

Liver transplantation

Liver transplantation was conceived and delivered by Tom Starzl (then of Denver, now of Pittsburgh) in the 1960s; it was nurtured by Starzl in the USA and Calne at Cambridge while in grave danger of perinatal mortality throughout the 1970s; began to grow through the 1980s; and has now come of age. The acceleration of clinical developments has been matched by a correspondingly exponential rise in the number of transplant centres and operations. On average, 11 patients per year received a new liver in Europe between 1968 and 1980, whereas in 1992 alone more than 2,000 had transplants. In total, more than 10,000 liver transplants have been performed in Europe, 2,000 of them in the UK, where activity has been largely restricted to designated centres in Birmingham (Queen Elizabeth Hospital), Cambridge (Addenbrooke's Hospital), Edinburgh (Royal Infirmary), Leeds (St James's Hospital), London (King's College and the Royal Free Hospitals), and Newcastle-on-Tyne (Freeman Hospital) (Fig 1).

Patient selection and timing of transplantation

General criteria

Certain broad principles can be applied in all cases. Disease should be irreversible and unacceptable in its effect on life expectancy and/or quality of life; no extrahepatic factors should be present which would seriously impair or prevent survival of the transplant patient and the patient's subsequent restoration to good health; selection is adversely influenced by a known tendency for early (within three years) symptomatic or fatal recurrence of disease.

Ideally, liver transplantation should be carried out at the latest stage in the course of the illness which is still compatible with the best chance for survival. Factors to be considered include donor availability (waiting list, blood group, liver size), and the predictability or otherwise of disease progression. Conversely, undue delay not only puts the patient at risk of dying before transfer to the transplant centre, or of death while waiting in hospital, but also diminishes the prospects of survival following transplantation. In practice, patients are serially monitored for signs of liver failure by simple analyses of the liver's metabolic, synthetic, and excretory function. One of the most important

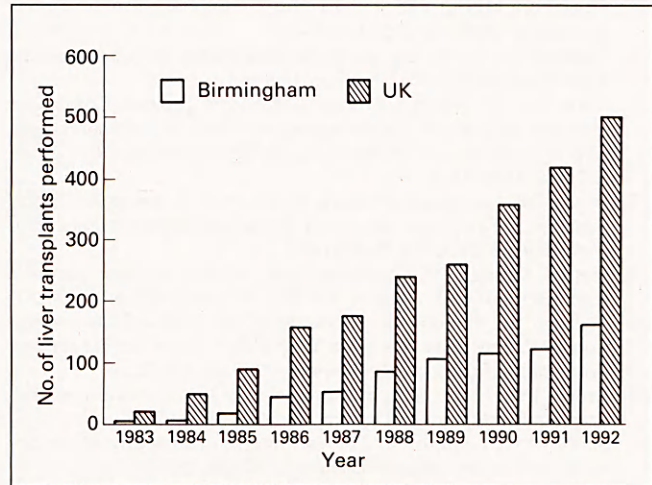


Fig 1. The total number of transplants performed within the UK and in the Birmingham Liver Unit's programme for each of the past 10 years

aspects, which is not clearly quantifiable, is the patient's quality of life. When a poor quality of life is the indication, all involved must be convinced that its alleviation justifies such a risky attempt.

Decompensated cirrhosis

Evidence that chronic liver disease has reached 'end stage' is frequently provided by complications of cirrhosis which influence the timing of transplantation regardless of the cause of the disease. Although only about 30% of cirrhotic patients will bleed from varices, 50% of them will die from their first bleed.

Variceal bleeding

Timing the transplant correctly therefore includes an assessment of the patient's risk of a major variceal bleed [1] (do they have large oesophageal/gastric varices?), and of the probability that they will survive such a haemorrhage should it occur. Very rarely a patient may have troublesome bleeding which cannot be treated satisfactorily by endoscopic means, and yet whose liver disease is insufficiently advanced to justify transplantation. In such a patient it may be acceptable to perform a spleno-renal shunt to prevent further variceal bleeding but only after discussion with a transplant centre. Surgery should use a left-sided approach to avoid interference with the portal vein which could preclude a future liver transplant.

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Encephalopathy

Transplantation should be considered after the first well-documented episode of porto-systemic encephalopathy (PSE). If the precipitating factor was severe (eg, major gastrointestinal bleeding) and is unlikely to recur, the decision will probably be made to defer the transplant. However, if the episode of PSE indicates that hepatic reserve is almost exhausted, that would weigh heavily in favour of early transplantation.

Ascites

When gross ascites becomes persistent, transplantation must be considered. It is wrong to prejudice chances of surviving a transplant by protracted medical treatment which is complicated by hyponatraemia, hepatorenal failure, and muscle wasting. Similarly, palliative measures such as paracentesis together with intravenous colloid infusion, should only be relied upon to keep the patient comfortable while on the active transplant list, and never as maintenance treatment for a patient who is a potential candidate for liver transplantation.

Peritonitis

Referral for transplantation is indicated after the first episode of spontaneous bacterial peritonitis (SBP) diagnosed by a neutrophil count in the ascitic fluid in excess of 500/ml. A patient with cirrhosis who develops ascites has a 40% chance of being alive two years later. Only 25% are alive one year after an episode of SBP [2]. Given the run-in period of several months

required to arrange optimal transplantation of a given patient, referral must not be delayed.

Disease specific indications (Fig 2)

Primary biliary cirrhosis

In primary biliary cirrhosis, bilirubin > 300 $\mu\text{mol/litre}$ is a strong enough indication even in the absence of any others.

More commonly, patients are given transplants when a combination of several of the following features is present:

- bilirubin > 100 $\mu\text{mol/l}$ and rising;
- ascites resistant to diuretics—with risk of hyponatraemia and hepatorenal syndrome;
- spontaneous bacterial peritonitis;
- either hepatic encephalopathy or grossly disabling lethargy;
- pain from osteoporotic bone disease;
- intractable pruritus;
- progressive muscle wasting;
- variceal bleeding resistant to sclerotherapy.

Cryptogenic cirrhosis and chronic active hepatitis

In cryptogenic cirrhosis and autoimmune chronic active hepatitis the commonest features indicating the time for transplantation are:

- diuretic resistant ascites;
- spontaneous bacterial peritonitis;
- hepatic encephalopathy or grossly disabling lethargy;
- low serum albumin (less than 26 g/l).

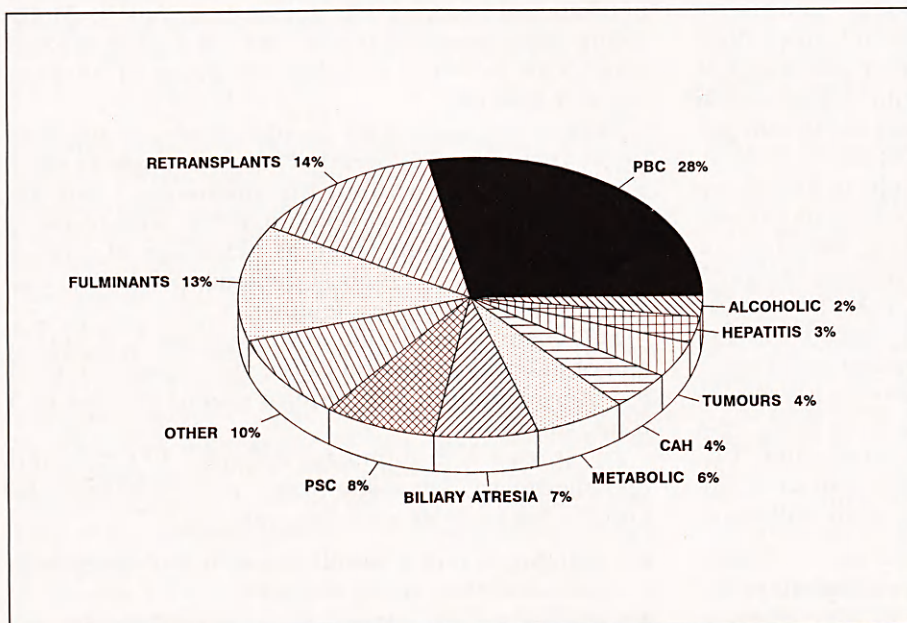


Fig 2. The indications for liver transplantation for the first 700 transplants performed in the Birmingham series

Primary sclerosing cholangitis

In primary sclerosing cholangitis (PSC), indications for transplantation are:

- deepening jaundice which is progressive, not fluctuant;
- intractable pruritus;
- weight loss and muscle wasting;
- decompensated cirrhosis.

Lesser procedures for relief of cholestasis have to be approached with extreme caution. Both endoscopic and surgical palliation of jaundice in PSC patients tend to be shortlived, involve hazardous procedures, and can significantly impair prospects of successful transplantation.

Timing of transplantation for PSC is difficult because bile duct cancer occurs in about 20% of cases. Any sudden worsening of jaundice and weight loss suggests this diagnosis. Dilation of intrahepatic ducts on ultrasound also suggests development of cholangiocarcinoma. The work-up for such a patient includes biliary cytology, biopsy of the stricture where possible, and imaging for a mass, enlarged nodes, vascular invasion, or distant spread.

In the absence of proven malignancy the patient proceeds to transplantation but has to be aware that the procedure will have to be abandoned should a cholangiocarcinoma be discovered intraoperatively. Because aggressive recurrence of disease is inevitable when cholangiocarcinoma has metastasised, it is correct to abandon the transplant so that the donor liver can be given to another patient.

Alcoholic liver disease

Liver transplantation in alcoholics arouses controversy [3]. It has been said that patients should prove their ability to abstain from drink for at least one year, but this begs the question since alcoholic patients who *survive* this interval of successful abstinence usually get back to a satisfactory state of health anyway.

Recent reports suggest that the results of liver transplantation in alcoholics are similar to those in patients with non-alcoholic liver disease [4,5]. Selection of alcoholic patients depends upon the absence of significant organic extrahepatic disease: eg, cardiomyopathy; thorough psychiatric evaluation that insists on acceptance of the diagnosis by both the patient and family; and assessment of prognostic indicators for continued abstinence and social stability that have been best defined in the University of Michigan programme [6].

It is appropriate to consider transplantation for patients with alcoholic liver disease in the following categories:

- severe alcoholic hepatitis (with encephalopathy and/or incipient renal failure); in these circum-

stances there is no opportunity for a qualifying period of abstinence;

- decompensated cirrhosis;
- early hepatocellular carcinoma complicating micronodular cirrhosis.

Budd-Chiari syndrome

Indications for surgery in acute Budd-Chiari syndrome are encephalopathy, jaundice, ascites, and abdominal pain. In chronic Budd-Chiari syndrome the usual indication is intractable ascites. When conditions permit, the treatment of choice is a meso-caval shunt. Transplantation should only be considered when such a shunt has failed or is technically not feasible.

Conditions which justify consideration of liver transplantation are:

- advanced cirrhosis on biopsy;
- occlusion of the retro-hepatic vena cava;
- failed meso-caval shunt;
- a primary thrombotic disorder (eg, protein C, protein S, or antithrombin III deficiency which is cured by liver replacement).

Fulminant hepatitis

Fulminant hepatitis is defined by the development of encephalopathy within eight weeks of the onset of this acute hepatitis. Fulminant hepatic failure is associated with high mortality, which depends on the age of the patient, aetiology of the liver disease, and the rate of onset, depth, and duration of encephalopathy.

Transplantation has been increasingly adopted in the management of acute liver failure, and some 50% of the patients who received transplants have made a full recovery. However, in a proportion of patients in whom the grafted liver has functioned satisfactorily neurological recovery has not been complete. Monitoring intracerebral pressure and developing reliable indices of cerebral viability are areas of current research interest.

Patients are selected for transplantation on the basis of the presence of factors that are most likely to carry a poor prognosis without transplantation, and the absence of features that would interfere with recovery after transplantation (such as neurological impairment secondary to cerebral oedema, psychiatric history of repeated suicide attempts).

Fulminant hepatitis due to virus agents A, B, and E, and of indeterminate viral cause, may be an indication for transplantation and require urgent referral to a transplant centre.

In patients with fulminant hepatitis, O'Grady and his colleagues [7] have shown that without transplantation the risk of death correlates with:

- aetiology—non-A non-B hepatitis and drug reactions carry the worst prognosis;
- age—less than 11 years or more than 40 years;

- jaundice for more than seven days before onset of encephalopathy;
- serum bilirubin above 300 $\mu\text{mol/litre}$;
- prothrombin time longer than 50 sec.

Patients are put on the emergency transplant list as soon as they have three of the factors listed above.

In fulminant hepatitis which has resulted from a paracetamol overdose, the poorest prognosis is indicated by:

- arterial blood pH under 7.30;
- prothrombin time longer than 100 sec;
- serum creatinine greater than 300 $\mu\text{mol/l}$.

Wilson's disease

Liver transplantation for Wilson's disease is indicated:

- in all patients presenting for the first time with fulminant hepatitis;
- for decompensated cirrhosis;
- in some patients in whom neurological dysfunction is progressing despite optimal medical treatment.

Because fulminant hepatitis due to Wilson's disease is invariably fatal without liver transplantation, the diagnosis should always be considered early in the course of severe hepatitis in patients aged 5–45 years, especially when accompanied by haemolysis, a low serum alkaline phosphatase, unusually deep jaundice, a low serum caeruloplasmin, or when there is a history of hepatitis or behavioural and neurological problems in a sibling.

All patients with such a diagnosis must be referred urgently for transplantation, if possible before the onset of encephalopathy. Kayser-Fleischer rings, discernible with slit-lamp examination of the eye, are frequently absent in teenagers, the peak age group for Wilson's disease presenting as hepatitis.

Chronic viral hepatitis

Hepatitis virus B, C, D, and of indeterminate viral origin may also become chronic and culminate in cirrhosis and death. Graft-damaging hepatitis B invariably follows liver transplantation in patients with chronic hepatitis B who, at the time of transplant, are serologically positive for HBV DNA. Persistence of HBV positivity is therefore a major contraindication to transplantation [8]. Viral replication is maximised by post-operative immunosuppression and leads in many patients to a rapidly fatal 'fibrosing cholestatic hepatitis' [9]. The emergence of new therapies, such as nucleoside analogues, which may effectively inhibit HBV replication in patients with transplants may make HBV DNA positivity less of a contraindication to liver transplantation.

Though HCV recurrence in the graft is also universal, the disease is generally benign, at least in the medi-

um term (up to five years) and is not regarded as a deterrent in patient selection [8].

Graft versus host disease (GVHD)

Liver transplantation is indicated when:

- the prognosis for cure from the disease which has been treated by bone-marrow transplantation is excellent;
- GVHD has produced advanced and irreversible liver disease, usually involving the 'vanishing bile duct syndrome' with progressive ductopenia involving more than 80% of portal tracts;
- GVHD involvement of tissues other than the liver is well controlled.

Haemochromatosis

Liver transplantation for haemochromatosis is performed when the patient has:

- decompensated cirrhosis; or
- early primary liver cancer discovered during serial screening of serum alpha fetoprotein and liver ultrasonography.

Contraindications include cardiomyopathy, diabetic microvascular disease, or advanced atheroma.

Protoporphyrria

Rarely, patients with protoporphyria develop progressively deepening jaundice leading to liver failure. Once encephalopathy has developed, survival is improbable without urgent liver replacement. Such patients should therefore be referred when they have progressively deepening jaundice. Referral is urgent when liver failure becomes manifest as a prolongation of the prothrombin time or pre-coma. Muscular weakness in the later stages is due to a porphyric neuromyopathy which can seriously compromise post-transplant recovery [10].

Primary hepatocellular carcinoma

Liver transplantation in malignant liver disease is a controversial area, and in general gives disappointing results [11]. Nevertheless, when otherwise inoperable primary liver cancer presents, without detectable extrahepatic disease, it is still common practice to offer the opportunity for transplantation; there is no alternative cure, and it may be the best palliation.

In such cases, 80% of patients can be expected to recover fully from the transplant, feel well and lead a normal life within one or two months of the operation, but only 25% or so will survive free of disease beyond two years. But because cholangiocarcinoma rapidly recurs with fatal results, it is no longer accepted as an indication for liver transplantation in most centres.

Contraindications to liver transplantation

Absolute contraindications are factors which render a successful outcome impossible. They include:

- active sepsis outside the liver and biliary tree;
- HIV positivity;
- metastatic hepatobiliary malignancy.

Relative contraindications are factors which place the patient in a high-risk category; renal impairment is the most sinister [12]. The most important factors are:

- impaired renal function;
- hyponatraemia;
- muscle wasting;
- hepatitis B or D;
- pulmonary hypertension;
- previous upper abdominal surgery;
- active post-sclerotherapy ulceration;
- bacteraemia;
- spontaneous bacterial peritonitis.

Surgery must be delayed until the reversible abnormalities have been corrected.

Hyponatraemia should be corrected by increasing plasma sodium level to above 125 mmol/l; otherwise there is a risk of central pontine myelinolysis.

Spontaneous bacterial peritonitis is diagnosed and treated on the basis of finding more than 500 neutrophils/ml of ascites in the diagnostic aspirate.

Post-sclerotherapy ulceration carries a risk of perforation with mediastinal abscess formation, weeks after an apparently successful liver transplantation [13].

Previous upper abdominal surgery: in the early days of liver transplantation, Starzl reported the risk of death within the first month after transplantation to be double that of patients who had not undergone earlier operations, but improved surgical technique has substantially reduced this risk.

Severe pulmonary hypertension, which occasionally complicates chronic liver disease, precludes liver replacement, except in the rare patient who is accepted for combined heart, lung, and liver transplantation. Arterial hypoxaemia due to intrapulmonary shunting may also be associated with cirrhosis, but tends to reverse after successful transplantation [14].

Other problems: many of the other high-risk factors indicate that transplantation has been left until too late. For example, renal impairment, hypoalbuminaemia, and gross muscle-wasting probably indicate a preterminal phase of the patient's chronic liver disease in which the optimal chances of surviving liver transplantation have been lost.

The operation

Donor organ availability

Although so far the number of livers available for transplantation within the UK has exceeded the num-

ber of recipients in any given year, patients die while on the active transplant list due to lack of a donor at the critical time. Thus strict timing requirements, as well as a broadening of indications which enlarges the number of recipients, maintain pressure for a greater supply of donated organs. Use of split livers (one donor for two recipients) or living-related donation (taking the left lobe from a healthy relative) are adventurous responses to the pressure to make liver transplantation more widely available.

Organ retrieval and preservation

Until recently, hypertonic citrate (Marshall's) solution was usually used for donor liver perfusion which allowed up to eight hours' preservation of the liver; however, the recent introduction of a lactobionate (Wisconsin) solution has made up to 20 hours' preservation possible. The shortage of size-matched donors for paediatric recipients has led to transplantation of anatomically reduced adult livers with encouraging early results.

Recipient operation

Preparation of the recipient for transplantation begins once reports from the donor hospital indicate that the donor liver appears satisfactory. Hepatectomy in the recipient can cause problems due to portal hypertension and associated coagulation abnormalities. In higher risk cases veno-venous bypass (shunting blood from the lower cava and portal vein through a centripedal pump into an axillary vein) stabilises haemodynamic variations during caval clamping and may reduce bleeding due to portal hypertension.

Once the recipient's hepatectomy is complete and haemostasis is achieved, the donor liver is inserted starting with the caval and then the portal vein anastomoses. Before the portal vein anastomosis is completed, the donor liver is perfused through the portal vein with 5% dextrose at 37°C, to wash out any toxic metabolites in the liver (potassium and hydrogen ions) and also to remove any air. It is then perfused with blood through the portal vein and the arterial anastomosis is completed. Early indications of graft function include rapid correction of the recipient's acidosis which develops during the anhepatic phase. Immediate function is necessary, otherwise refractory acidosis, coagulopathy, and hypotension lead to early death. Direct duct-to-duct biliary anastomosis with or without a T-tube has superseded the use of the donor gall bladder as a conduit for biliary reconstruction.

Results

The outcome of liver transplantation depends on the timing of the surgery, selection of the patient, the severity of the disease, and the extent of failure of other organ systems. The actuarial two-year survival

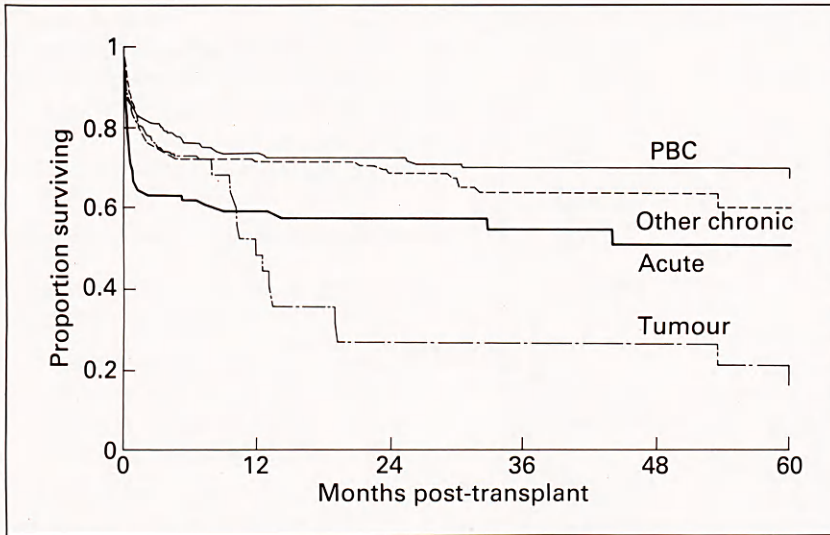


Fig 3. The actuarial 5-year patient survival according to disease for the first 600 transplants in the Birmingham programme. (PBC = primary biliary cirrhosis; Other chronic = other chronic liver disease; Acute = acute liver failure; Tumour = malignancies)

after transplantation in the entire Birmingham series is 70–80% in chronic liver disease, 50–60% in acute liver failure, and 25–30% for malignancies (Fig 3); this is broadly representative of worldwide experience.

In future, improved results are likely to come with more stringent patient selection, opportune timing of liver replacement, and more effective immunosuppression. Fatal delays occur as a result of late presentation and referral, rapidly progressive disease, difficulty in procuring organs at short notice, and logistic problems in the transplant programme, such as influx of more urgent cases. Patients should be offered the option of receiving a transplant when the chances of success are still optimal (currently better than 80%) (Fig 4). In acute liver failure, it is essential to assess the prognosis as early as possible so that the decision to transplant can be taken in good time for obtaining a

donor organ, to avoid death due to cerebral oedema before transplantation becomes a possibility (Fig 5).

Postoperative complications

Early complications include cardiovascular instability, usually associated with intraoperative haemorrhage, primary non-function of the implanted liver, and acute renal failure.

Early hepatic artery thrombosis is one of the most serious complications. It causes graft ischaemia with massive elevation of serum transaminases, and is an indication for urgent re-grafting. The hepatic artery is postoperatively routinely imaged by Doppler ultrasound, and any suspected thrombosis is confirmed angiographically.

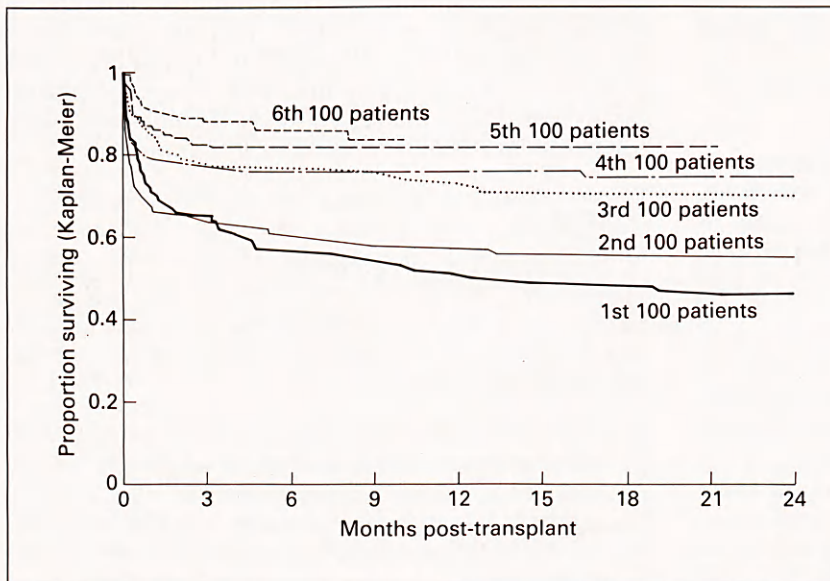


Fig 4. The 2-year actuarial survival for successive cohorts of 100 patients since the start of the Birmingham Liver Unit's programme in 1982. There was a progressive improvement in outcome

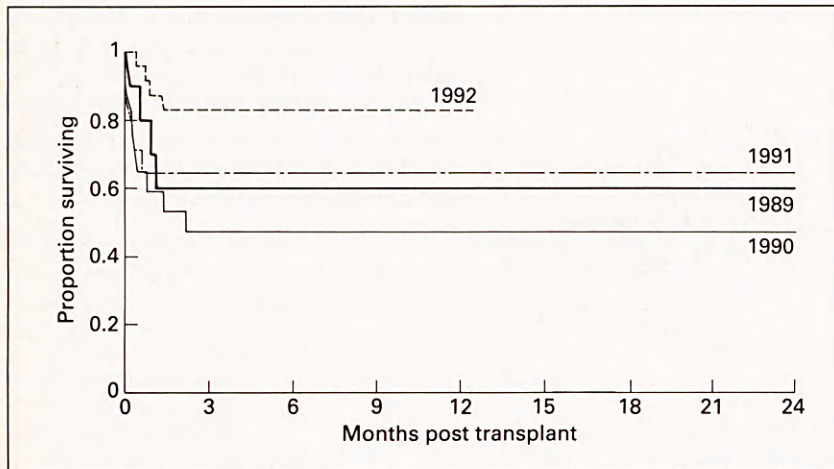


Fig 5. The proportion of patients surviving liver transplantation for fulminant hepatic failure in the Birmingham series for each of the past 4 years

Rejection

Acute rejection: although animal studies have suggested that the liver is less susceptible to rejection than other organs, in humans the liver does not seem to be protected. Histological features of acute rejection consist of a mixed inflammatory infiltrate concentrated around the bile ducts in the portal tract and the endothelium of the portal and hepatic vein radicals [15].

Chronic rejection: the cardinal feature of chronic rejection is the sudden or gradual disappearance of small intrahepatic bile ducts; the hepatic arterial lumen is occluded by foam cells, and the parenchyma shows evidence of secondary cholestasis and ischaemia.

Immunosuppression: cyclosporin is the most commonly used maintenance drug, often combined with corticosteroids and azathioprine, but regimens vary considerably between transplant centres. The Birmingham protocol involves triple therapy with:

- cyclosporin, 2 mg/kg/day iv converting to 10 mg/kg/day po, and adjusted to maintain blood levels of 100–300 mg/l;
- low-dose prednisolone, 20 mg/day (reducing stepwise to 0 g/day at three months);
- azathioprine, 2 mg/kg/day.

Acute rejection is treated with methylprednisolone, up to 1 g/day for three days. Patients who fail to respond to one or two courses of corticosteroid bolus are treated for 10 days with the monoclonal anti-lymphocyte antibody OKT3.

The early experience with a new agent, FK506, suggests that it will provide a useful alternative to cyclosporin, but a significant risk of nephrotoxicity remains, and the results of controlled trials are awaited [8].

Immunosuppression must be balanced to minimise the risks of rejection and opportunistic infection. Infections (bacterial, viral, and fungal) are common causes of liver dysfunction or systemic disease.

Cytomegalovirus (CMV) infection is one of the most common infections after transplantation; when possible, CMV-negative donors are matched to CMV-negative recipients. Reduction of immunosuppression is often sufficient to allow patients to recover from symptomatic CMV infection, but in severe cases treatment with ganciclovir and specific immunoglobulins has to be given.

Late complications

Recurrent disease

This is most likely to occur when transplantation has been performed because of malignancy and viral hepatitis (hepatitis B, C, and indeterminate).

Biliary obstruction and cholangitis

These may be manifest as a high alkaline phosphatase, jaundice or dark urine, pruritus, rigors, or a tendency to diarrhoea. Early recognition is important because of the risk of sepsis from cholangitis and bacteraemia and of rejection secondary to malabsorption of immunosuppressive agents during episodes of cholestasis. Early correction of the biliary problem is recommended.

Rejection

De novo rejection is extremely rare in the stable patient with good graft function more than one year after transplant, and patients should be reassured accordingly. Rejection is then only encountered in one of the following circumstances:

- immunosuppressive drug concentrations fall to subtherapeutic levels because of a change in regimen (eg, reduced dose, alteration of a co-prescribed pharmacokinetically interactive compound), or because of malabsorption due to an intercurrent diarrhoeal illness or cholestasis;

- incipient chronic rejection, early signs of which will usually have been noted by the transplant centre who will usually have taken precautions by keeping the patient under intensive surveillance—chronic rejection will produce cholestatic jaundice if allowed to progress.

Complications of immunosuppression

The most common long-term side-effects of immunosuppressive drugs are:

- osteoporosis in patients on corticosteroids;
- hypertension and renal impairment in patients on cyclosporin A; if severe, it may be necessary to substitute cyclosporin [16].

Long-term immunosuppression significantly increases the risk of malignancy in the recipient. Azathioprine is particularly associated with skin cancer, and all skin lesions should be carefully examined. Lymphoproliferative disorders are also a serious long-term hazard—cranial nerve palsies and other manifestations of early cerebral involvement being a curiously frequent characteristic.

Precautions in the post-transplant patient

Patients will generally be advised to avoid pregnancy if taking an immunosuppressive agent other than prednisolone (usually discontinued at this stage), azathioprine, and cyclosporin. Prospective parents can be reassured that these agents have been taken throughout pregnancy with a happy outcome in more than 100 instances. There is no proof that these drugs constitute a significantly increased risk to the baby during pregnancy, but the overall numbers are too small to be sure that there is not an increased risk of miscarriage and for the babies to be born at low birthweight.

Parents should be advised that small risks such as these may be substantiated in the fullness of time, but be prepared to accept the outcome should such eventualities arise. Because of a tendency to hypertension in patients on cyclosporin, extra careful monitoring of blood pressure and renal function is recommended throughout pregnancy.

Generally speaking, all intercurrent illnesses should be treated in the standard way. This particularly applies to short-term medication such as antibiotic therapy for acute infection. A check may be required on the effect of any interaction between the new agent and the patient's immunosuppressive regimen (eg, erythromycin will tend to increase CyA blood levels). Such a check is mandatory with a view to readjusting dose levels if the new agent is to be used in the long term. Although the direction of change is known for many agents (nifedipine and cimetidine will increase CyA blood levels whereas phenytoin and warfarin will reduce them), the precise effect should be monitored with weekly estimations of trough blood levels until

Table 1. Complications after liver transplantation

Immediate complications:

Haemorrhage
Renal failure

Early complications:

Day 0–3:

Primary graft failure
Hepatic artery thrombosis
Cerebral death (in acute liver failure)

Weeks 0–2:

Sepsis (pulmonary, abdominal, biliary)
Acute rejection (70–80%)
Chronic rejection (rare < 1%)

Weeks 2–8:

Sepsis (perihaptic, biliary leak or sludge in bile duct)
Acute rejection
Chronic rejection
Opportunistic infections – fungal, viral (eg cytomegalovirus, herpes virus)
Over-immunosuppression

Late complications:

Chronic rejection (10–15%)
Acute rejection (rare < 1%)
Recurrent disease
HBV
Malignancy
Biliary strictures

Drug toxicity:

Cyclosporin nephrotoxicity, hypertension, hypertrichosis, dyspepsia, fine tremors, paraesthesia
Azathioprine myelotoxicity
Lymphoproliferative disorders

three successive estimations have given satisfactory readings.

Psychoactive treatments should be used as indicated in liver transplant recipients. Although most patients are elated by the successful outcome of a liver transplant, some continue to experience significant symptoms of an affective disorder. They need to be listened to carefully and sympathetically in quiet surroundings and reassured that their symptoms are understandable, far from unique, and generally associated with a very good prognosis. It probably takes the average patient some two years to become fully adjusted to being a liver recipient. Some have a sense of guilt because someone else had to die to enable them to survive. Many find that they are unable to fulfil what they

believe are people's (family, healthcare team) expectations of them to bounce back to full vivacity and vitality, and fear their failure to do so will be interpreted as ingratitude. The overwhelming majority of survivors manage to resume normal activity without any restrictions and with a complete sense of wellbeing.

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Current Themes in Diabetes Care

*Based on an Interfaces in Medicine Conference
organised by the Royal College of Physicians*

Edited by Ian Lewin, FRCP and Carol Seymour, FRCP

Many people participate in diabetes care. First and foremost is the individual with diabetes who is advised and supported by the general practitioner and practice nurse. They in turn are backed up by the diabetic clinic or centre, based at the hospital with medical and nursing staff, dieticians, chiropractors, laboratory staff and other specialists. But diabetes care also needs the support of the pharmaceutical and instrument companies that manufacture insulin, anti-diabetic drugs and glucose measuring devices. To emphasise the need for all these agencies—and the advantages to the patient of co-operation between the hospital clinical and general practice—the Royal College of Physicians held a conference in 1991 which formed the basis of this book.

Contents:

- Preface by David Pyke. Editors' introduction. ● Provision of diabetes care in the UK ● The aims of diabetes care ● Which diabetics need hospital follow-up? ● Non-insulin dependent diabetes: a wolf in sheep's clothing? ● Obesity and hyperlipidaemia in the non-insulin dependent diabetic patient ● Update on long-term diabetic complications ● Practical aspects of insulin therapy ● Starting insulin at home ● Good control or a happy life?

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