Scintigraphic Evaluation of Liver Transplant Function

Merle K. Loken, Nancy L. Ascher, Robert J. Boudreau, and John S. Najarian

Division of Nuclear Medicine, Department of Surgery, University of Minnesota Hospitals, Minneapolis, Minnesota

Since the initiation of liver transplantation at our institution 9 yr ago, 73 patients ranging in age from 8 mo to 64 yr have undergone this procedure. In the immediate postoperative period and at various times thereafter as deemed necessary, radionuclide studies were performed using one of the iminodiacetic acid (IDA) derivatives labeled with ^{99m}Tc. Initially, these studies were performed using labeled PIPIDA with a shift to diisopropyl IDA when this latter agent became available. The IDA agent is administered as a bolus so that the "flow" and "pooling" may be viewed immediately after injection. This is followed by sequential imaging at various times up to 24 hr, with optional graphic tracings of hepatic and bowel patterns of uptake and clearance of radioactivity. An analysis of the initial portion of the IDA scan yields useful information regarding the arterial and portal venous supply of the liver. The rapidity of hepatic concentration and excretion provides a direct measure of hepatocyte function which is particularly helpful when used sequentially to follow the response of the liver to therapy for rejection or infection. The study is also used to assess the biliary system for obstruction or leaks.

J Nucl Med 27:451–459, 1986

Since the introduction of human orthotopic liver transplantation by Starzl and associates in 1963, more than 1,000 liver transplants have been performed at various medical centers throughout the world (*1,2*). This procedure is increasingly recognized as the appropriate treatment for a number of disease processes involving the liver (*1–5*). Increased interest in hepatic transplantation has paralleled improved survival results which have been attributed in large part to the use of cyclosporine (*1,2*), but also relate to improved surgical technique and better diagnoses and treatment of complications. Interest in liver transplantation at our institution has also increased considerably with the availability of cyclosporine. Although 16 liver transplants were performed prior to the use of cyclosporine in 1982, only two patients survived longer than 1 yr. Since then, 57 transplants have been performed with 33 survivors at present.

The postoperative period is an uncertain one for the transplant patient; complications include bleeding, vascular accidents, rejection, biliary disruption, and infection. Liver enzyme abnormalities do not identify the specific pathology (*5*). Although routine post-transplant percutaneous biopsies are used to delineate hepatic pathology, it would be preferable to develop a noninvasive examination instead. We are, therefore, utilizing radionuclide scintigraphy as introduced by Klingensmith et al. (*6,7*) to determine the efficacy of this procedure in defining graft function and specific post-transplant pathology in our patients (*8*). In this paper, we report our efforts to date with this noninvasive examination. Other details of our experience have been considered in other publications (*3–5*).

MATERIALS AND METHODS

Donors who met brain death criteria (no evidence of either intracranial blood flow or electroencephalographic activity) were matched to prospective transplant recipients according to blood group, size, and weight. A cross-match between recipient serum and donor lymphocytes was performed for retrospective analysis. The preoperative donor assessment included tests of hepatocyte function (coagulation parameters), hepatocyte integrity (serum transaminase-AST), and evidence of adequate oxygenation and blood pressure maintenance.

Received June 27, 1985; revision accepted Nov. 15, 1985.

For reprints contact: Merle K. Loken, MD, PhD, Div. of Nuclear Medicine, University of Minnesota Hospitals, 420 Delaware St. SE, Minneapolis, MN 55455.

Visual inspection of the donor organ completed its evaluation prior to transplant.

Sixty-one orthotopic liver transplants have been performed at our institution from 1980 to the present and serve as the basis of this report. Of 43 pediatric patients, 30 had biliary atresia, five had alpha-1-antitrypsin deficiency, two had Wilson's disease, and one each of chronic aggressive hepatitis, fulminant hepatitis and tyrosinemia, glycogen storage disease, chronic cholangitis and hepatoblastoma. Of 18 adult patients, seven had primary biliary cirrhosis, three had sclerosing cholangitis, two had cancer, one each had chronic active hepatitis, photoporphyria, fulminant Wilson's disease and alpha-1-antitrypsin deficiency, and two had unknown causes of liver failure.

The evaluation of each patient scheduled to receive a liver graft has several purposes: (a) to optimize the patient's general condition prior to graft placement. Nutritional and respiratory functions receive special attention. Short courses of broad spectrum antibiotics are used when considered necessary. Judicious use of furosemide and aldactone diuretic treatment of ascites is weighed against the possibility of exacerbating renal insufficiency. Blood volume is maximized using colloid to treat the pre-renal component of the hepatorenal syndrome, (b) to characterize defects of hepatic, pulmonary or cardiac function that might influence the patient's chance of survival, (c) to determine whether the transplant is technically feasible given an individual patient's anatomy, and (d) to search out sites for occult infection and/or malignancy. The details of protocols followed for this purpose have been considered elsewhere (*4*,*5*).

Techniques similar to those developed for renal preservation have been adapted for preserving the donor liver (*9*). After the donor liver is isolated and its vessels skeletonized, inflow cannulas are placed in the portal vein and aorta. An outflow cannula is placed in the distal vena cava and a slow in situ flush is begun with cold heparinized lactated Ringer solution through the portal system. After the liver has been cooled and flushed for ~20 min, both portal and aortic systems are flushed with cold heparinized Collins solution. The hepatectomy is then completed and the liver transported on ice to the operating theater where the recipient is being prepared. This method provides for ~8 hr of preservation of the graft prior to implantation.

The recipient hepatectomy is often the most dangerous and tedious aspect of liver transplantation in that portal hypertension and adhesions can result in excessive bleeding. A rapid infusion system, the cardiopulmonary bypass pump, is used to deliver washed blood (free of white blood cells and low in potassium) at a rate of up to five l/min.

The liver graft is placed in an orthotopic position. The donor and recipient suprahepatic vena cavae are anastomosed first; this anastomosis can be difficult because of limited exposure. Next, the infrahepatic vena cavae of donor and recipient are anastomosed leaving a small defect in the anterior suture line. Third, the portal veins of donor and recipient are anastomosed after cutting each vessel on a bias to maximize the diameter of the anastomosis. Release of the portal vein vascular clamp without release of the suprahepatic vena cava results in flushing of the potassium rich Collins solution out the defect in the infrahepatic vena cava and protects the recipient against sudden hyperkalemia. After this fluid is flushed into the peritoneal cavity, the infrahepatic suture line is completed and the suprahepatic vena cava is released, returning portal flow to the circulation. Arterial flow is established by way of the hepatic artery to hepatic artery anastomosis or an aorto-aortic anastomosis. Biliary drainage in adults is by way of a choledocholedochostomy over a T-tube stent, and in children a choledochojejunostomy is performed.

Prior to April 1984, cyclosporine and prednisone were used for immunosuppression. Since then, cyclosporine, prednisone, and azathioprine have been used for immunosuppression. Intravenous cyclosporine at a dose of 3 mg/kg/24 hr is started after surgery. Oral cyclosporine is added as bowel activity resumes and the i.v. cyclosporine is tapered. A whole blood level of 200–350 ng/ml, as measured by high performance liquid chromatography, is maintained. Prednisone at 2 mg/kg is begun prior to transplantation and rapidly tapered to a maintenance of 0.2 mg/kg at 3 mo. Azathioprine is begun at a dose of 2 mg/kg and adjusted according to the white blood count.

A TRU CUT needle biopsy is performed at the time of revascularization, and percutaneous biopsies are obtained weekly until discharge. Subsequently, 6-mo and yearly biopsies are obtained. In the immediate postoperative period (usually within 24 hr of surgery) and subsequently as deemed necessary, radionuclide studies are performed using one of the iminodiacetic acid (IDA), derivatives labeled with technetium-99m. Initially, the studies were performed using labeled PIPIDA with a shift to diisopropyl IDA when this latter agent became available. For these studies, patients are placed supine below a large field-of-view scintillation camera fitted with a low-energy, all-purpose collimator and positioned such that the liver graft is located centrally within the left upper quadrant of the camera's field-of-view. The amount of radioactivity administered has ranged from 1 to 5 mCi depending upon the patient's age and/or weight with the 5 mCi dose used routinely in adults. When the dose that has been administered as an i.v. bolus appears in the abdominal aorta, data from the camera are entered into a computer and framed at 2-sec intervals for 1 min as a means for assessing blood flow to the graft. A 500k count image is then obtained of the blood pool in and around the graft. Data are

continually entered into the computer and framed at 30-sec intervals for 1 hr. Sequential digitized scintiphotos and/or graphic analyses of the uptake and clearance of radioactivity from the graft are generated from this data bank as desired. The time required at 5 min postinjection to obtain an analog image with 100k counts is used for that and all subsequent scintiphotos, usually obtained at 10, 15, 30, and 60 min. Analog images are also obtained at various times beyond 1 hr to 24 hr postinjection depending upon the need for such images as assessed from the pattern of extraction and excretion that is observed in each study. Ordinarily, only anterior views of the abdomen are recorded. However, other projections are obtained as deemed necessary when questions arise concerning bile leaks, radioactivity in the GU compared with the GI system, and the like.

RESULTS

Seventy-three patients have received orthotopic liver allografts since the introduction of this technique at our institution in 1968; these patients have ranged in age from 8 mo to 64 yr. During the first 5 yr of this effort, 11 patients received liver allografts with no recipient surviving more than 6 wk after transplantation. Due largely to these failures, no patients received a liver allograft for the next 4 yr during which time consider-

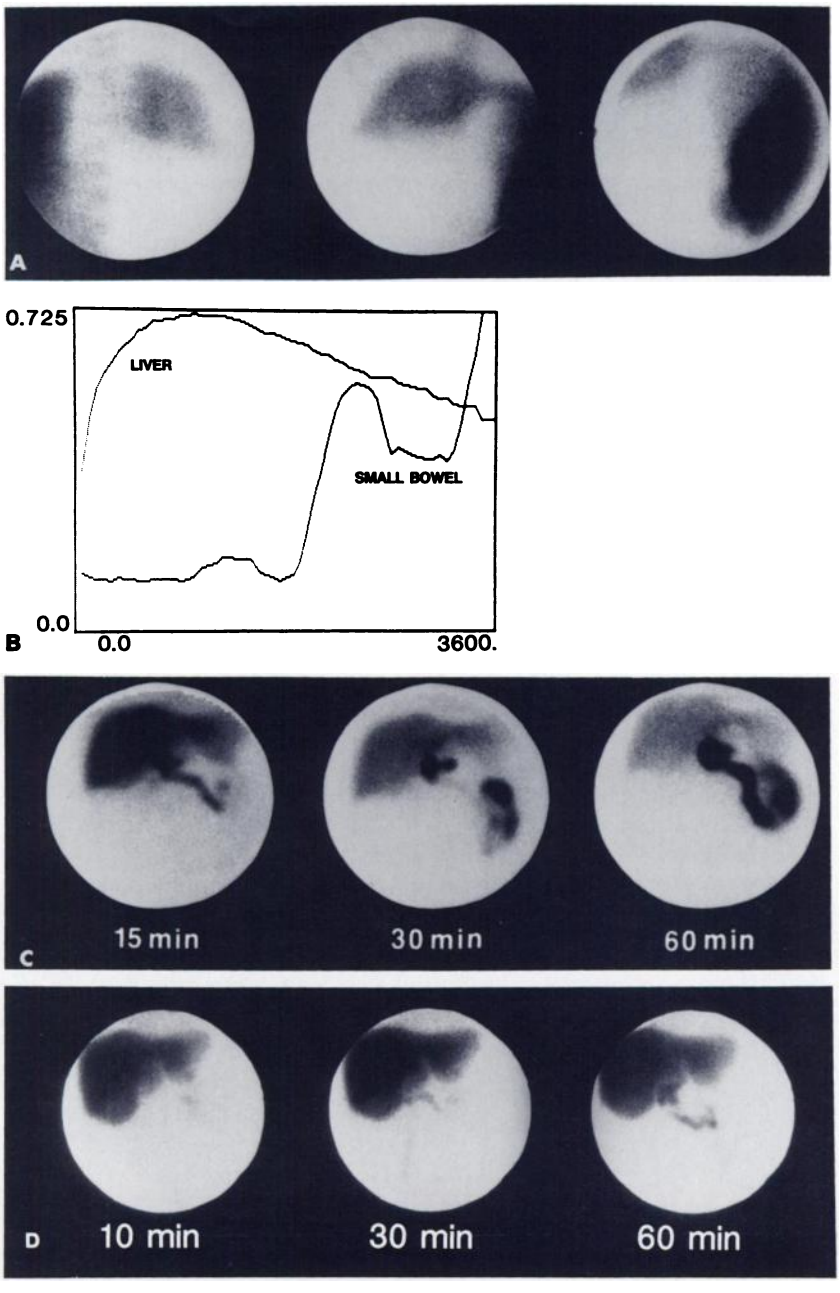

FIGURE 1
A: [^{99m}Tc]sulfur colloid study performed on 6-16-77 on young girl reveals small, poorly functioning liver with attendant ascites, bone marrow uptake, and marked splenomegaly. B: On 6-5-80, 1 mo following liver transplantation, these tracings of uptake and clearance of PIPIDA show graft to be functioning well. C: Selected scintiphotos from PIPIDA study of 6-5-80 also show good graft function. D: This PIPIDA study performed during episode of rejection shows delay in transit and clearance of radioactivity

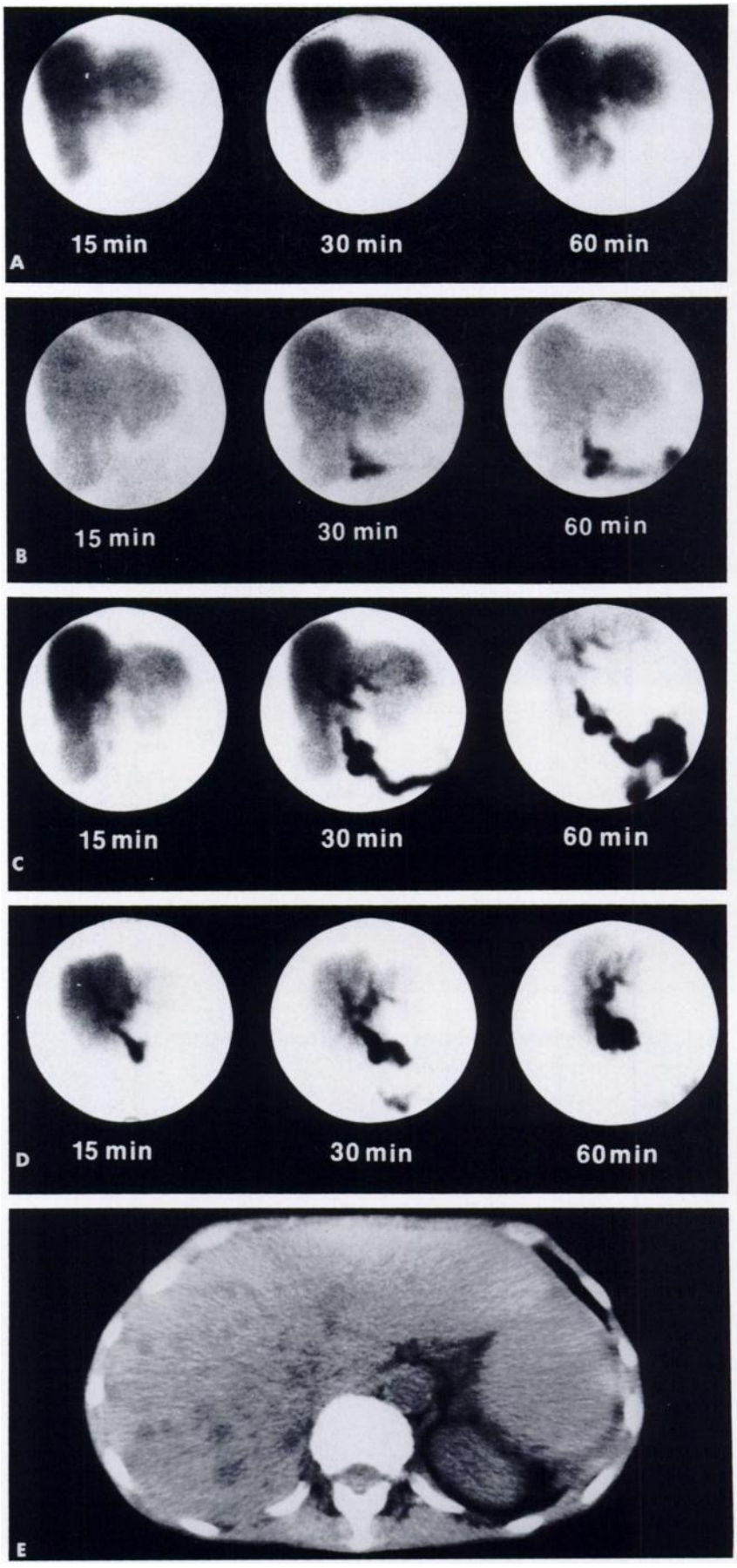

FIGURE 2
A: Diisopropyl IDA study performed 2 days after man had received liver transplant for treatment of cholangiocarcinoma reveals good graft function. Delay in passage or radioactivity into bowel is attributed to edema present at site of biliary anastomosis. B: One week later, this patient experienced episode of rejection as evidenced by marked delay in extraction, and, hence, in clearance of diisopropyl IDA. Some bowel activity is seen at 30 min indicating that edema at site of anastomosis has subsided. C: Following 2 wk of intensive antirejection therapy, graft function has returned to normal. D: Diisopropyl IDA study performed 1 yr after surgery shows excellent graft function. Some delay in transit is encountered secondary to tumor involvement of small bowel. Left lobe and inferior right lobe are poorly visualized for technical reasons. E: TCT examination performed shortly before patient died, reveals presence of multiple metastases in graft

able effort was spent in improving surgical technique and ascertaining means for minimizing various complications, the most notable being rejection. In 1979, a single patient received a graft that continued to function well for 5 mo before sepsis and hemorrhage combined with other complications led to the patient's demise. One of two transplants performed in 1980 continues to do well and is our longest survivor. Liver failure secondary to posthepatitis necrosis necessitated a graft placement in this patient. One of the two recipients of a liver transplant in 1981 succumbed 2 mo after surgery. The other survived for 14 mo during which time the liver allograft continued to function well despite a recurrent cholangiocarcinoma which led to death. Representative scans of these patients are presented as Case 1 and 2 of this report for the purpose of illustrating results from our "pre-cyclosporine" experience (Figs. 1 and 2).

With the availability of cyclosporine in 1982 to prevent rejection, the survival of our patients with liver allografts has improved significantly. Using cyclosporine and prednisone immunosuppression, 6-mo actuarial survival was 51%. Since triple therapy was introduced in April 1984, 35 patients have been transplanted with a 6-mo survival of 76%. A total of 57 liver transplants have been performed since 1982 with 33 of them alive and well at present. When each patient has stabilized after receiving a liver graft, a radionuclide liver function study is performed. These studies have been repeated as many as 15 times in several of our patients whose postoperative course has been complicated by one or more clinical problems, the most common ones being rejection and infection (Table 1). More than 200 of these radionuclide studies have been performed to date. Except for a few scans performed in 1980 and 1981 with PIPIDA, all have been done with [^{99m}Tc] diisopropyl IDA. In our experience, all conditions listed in Table 1 are identifiable on these scans in a manner similar to nontransplant cases except for rejection which, of course, does not occur without an allograft.

Two additional cases are presented here to illustrate our use of the IDA scan for evaluation of graft function in patients who are receiving both cyclosporine and prednisone. The first of these involves an 11-mo-old white female with congenital biliary atresia. A Kasai procedure at an outside hospital was not successful. A liver transplant was performed on November 5, 1982. Various studies performed in the care of this patient are shown (Figs. 3A-E). Postoperatively, the graft has continued to function quite well up to the present time although in the early postoperative period the patient experienced fever, jaundice, and elevated liver function enzymes. She failed to respond to antimicrobial antibiotics. A hepatobiliary study performed at that time (Fig. 3D) showed evidence of retention of radioactivity within the graft several hours postinjection. This pattern was thought to be compatible with but not pathognomonic of rejection. A liver biopsy revealed focal hepatocellular necrosis indicative of a viral hepatitis and highlights the inability of the IDA scan to differentiate among the various causes of hepatocellular dysfunction. The patient responded satisfactorily to a 2-wk regiment of acyclovir therapy with return to essentially normal liver function within the next several weeks. Subsequently, the patient experienced a second febrile episode (fever up to 104°). A diisopropyl IDA study performed at that time showed continued normal function despite a bacterial infection that was successfully treated with antibiotics. Followup hepatobiliary studies on November 7, 1984 and October 24, 1985 (not presented here) have continued to show essentially normal liver function.

TABLE 1
Complications Among 56 Liver Graft Recipients from August 1982 Through September 1985

Item	No. of occurrences*	No. of deaths†
Rejection	30	5
Infection	27	12
Vascular Compromise	7	3
Bile Duct Stenosis	6	2
Tumor (Recurrent)	2	2
Biliary Leak	2	1
Hemorrhage	1	0

* Most patients had more than one complication.
† Indicates principal cause of death.

The final case included here involves a white girl in whom the diagnosis of biliary atresia was made at the age of 2 mo. A Kasai procedure was performed which functioned well for several months until the patient developed ascending cholangitis with E-coli sepsis and a liver abscess. Because of ascites, hepatosplenomegaly and continued liver dysfunction, a liver transplant with a concomitant splenectomy was performed on April 28, 1983. Selected post-transplant studies on this patients are shown (Figs. 4A–C). These illustrations indicate that the graft has functioned well except in the immediate postoperative period at which time the presence of edema at the site of the biliary-jejunal anastomosis caused some delay in clearance of radioactivity. During more recent clinical visits (March 17, 1984 and April 30, 1985) repeat IDA studies (not included here) have shown a continuation of normal hepatic function.

DISCUSSION

The evaluation of hepatic function using techniques of nuclear medicine began in 1955 at which time iodine-131 ([^{131}I]) rose bengal was introduced by Taplin et al. (*10*). The administration of rose bengal followed by

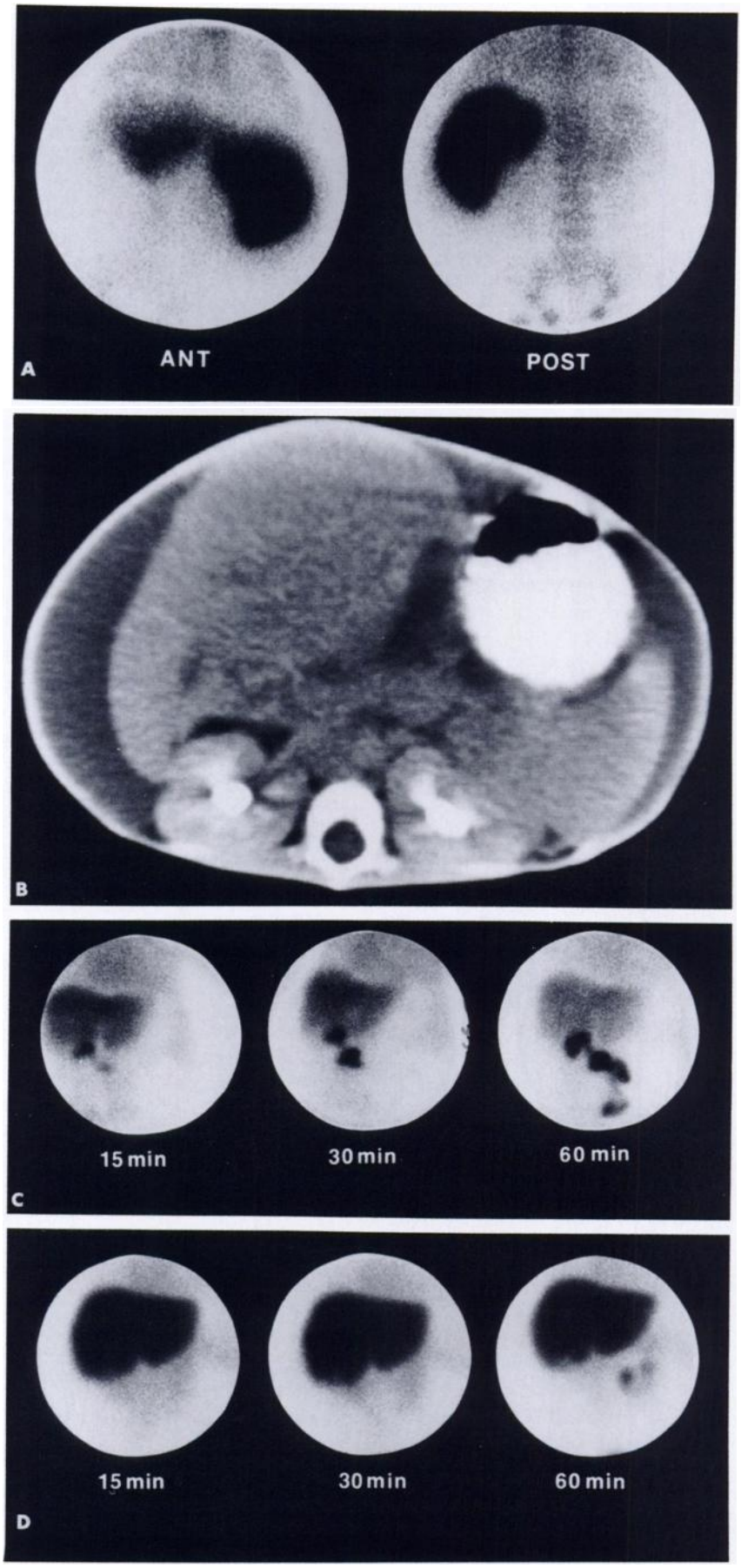

FIGURE 3
A: Liver-spleen scan performed with [^{99m}Tc]sulfur colloid on infant girl with biliary atresia, reveals shrunken liver with poor uptake, splenomegaly, and ascites. B: TCT examination also performed at that time (9-24-82) provides further evidence of the sequellae of hepatic failure. C: Diisopropyl IDA study performed 3 days after liver transplantation shows graft to extract well with gradual passage of radioactivity into small bowel through choledochojejunostomy. D: Diisopropyl IDA study performed during bout with viral hepatitis (11-21-82) shows good extraction but marked retention of radioactivity within liver. Retention persisted for several hours postinjection

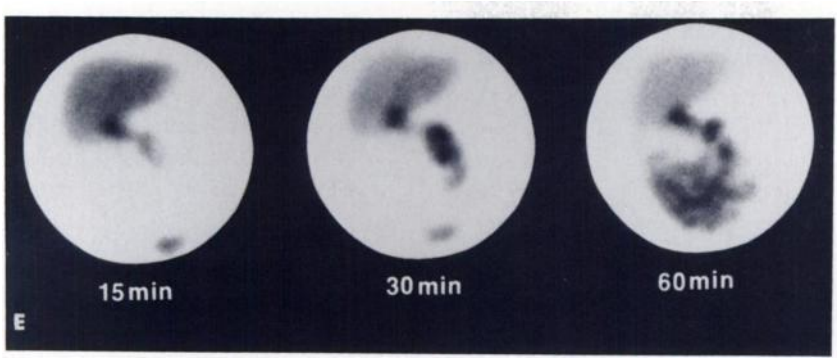

FIGURE 3
E: Following 2-wk regimen of acyclovir therapy, graft function has returned to normal as seen on diisopropyl IDA study on 1-31-83

imaging and/or stool collections has permitted hepatocellular disease to be distinguished from an obstruction (partial or complete) of the common bile duct. Its major use has been in differentiating neonatal hepatitis from biliary atresia. Rose bengal was also employed by Klingensmith et al. in some of their early investigations of liver transplants (*6,7*). Although the results of these various studies with rose bengal have proven to be clinically useful, the relatively high radiation dose to the patient and the poor imaging characteristics of ^{131}I have prevented wide acceptance of this procedure. In the early 1970s various organic compounds, such as

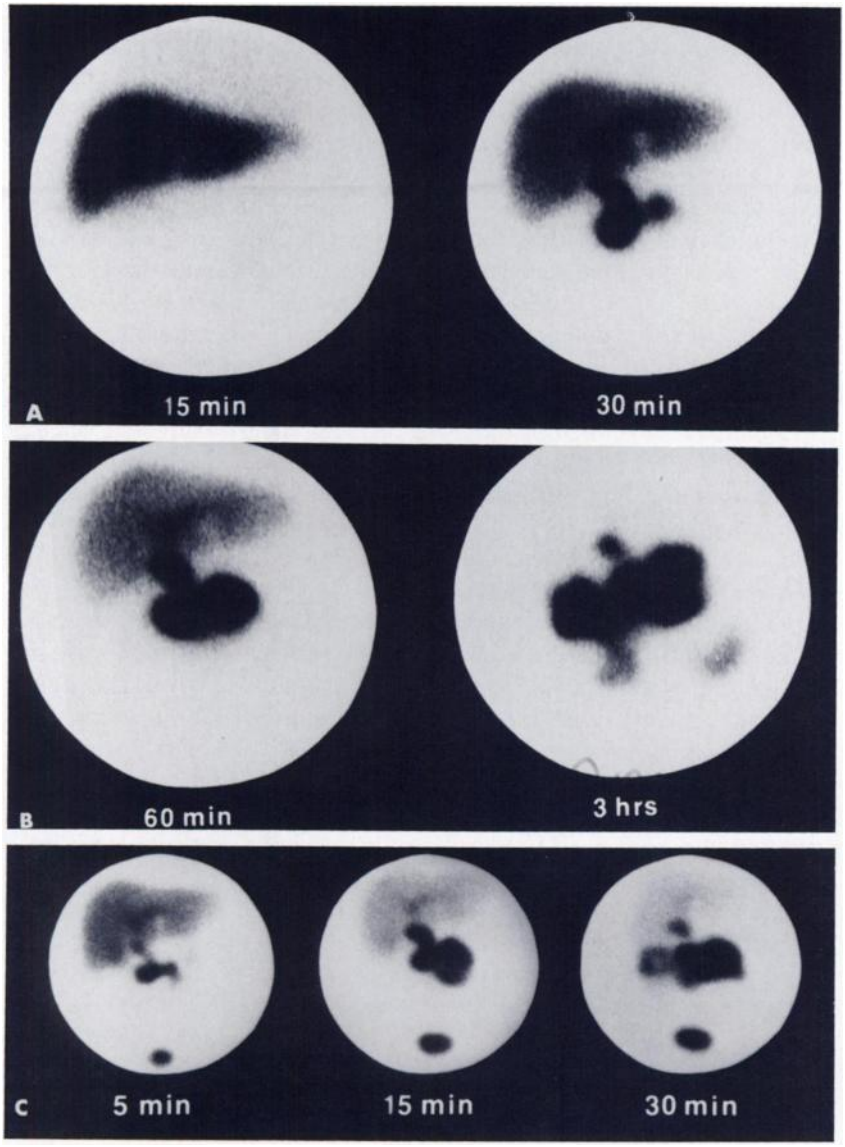

FIGURE 4
A: Diisopropyl IDA study performed on infant shows excellent extraction by liver graft but significant retention of radioactivity at site of biliary anastomosis. B: Delayed images up to 3 hr from study of 5-2-83 reveal gradual passage of radioactivity into small bowel. C: Repeat diisopropyl IDA study performed 4 days later shows that edema at anastomotic site has subsided and bowel transit is essentially normal

pyridoxylidine glutamate and dihydrothioctic acid were employed. Their potential for evaluation of liver function was immediatley recognized. However, problems associated with stability of many of these ^{99m}Tc-labeled compounds, as well as with their excretion, in part by the kidneys, particularly in instances of impaired hepatocellular function, has served as a deterrent to their clinical use at various centers including our own. In addition, their distribution and pharmacokinetics appear to depend more upon the concentration of serum bilirubin than on liver function.

Following the introduction of the IDA group by Loberg's group in 1975 (*11*), rapid strides have been made in "perfecting" a radiotracer for assessment of hepatocellular function in both native and transplanted livers (*6,7,12*). The first of these agents developed by this group was ^{99m}Tc (6-dimethylphenylcarbamoylmethyl) iminodiacetic acid [^{99m}Tc]dimethyl IDA). The complexation of reduced ^{99m}Tc with this agent using stanous chloride as a reductant at room temperature is similar to the well-established preparation of various other radiopharmaceuticals labeled with ^{99m}Tc.

The desirable biliary imaging characteristics of ^{99m}Tc-labeled dimethyl IDA spurred interest in the development of other derivatives of N-substituted iminodiacetic acids. The properties of these various agents have been tested extensively in a variety of laboratories throughout the world. It appears at present, that the diisopropyl IDA derivative (disofenin) because of its somewhat longer substituted side chain allows for increased biliary excretion and visualization of the hepatobiliary system at somewhat higher serum bilirubin levels (approaching 20 mg/dl) than has been possible with the shorter chain derivatives such as dimethyl IDA or PIPIDA (p-isopropyl IDA) (*11–13*).

The rate at which a liver graft accumulates and ultimately excretes the various IDA derivatives provides a sensitive indicator of hepatocyte function (*6–12*). Because of this attribute together with its use in assessing the integrity of biliary drainage, it is employed routinely at our institution to evaluate the liver graft within 48 hr after transplantation. Subsequently, it is used for routine follow-up as well as an aid in the assessment of one or more of the postoperative complications listed in Table 1. As indicated in this table, rejection and infection are the two most common complications observed among our liver graft recipients. Both may cause a significant reduction in hepatocyte function and thus both may markedly depress the uptake and clearance of labeled IDA by the liver. This in turn leads to enhanced renal excretion of the radiotracer which must be differentiated from that appearing in the abdomen secondary to excretion by way of the biliary system. The presence of radioactivity in the kidneys, particularly on the right side, must be taken into account when selecting a region of interest from which a tracing of uptake and clearance of tracer by the liver graft is to be generated.

Since rejection and disease states such as viral hepatitis and ascending cholangitis all depress hepatocyte function and consequently alter the IDA scan study in a similar manner, a second diagnostic procedure, the percutaneous liver biopsy, is routinely employed in these instances because of its diagnostic accuracy. Microscopic evaluation of the biopsy specimen aids in the differentiation of the various causes of hepatocellular injury and thus improves the overall specificity of our diagnostic testing. Unfortunately, the biopsy is not without finite risk. Although we have not experienced patient death following biopsy (>250 biopsies total), blood transfusions have been necessary in three instances to correct a fall in hemoglobin with an associated mild hemodynamic instability.

The various complications observed following placement of liver grafts are summarized in Table 1 along with their frequency of occurrence and their effect on clinical outcome. Rejection, the most frequent complication, was experienced in more than half of our patients. Infections, either bacterial or viral (or both) were found in 27 of patients with liver grafts and led to the demise of 12 of them. It was in these two groups of patients that the liver biopsy was used most frequently. The other complications listed in Table 1 are usually readily identifiable using the IDA scan. Quantitation of the initial uptake of radioactivity into the graft and examination of the blood-pool images yields information regarding the adequacy of the arterial and portal venous supply to the liver. Compromises in arterial or in portal venous flow were demonstrated in two and three of our patients, respectively. Although vascular occlusion may be secondary to acute rejection as was recently reported (*14*), our experience indicates that technical problems, such as stenosis at a site of anastomosis, are much more likely to be the cause of a vascular compromise.

In instances of biliary stenosis and/or obstruction, the finding on the IDA scan has been quite specific. The extraction (uptake) of radioactivity of the graft is usually good whereas excretion is delayed. Scintiphotos obtained a half-hour or more after administration of the tracer show clear evidence of parenchymal retention with gradual filling of dilated biliary radicals. It is in these instances that graphic analyses are particularly useful as a reliable means for assessing functional changes occurring in sequential studies. If the integrity of biliary outflow is compromised as with a leak at the anastomotic site, the appearance of radioactivity in the peritoneal cavity is easily identified.

The presence of a mass lesion within the liver has been detected from scintiphotos obtained during the first few minutes after administration of an IDA agent. The usual cause of a mass effect has been hemorrhage,

although a mass secondary to recurrent tumor was found in one case. By use of other information (earlier scans, clinical history, or knowledge of a recent liver biopsy, etc.), it is usually possible to determine the etiology of a mass although CT is more commonly employed for this purpose.

CONCLUSION

The IDA scan presently performed at most institutions using the diisopropyl derivative labeled with ^{99m}Tc is a sensitive indicator of hepatic blood flow, hepatocyte function, and biliary drainage, and permits mass lesions of the liver to be identified. As such, this procedure is employed early on in the evaluation of our patients with liver transplants. However, this test does not permit a differentiation to be made of various causes for depressed graft function, and a liver biopsy is required to establish specific diagnosis. Nevertheless, because of its sensitivity in the detection of the various abnormalities associated with liver transplants and the noninvasive nature of this test, the IDA scan is a diagnostic modality that is routinely used to serially monitor the hepatic graft.

ACKNOWLEDGMENTS

The authors thank Salma Mikhail, MD for assistance in the selection of the case material and Ms. Judy Thompson and Mr. Steven Anderson for assistance in the preparation of this manuscript.

REFERENCES

1. Starzl TE, Marchioro TL, VonKaulla KN, et al: Homotransplantation of the liver in humans. *Surg Gynecol Obstet* 117:659–676, 1963
2. Starzl TE, Iwatsuki S, VanThiel DH, et al: Evolution of liver transplantation. *Hepatology* 2:614–636, 1982
3. Bloomer J, Ascher NL, Najarian JS, et al: Liver transplantation. In *Research Advances, Opportunities, and Needs in Digestive Diseases: A Report of the Nat'l Digestive Diseases Advisory Board*, McGuigan JE, Trier JS, eds. U.S. Dept. of Health and Human Services, NIH Publication No. 84-2658, Oct. 1983, pp. 113–117
4. Ascher NL, Najarian JS: Hepatic transplantation and biliary atresia: Early experience in eight patients. *World J Surg* 8:57–63, 1984
5. Najarian JS, Ascher NL: *Current Status of Liver Transplantation.* Najarian JS, Delaney JP, eds. Chicago, Year Book Medical Publishers, Inc., pp 433–440, 1984
6. Klingensmith WC, Fritzberg AR, Koep LJ, et al: A clinical comparison of ^{99m}Tc-diethyl-iminodiacetic acid, ^{99m}Tc-pyridoxylideneglutamate and ^{131}I-rose bengal in liver transplant patients. *Radiology* 130:435–441, 1979
7. Klingensmith WC, Fritzberg AR, Koep LJ: Comparison of Tc-99m diethyl-iminidiacetic acid and I-131 rose begnal for hepatobiliary studies in liver transplant patients: Concise communication. *J Nucl Med* 20:314–318, 1979.
8. Loken MK, Ascher NL, Mikhail S, et al: Functional imaging of liver transplants. *J Nucl Med* 24:P98–99, 1983 (abstr)
9. Rosenthal JT, Shaw BW, Hardesty RL, et al: Principles of multiple organ procurement from cadaver donors. *Ann Surg* 198:617–621, 1984
10. Taplin GV, Meredith OM, Kade H: The radioactive I-131 tagged rose bengal uptake excretion test for liver function using external gamma ray scintillation counting techniques. *J Lab Clin Med* 45:665–678, 1955
11. Harvey E, Loberg MD, Cooper M: A new radiopharmaceutical for hepatobiliary imaging. *J Nucl Med* 16:533, 1975
12. Chervu LR, Nunn AD, Loberg MD: Radiopharmaceuticals for hepatobiliary imaging. *Semin Nucl Med* 12:5–17, 1982
13. Klingensmith WC, Fritzberg AR, Spitzer VM, et al: Clinical evaluation of Tc-99m-trimethylbromo-IDA and Tc-99m diisopropyl IDA for hepatobiliary imaging. *Radiology* 146:181–184, 1983
14. Williams HC, Pope CF, Siskind BN, et al: Vascular thrombosis in acute hepatic allograft rejection: Scintigraphic appearance. *J Nucl Med* 26:478–481, 1985