead of azathioprine during the first three days after operation, when ischaemic damage is presumably at its greatest.

Further episodes of jaundice have occurred after a short interval or occasionally directly, when immunological or histological evidence of rejection has been obtained. Such episodes were observed in 10 of

the first 26 patients. Six patients responded rapidly to a temporary increase in immunosuppressive treatment. In four patients, however, the jaundice continued and severe rejection was considered to have been the major cause of death. These included one patient in whom immunosuppressive drugs were withheld because at the time (1968) we thought that the hepatitis virus that was presumed to be the cause of his subacute hepatic necrosis might be reactivated. The other three patients became deeply jaundiced with a grossly raised serum alkaline phosphatase concentration and a moderate increase in serum transaminase concentration. The final morphological changes in the allograft in two patients (cases 3 and 19), who survived for three and four months respectively, were characteristic of chronic rejection with intimal thickening of the hepatic arterioles by foamy lipid-laden histiocytes. Among the more recent patients, we encountered one further case of severe cholestatic jaundice due to chronic rejection (case 50). This patient died at four months, and an additional feature of the hepatic histological changes found at necropsy was the absence of interlobular bile ducts.

Hepatitis B infection—One of the patients with a primary hepatoma who underwent operation in 1975 (case 43) was known to be positive for hepatitis B surface antigen (HBsAg). There was no underlying liver disease, but two other brothers, one of whom had died two years earlier from a primary hepatoma,[10] had been found to have HBsAg in the serum. Because of Starzl's experience with a patient in whom serum HBsAg reappeared two months after the transplant, with the subsequent reappearance of chronic active hepatitis,[11] we used large doses of specific immunoglobulin. The first dose was given during the operation immediately after the diseased liver had been removed with the aim of neutralising HBsAg circulating in the serum and so preventing reinfection of the transplanted liver. By the next day the antigen titre, which was over 1/4000 initially, had decreased to 1/32. Further immunoglobulin was given, and the patient remained antigen free. One year after transplantation he was clinically well, back to work full time, and with no evidence of tumour recurrence.

Recurrence of tumour and new malignancy

Eighteen of the 25 patients with a primary hepatoma died. Of the five who died within two weeks of the operation, two had residual tumour in the retroperitoneal or porta hepatis lymph nodes, and residual or recurrent tumour was found at necropsy in eight of the 13 who survived for longer periods. The amount of tumour tissue was not necessarily very great. In one patient who lived 11 months the single metastasis in the right adrenal was only 2 cm. Five patients had worthwhile palliation and survived for 5, 6, 6¾, 7½, 11, and 23 months. Each regained normal weight and was discharged from hospital for a spell of normal activity before evidence of tumour became manifest again. The seven patients currently alive who have shown no evidence of tumour recurrence include one patient who has survived nearly three years (case 34) and two patients (cases 42 and 43) who underwent operation in December 1975. The eight patients in whom no tumour was detectable at necropsy died of various causes. These include the patient who lived for five years and three months (case 9) and the two patients already referred to (cases 3 and 19), who died after some months of chronic rejection and who had received very high doses of immunosuppressive drugs.

Recurrent tumour was also observed in four of the five patients in the earlier series who underwent transplantation for the characteristically small primary carcinoma arising at the junction of the hepatic ducts. All had undergone a previous attempt to intubate the growth, which probably disseminated tumour cells in the porta hepatis. This also applied to two of the three cases in the recent series, one of whom (case 40) did well for a year before showing evidence of recurrent growth. The one survivor (case 47) of the eight cases with this type of growth in the total series was transplanted at a much earlier stage (within two months of the first symptom) and had not had previous surgery. At the time of writing he was in his seventh month and was well and back to work.

Of the four patients who received a transplant for hepatic metastatic growths, three died between two and six months, one from sepsis (case 18) and the other two from disseminated malignancy (cases 21 and 50).

Reticulum cell sarcoma—This occurred in a woman with cirrhosis and encephalopathy (case 22) who died of septicaemia and cholangitis at six months after a very satisfactory initial course.[12] At necropsy small discrete nodules of tumour were found within the graft and in the porta hepatis. These showed the typical appearances of reticulum cell sarcoma on histological examination.

Discussion

Our recent improved results are due not only to the quality of the donor organs being transplanted but also to the progress we have made in solving problems relating to the immediate postoperative period and in reducing the frequency of the biliary tract complications.

BILIARY TRACT COMPLICATIONS

These complications have for some time constituted the main cause of morbidity and mortality with later transplantation. Fistulae may develop after direct duct-to-duct drainage because of a poor blood supply to the lower end of the donor duct and tension on the anastomosis. But, whatever type of anastomosis is used, breakdown is more likely if there is already infection at the operation site, particularly as the immunosuppressive regimen will further impair healing. Starzl, who has also reported biliary obstruction by sludge developing some months after transplantation, relies on a cholecystojejunostomy with a long jejunal loop.[13] If complications develop his second-stage operation is to detach the Roux loop, remove the gall bladder, and remake the anastomosis to the then usually dilated common bile duct.[14] We think that the technique we use in our patients fulfills the objectives of biliary drainage. Firstly, it preserves the sphincter of Oddi to prevent ascending cholangitis. Secondly, it provides a wide anastomosis with a good blood supply and no sump such as the blind end of the common duct for the accumulation of biliary sludge. Thirdly, it provides ready access to the biliary ducts for both irrigation to prevent sludge blockage and radiography for diagnostic purposes.

The possibility of an abnormality of bile secretion underlying the formation of sludge was investigated in three of our recipients.[8] Supersaturation of bile with cholesterol was found in two patients immediately after surgery and during episodes of acute rejection. Bile was never lithogenic in the third, and a more important factor is almost certainly a change in composition consequent on infection. Chemical analysis of casts found at necropsy showed that free bilirubin was the major component, and in one recipient the *Escherichia coli* organisms grown in cultures of the casts possessed glucuronidase activity.

Damage to bile duct mucosa will also favour precipitation of calcified salts and bilirubin, and there was evidence of this in one of our cases. Cytomegalovirus and monilial infections of the bile duct mucosa, leading to sloughing of the mucosa with subsequent precipitation of biliary constituents, have also been described by Starzl *et al.*[14] Further evidence in favour of mucosal sloughing[15] comes from analyses of sludge obtained from our more recent patients in which collagen was shown to be a major component. Another important factor underlying such mucosal shedding, in addition to infection, almost certainly includes ischaemic damage to the epithelium and subepithelial collagenous tissue during the preservation procedure. Rejection of the mucosa is another possibility, but of this little is known.

REJECTION

Liver allografts seem to be distinctly less severely rejected than those of the kidney. In a collaborative study with the Denver group we showed that the deposition of immunoglobulins and complement was less common and less intense than in renal or cardiac allografts protected by similar immunosuppressive regimens.[16] Two of our patients were completely weaned from prednisone, and we were never able to do this in a series of more than 400 kidney grafts from unrelated cadaver donors. Neither in our patients nor in those of Starzl has the degree of histocompatibility between donor and recipient seemed to be relevant to the occurrence of rejection. One of our patients was found to have cytotoxic antibody reacting with donor cells before transplantation, yet there was no evidence of rejection over six months. Starzl has had the same experience, and in three of his

patients transplantation was successful despite red blood group incompatibility. Rejection of the liver accounted for less than 10% of the deaths in his series,[13] and our figure of five deaths from this cause is similar.

In this respect the human experience is similar to the observations made in animals.[17] The most recent of these have shown that in the pig liver cells possess less major histocompatibility complex surface antigenic specificities than kidney cells, and hepatocytes are more resistant to killing by allogeneic lymphocytes in tissue culture than kidney cells.[18 19] The difference in expression of surface antigens on liver cells might be an important factor in the relatively privileged immunological status of the liver. Hepatic metabolism and contributions of Kupffer cells might also be relevant.

The importance of an accurate diagnosis of rejection cannot be overemphasised, as many of our earlier patients were almost certainly overtreated with immunosuppressive drugs and this caused some of the infective complications. The jaundice of rejection may have obstructive features due to intrahepatic cholestasis. If there is no T tube in place, transhepatic cholangiography using the fine needle technique is useful in excluding extrahepatic biliary tract obstruction. The leucocyte migration test, carried out with donor antigen obtained from white cells, has proved a reliable indicator of rejection, particularly during the first few weeks after transplantation.[20]

SARCOMA

The development of a reticulum cell sarcoma in one of our patients is the only case in a liver allograft so far reported, although there are many described after renal transplantation. Najarian et al[21] have suggested that the pathogenesis of these lymphoproliferative tumours entails the reactivation of latent oncogenic viruses of the herpes group by the chronic antigenic stimulation of the graft in the immunosuppressed patient.

Nuclear sex determination in our patient based on both X and Y chromosome counts clearly showed that the tumour was of host origin and had not been transplanted along with the donor graft.[12]

INDICATIONS

The indications for transplantation are becoming clearer. The largest group of potential recipients are those with end-stage cirrhosis, particularly when chronic encephalopathy is the main clinical feature. Several will be found on investigation to have developed a hepatoma. An assessment of pulmonary function is also important, for interstitial fibrosis and disturbances of ventilation-perfusion balance (with arteriovenous shunting in some) are common. These patients are also likely to have electrolyte imbalance and they are highly susceptible to infection. The timing of the operation in these patients is particularly difficult, although with the progress being made in techniques of artificial liver support this should become less of a problem.[22]

A small group of patients for whom transplantation should be considered, and in whom the prognosis was previously very poor, are those with Budd-Chiari syndrome. Two were included in our series. One died with widespread thrombosis in portal and hepatic venous systems, and because of this experience the second, who was operated on only recently, was maintained on low dose subcutaneous heparin. An excellent longer term result from Starzl's series has also recently been reported.[23]

Only a small percentage of those with primary liver cancer will finally prove suitable for grafting since metastases are so often present by the time the lesion is diagnosed. Undoubtedly, however, the tumour can be completely removed, as shown in one patient who survived for five years and had no evidence of tumour at necropsy (case 9) and in another who remains well nearly three years after transplantation (case 34). Bone scanning is essential in excluding metastases outside the liver, and both inferior venacavography and lymphangiography are valuable in detecting involvement of retroperitoneal abdominal lymph nodes. It is, however, virtually impossible to exclude small metastases in lymph nodes within the porta hepatis. In those patients with a malignant hepatoma arising in a non-cirrhotic liver, it is essential to eliminate the possibility of treatment by resection. Of all the investigations available, hepatic arteriography is the most helpful in determining whether one or both lobes are affected.

With respect to carcinoma of the hepatic ducts, tumour recurrence has occurred in most of our cases despite the intrinsic low malignancy of the growth. Terblanche et al[24] have argued that good palliation can be obtained with a T-tube cannulation and x-irradiation. But cases such as case 48, where transplantation was carried out at an earlier stage and where attempts to cannulate the growth had been resisted, augur well for the future. The results of liver grafting for metastatic tumour, both in the present studies and in that of Starzl, have been poor due to early tumour recurrence.

We have been reluctant to advise liver transplantation for children or infants with biliary atresia or other forms of chronic liver disease, partly because of the side effects of prolonged immunosuppressive treatment, which include growth retardation, as well as the lack of donors in this age group. Nevertheless, these constitute the most successful group of cases in Starzl's series.[13 25] He has also had encouraging results in patients with certain inborn errors of metabolism, particularly Wilson's disease, in which the primary defect may reside in the liver.[26] One patient lived for six years, and the other is doing well at five and a half years. Neurological dysfunction gradually improved after the transplant and liver biopsy specimens showed no recurrence of copper overload. Starzl has also carried out liver transplantation for α_1-antitrypsin deficiency and tyrosinaemia[27] and there was also one case of Niemann-Pick disease.[28]

DENVER SERIES

In Starzl's series there has been a steady improvement in overall survival figures. Of 103 patients who were transplanted a year or more ago, 30 (29%) have survived for at least one year. One-year survival figures were as high as 45% in some groups. Nevertheless, the early morbidity was high, although most of the patients who reached the one year mark continued to do well thereafter, as has been shown in our series. In the Denver series half of those who survived for one year were still alive at the time of writing. Fifteen survived for two years, eight for three years, and four for five years. The longest survivor in Starzl's series (and in the world) has lived for 6 years and 4 months since transplantation. She is living at home, attending school, and has normal liver function. Two other five-year survivors are also completely well.[27]

As confidence in liver transplantation increases, with earlier operation and the diminished tendency of the recipient to reject the grafted liver, both the overall and long-term results of liver transplantation might be better than those of kidney grafting. Indeed, during the past 12 months our immediate results for liver grafting have been better than those obtained with cadaveric renal transplantation.

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Incidence of post-abortion psychosis: a prospective study

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Summary

Twenty-one consultant psychiatrists participated in a prospective study of post-abortion psychosis among a population of 1 333 000 people. During the 15-month study only a single case was reported, concerning a woman who had a history of two previous attacks of puerperal psychosis. The incidence of post-abortion psychosis was 0·3 per 1000 legal abortions. The incidence of puerperal psychosis, which was also studied as an index of validity, was 1·7 per 1000 deliveries. This conforms with currently accepted figures and indicates that the study population was representative. I suggest that physiological changes, which are probably more profound after childbirth than after abortion, may be responsible for the higher incidence of puerperal psychosis.

Introduction

Although the incidence of serious mental disturbance after legal abortion is generally held to be low, no British studies provide any precise figures. Jansson[1] reported an incidence of 19·2 admissions per 1000 legal abortions and 2·7 admissions per 1000 illegal and spontaneous abortions within 12 months of abortion, but this study related to a period (1952-6) when abortion in Sweden was not freely available. A significant proportion of those aborted had a history of serious psychiatric disorder. Jansson's findings are of doubtful relevance to conditions in Britain today since most aborted women have no such history and changing attitudes to abortion may have made it a less disturbing experience.

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This conclusion certainly may be drawn from a recent study in the USA by Tietze and Lewit.[2] In a follow-up of 73 000 legally aborted women they found that the incidence of "major psychiatric complications" (virtually synonymous with admission to a psychiatric ward) was 0·2-0·4 per 1000 abortions. Diagnostic concepts and admission procedures in the USA, however, differ from those used here, and the follow-up period was short.

Even if the incidence of post-abortion psychosis were similar to that of puerperal psychosis—that is, between one and two per 1000 deliveries—it would be necessary to survey at least 3000 aborted women to obtain valid figures. No published British study has entailed anything like such numbers. A different approach is to find out how many women are admitted to particular psychiatric hospitals within a given period after a legal abortion and to relate it to the number of abortions performed in their catchment area populations during the study period. This method was adopted by Jansson, and the existence of reliable regional abortion statistics as a consequence of the 1967 Abortion Act enabled me to use a similar method in the present study.

Method

Twenty consultants in adult general psychiatry practising in the West Midlands Region, and the consultant in charge of the regional unit for adolescents took part in a prospective survey that began on 1 July 1975 and ended on 30 September 1976. They recorded all patients admitted under their care who had had a legal abortion during the previous three months. Patients were divided into two categories, namely—primary post-abortion psychosis (category A) or secondary post-abortion psychosis (category B). Category A was defined as "a serious disorder requiring admission, and manifesting delusions and/or hallucinations, or gross overactivity, in the absence of a previous history of significant psychiatric disorder." Category B was defined as category A but referred to women with a previous history of psychiatric disorder requiring admission to hospital.

The record form made it clear that these categories were intended to embrace "such diagnoses as mania, schizophrenia, delirium, and the more serious cases of depression." The consultants were also asked to record any patients who did not satisfy the rather narrow criteria of the two categories, but who had been legally aborted during the previous three months.

To calculate the approximate number of abortions occurring during the study period in their catchment areas, each consultant was asked to state the population for which he was responsible (excluding the