

# Progress in Liver Transplantation and the Treatment of Bile Duct Carcinoma

JOHN TERBLANCHE, CH.M., F.R.C.S. (ENG.), F.C.S. (S.A.), *Senior Lecturer in Surgery, University of Cape Town, and Principal Surgeon, Groote Schuur Hospital*

## SUMMARY

The present position of transplantation of the liver in man is briefly reviewed and the indications for this procedure are critically analysed. These are primary carcinoma of the liver, congenital biliary atresia, cirrhosis, secondary carcinoma of the liver, and carcinoma of the bile ducts situated at the main hepatic duct junction. The treatment of this latter condition by palliative procedures on the professional surgical unit at Groote Schuur Hospital is presented and a case is made for the use of a 'U-tube' procedure as the best palliative measure available at the present time.

*S. Afr. Med. J.*, 45, 1149 (1971).

## LIVER TRANSPLANTATION

Due to a better understanding of the requirements and value of organ transplantation by medical practitioners in general, the availability of organ donors is improving in a number of centres, including our own. The logistics for all organ transplants are, however, likely to remain a problem.<sup>1</sup>

Although there has been progress in the field of liver transplantation in the past two years, many of the original problems still remain unsolved.<sup>2-5</sup> During this period the indications have been further clarified. The technique, having been fully worked out in the laboratory, has been successfully employed in patients for some years, but minor modifications are still being introduced.

As the liver withstands ischaemia poorly, the lack of a simple, readily available, but satisfactory method of liver storage has been one of the main factors delaying liver transplantation in many units, including our own. With the development of such a system in the laboratory,<sup>6</sup> it is our intention to consider patients for liver transplantation once again.

No recent progress has been made in preventing rejection of liver transplants and the immunosuppressive regimens used in most centres are similar to those used for renal transplantation, with all the attendant problems.

In many countries, including South Africa, advances in the legal problems of organ transplantation have been made recently. Although there are still problems in South Africa's proposed legislation dealing with organ transplantation, it is pleasing to note that the government authorities and legal profession are studying ways to provide better laws to cover organ transplantation procedures.

A considerable number of human liver transplants have been performed in a limited number of centres around the world to date.<sup>2-5</sup> The majority have been orthotopic, or total-replacement liver transplants and in these cases occasional survival of over 2 years has been attained. It must be emphasized, however, that most of the patients have died much earlier. With continued experience, there is no reason why liver transplantation should not progress to the same degree as renal transplantation, which is now of unquestioned therapeutic value. Heterotopic liver transplantation (i.e. auxiliary or accessory transplantation) has been performed on a few occasions. Here the patient's own liver is left *in situ*. However, mainly due to technical problems, the majority have failed to function for any length of time. The problems of heterotopic liver transplantation are being investigated in many laboratories, including our own, and it is possible that this form of transplantation of the liver may be successfully employed in patients in the future.

## Primary Carcinoma

The main indications for the liver transplants that have been performed in patients to date have been primary carcinoma of the liver; carcinoma of the intrahepatic bile ducts; congenital biliary atresia; cirrhosis with end-stage liver failure; and secondary carcinoma of the liver.

As primary carcinoma of the liver is a common condition in the Bantu, and is seldom amenable to hepatic lobectomy as a form of therapy, our group initially felt that this would constitute an important indication for liver transplantation in South Africa. Subsequent evidence from Starzl's group in the USA that patients with primary carcinoma who have received liver transplants and survived for longer than 2 months tend to die of spread of the carcinoma,<sup>2</sup> made us reject these patients as potential liver recipients. Our current view is that patients with primary carcinoma of the liver who cannot be treated by hepatic lobectomy die so quickly of their disease that a limited number of these patients should be considered, once again, as potential transplant recipients after careful assessment. If a well-motivated patient can be given 2 years of reasonably comfortable life, we believe this to be a worthwhile proposition.

A number of patients with inoperable carcinoma of the bile ducts have undergone liver transplantation. The majority of these have died early after the procedure and the best that can apparently be achieved at present is occasional survival of in the vicinity of 2 years. For this

reason, we have investigated various forms of palliative treatment for these patients and this will constitute the second part of this article. It is our current view that patients with bile duct carcinoma should be treated by palliative surgical therapy because of the prolonged survival that is possible by those measures. Once liver transplantation has advanced further, patients with this condition can again be considered as transplant recipients.

### **Congenital Biliary Atresia**

Congenital biliary atresia still remains a problem and most cases are not amenable to standard surgical procedures. Transplantation has been offered to a number of these children, mainly by Starzl,<sup>2</sup> but survival is still limited. An additional problem has been the complications of immunosuppression in children, especially those related to growth. Furthermore, difficulty in obtaining donors with livers of a size suitable for transplantation into children has been a major stumbling block in many centres, including our own.

### **Cirrhosis**

Patients suffering from cirrhosis with liver failure will eventually constitute the main group who will be treated by liver transplantation. It is a condition seen commonly at the Liver Clinic, Groote Schuur Hospital, but we have experienced great difficulty in diagnosing the end-stage of the disease in most of these patients. Some patients considered for transplantation have lived for months or years, and others not considered at the end-stage of their disease have rapidly died. In the future, when liver transplantation has progressed to the point where most of the patients can expect to live for some years, this group of patients could be considered for transplantation earlier in the course of their disease. At present it is felt unjustified to perform a liver transplant on a patient who is not in end-stage disease.

### **Secondary Carcinoma**

At present we do not consider patients with secondary carcinoma of the liver for transplantation. Here the same arguments hold as for primary carcinoma of the liver. It is possible that the occasional highly selected case will be considered in the future.

It is clear that further advances in the field of liver transplantation will be required before this procedure can be offered as a routine, as now pertains to kidney transplantation. With the amount of laboratory work being undertaken in this field at present, it is hoped that these advances will be made in the not too distant future. In addition, limited clinical progress should continue in specialized centres, as it is only in this way that the problems can be defined, and then subsequently investigated in the laboratory. It is also considered that, for the present, 2 years' palliation is a reasonable aim for patients who

have already reached the end-stage of their liver disease, and that some of these patients should be offered liver transplantation after very careful selection.

### **Bile Duct Carcinoma (Carcinoma of the Main Hepatic Duct Junction)**

Carcinoma of the main hepatic duct junction, which is not amenable to hepatic lobectomy, has been considered an ideal indication for liver homotransplantation because of its slow growth, and the fact that it tends to remain localized until late in the course of the disease. Although some authorities still consider these patients for liver transplantation, it is our view that they should not be transplanted at the present stage of development of liver transplantation. This is based on the experience of the prolonged palliation that can be achieved by other means. They can be offered more by various forms of palliative surgical therapy than by liver transplantation.

Although rare, the condition is often misdiagnosed, even at surgery, and may therefore be more common than previously thought. Klatskin from the USA has reported on a series of 13 cases seen over a period of 16 years,<sup>7</sup> and Whelton and others of Sherlock's group from the United Kingdom have recently reported on a series of 23 cases.<sup>8</sup> In both series, the diagnosis was missed at the initial operation in most instances.

These patients commonly present with obstructive jaundice, which is usually progressive, early pruritus, absence of pain, and they often have a marked hepatomegaly which is smooth and firm. At operation the gall-bladder and common bile duct are classically collapsed and it is for this reason that the diagnosis is so often missed. In addition, the lesion situated in the porta hepatis area of the liver may not be obvious to the operating surgeon. The diagnosis can best be made by means of transhepatic cholangiography.

In the Professorial Surgical Unit at Groote Schuur Hospital 20 patients with this condition were seen in the 9½-year period from 1961 to June 1970. The last 9 cases constitute a personal series which have been followed up prospectively and were first diagnosed in the 2½-year period from January 1968 to June 1970. In all cases the lesion was situated in the porta hepatis at the junction of the main hepatic ducts and was not amenable to curative surgery other than by total hepatectomy and transplantation. A number of these patients were operated upon and diagnosed elsewhere before being referred to Groote Schuur Hospital for consideration for liver transplantation. Four of the 9 patients were accepted on the liver transplant programme, but none received hepatic transplants as suitable donors did not become available while these patients were still considered suitable transplant candidates. Most of the patients were treated by various palliative manoeuvres and 3 of the 9 patients are still alive at over 2½ years, over 2 years, and over 1½ years respectively after the initial laparotomy at which the diagnosis was made. Additional cases seen since June 1970 have not been included for analysis and therefore all the patients have been followed up for at least 6 months or until death.

Of the 6 patients that died during the follow-up period, 3 lived for longer than 1 year. Of the 3 who are still alive, 2 are well at the present time with no significant symptoms. It is our belief that this group of patients received better palliation than would have been provided had they received hepatic transplants. The palliative procedures utilized included dilatation of the carcinoma in 7 with the passage of a tube through the lesion in an attempt to maintain patency. Standard T-tubes were utilized at the first procedure in 4 cases and 1 of these received cobalt therapy to the localized area subsequently, and is still alive. Another had the T-tube replaced by a transhepatic tube at a subsequent operation after the T-tube had occluded and she, too, is still alive. Three of the patients had 'U-tubes' inserted and this is the procedure favoured at the present time. In the 'U-tube' procedure either a Meredith Thoracic Catheter (16 Ch)\* or silastic tubing is passed through the dilated carcinoma via the common bile duct and then up through the surface of the liver and out of the skin through a stab incision. The other end is brought out through the incision in the lower end of the common bile duct and out of the skin through a separate stab incision. Two holes are cut in the tube and are sited, under radiographic control, just above and just below the carcinoma. This allows bile to drain past the carcinoma and via the common duct into the duodenum. The 'U-tube' has great advantage over the other tubes utilized in that it

\*Meredith Plastics, Eschmann, England.

can be easily replaced without a further operative procedure when it blocks, as invariably happens. In the third long-term survivor in whom a 'U-tube' was utilized, it was replaced recently and the patient is once again fit and well.

It is important to note that out of an interest in transplantation of the liver has arisen the opportunity to provide better palliative treatment for carcinoma of the main hepatic duct junction by means other than transplantation, in a group of patients who were referred for liver transplants. Because of the slow growth of these tumours and their tendency to spread late, palliative procedures—particularly the 'U-Tube' procedure—are recommended as better therapy than transplantation at the present stage of our knowledge of hepatic transplantation.

I wish to thank Prof. J. H. Louw, Head of the Department of Surgery, University of Cape Town, for his continued interest and support, and Dr J. G. Burger, Medical Superintendent, Groote Schuur Hospital, for permission to publish details of the patients.

#### REFERENCES

1. Terblanche, J. and Riddell, A. G. in Read, A. E., ed. (1967): *Colston Papers: The Liver*, Vol. 19, p. 321. London: Butterworths.
2. Starzl, T. E. and Putnam, C. W. (1969): *Experience in Hepatic Transplantation*. Philadelphia: W. B. Saunders Company.
3. Starzl, T. E., Porter, K. A., Brettschneider, L., Penn, I., Bell, P., Putnam, C. W. and McGuire, R. L. (1969): *Surgery*, **128**, 327.
4. Calne, R. Y. (1969): *Brit. J. Surg.*, **56**, 730.
5. Williams, R. (1970): *Brit. Med. J.*, **1**, 585.
6. Spill, H., Uys, C. J., Hickman, R., Saunders, S. J. and Terblanche, J. (1971): *Transplantation*, **11**, 457.
7. Klatskin, G. (1965): *Am. J. Med.*, **38**, 241.
8. Whelton, M. J., Petrelli, M., George, P., Young, W. B. and Sherlock, S. (1969): *Quart. J. Med.*, **38**, 211.