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**Case No. 8**

**LIVER AND SMALL BOWEL TRANSPLANTATION  
FOR SHORT GUT SYNDROME  
IN A CHILD**

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A 3 year old girl was referred to us for treatment of short gut syndrome and liver failure secondary to chronic administration of total parenteral nutrition (TPN).

Shortly after birth, the child underwent resection of the small bowel distal to the ligament of Treitz and ascending colon for necrotizing enterocolitis and was placed on TPN. At the age of two years she developed hypersplenism for which she underwent splenectomy. Two months later she underwent cholecystectomy and common bile duct exploration for progressive jaundice. Other surgeries included a fundoplication at the age of two months and multiple TPN line placement and removal procedures.

At the time of her referral to us she was jaundiced (total bilirubin 14 mg %) and had overt signs of portal hypertension including bleeding esophageal varices not controllable with sclerotherapy.

An appropriate donor (Table 1) became available and a combined liver and small intestinal transplant was performed.

TABLE 1

	<i>DONOR</i>	<i>RECIPIENT</i>
Sex	Female	Female
Age	31 months	38 months
Weight	12 kg	12.4 kg
Height	86 cm	87 cm
ABO Type	O	O
HLA Type	A2, 28, B57, 60	A19, 24, B13, DR6, 7, BW4, 6
CMV Status	(+)	(-)

**DONOR**

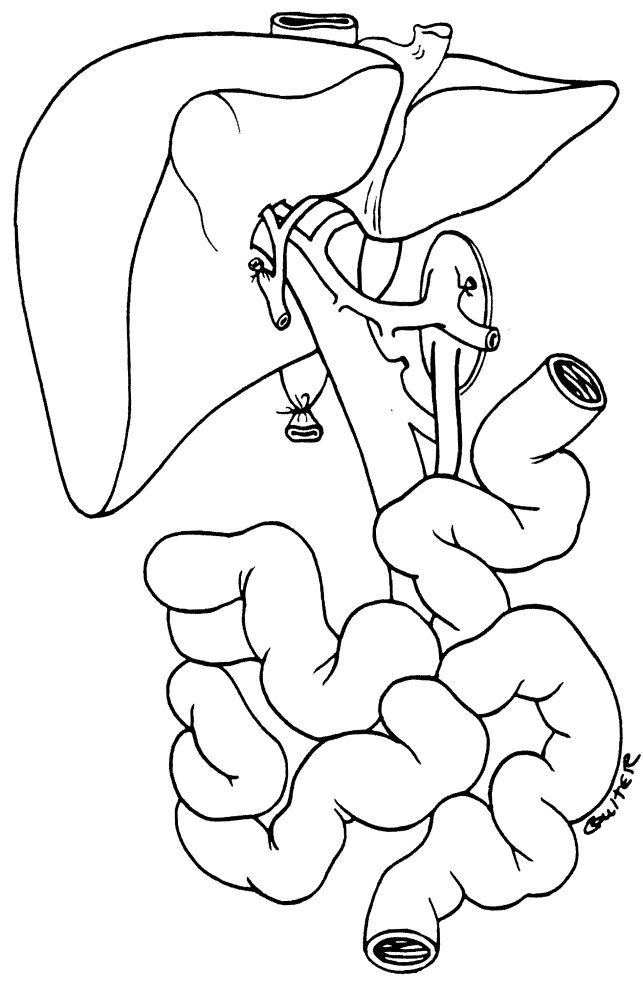


Fig. 1. Composite liver-intestinal graft.

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*The donor operation.* The graft included the liver and entire small intestine distal to the ligament of Treitz and was procured using a modification of the "Flexible Procedure for Multiple Cadaveric Organ Procurement."\* The pancreas and duodenum were stripped off the SMV and SMA. An aortic patch containing the ostia of both celiac axis and SMA was included in the specimen (Fig. 1). Cooling of the graft was started in situ through the aorta and splenic vein and completed with

\*Surg Gynec Obstet 1984; 158: 223-30

## RECIPIENT

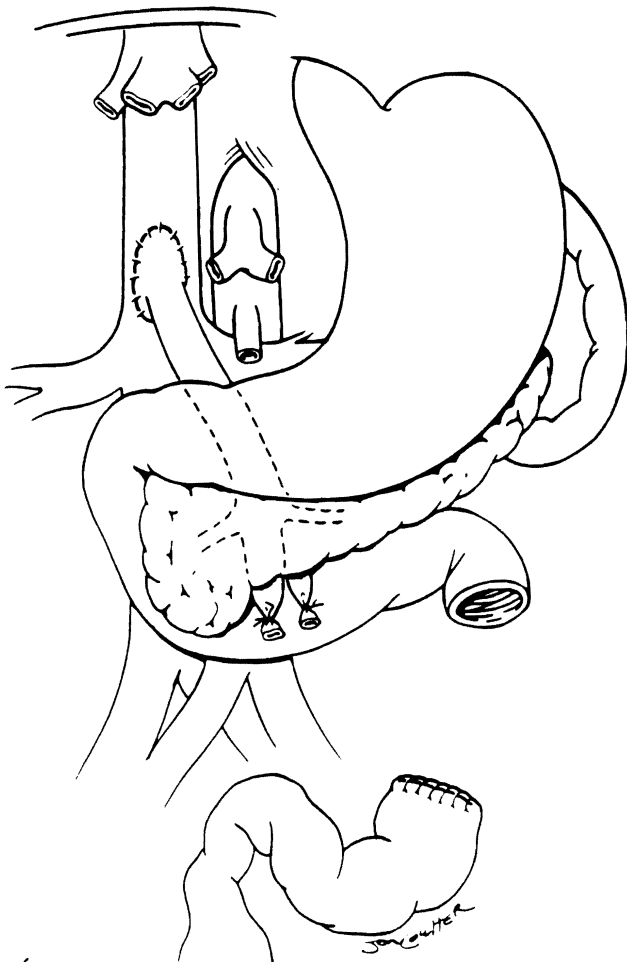


Fig. 2. The recipient after hepatectomy. Note the end-to-side portacaval shunt onto the native vena cava which was preserved.

a back table flush of the liver through the splenic vein cannula. UW solution was used at the preservation fluid.

*The recipient operation.* The recipient operation was performed through a cruciate abdominal incision. After the hilar structures of the liver were identified, an end-to-side portacaval shunt was performed and then a total hepatectomy with preservation of the native inferior vena cava (Fig. 2).

The outflow of the graft was by an end-to-end anastomosis of the donor suprahepatic cava onto the opening created by joining the ostia of the left and middle hepatic veins. The right native hepatic vein was oversewn. The donor infrahepatic cava was ligated. The arterial patch with the celiac artery and SMA was implanted onto the infrarenal aorta of the recipient which was exposed after the duodenum had been Kocherised (Fig. 3).

Mature stomata were created using the two ends of the intestinal graft. The distal end of the recipient duodenum was connected end-to-side to the graft, just below the proximal stoma.

Biliary drainage was accomplished with a choledocho-jejunostomy into a Roux-en-Y loop created with donor jejunum. Complete GI continuity was established two months after transplant, at which time the proximal stoma was closed and the distal was connected to the colon (ileocolostomy) (Figs. 4 and 5).

*Immunosuppression.* Immunosuppression was accomplished with FK506 which was given intravenously for four weeks and then orally---except perioperatively at the time of the closure of the stomata, at which time a short course of intravenous FK506 was administered. Prednisolone (10 mg/day) was given intravenously for eight days after transplantation. A single bolus of 500 mg of hydrocortisone was given on the twenty-seventh

TABLE 2

### PREVENTION OF INFECTION

DONOR: Intestinal Decontamination, N.G.:

Amphotericin  
Mycostatin  
Tobramycin  
Polymycin

SYSTEMIC ANTIBIOTICS:

Cefotaxime  
Ampicillin

RECIPIENT: Intestinal Decontamination, P.O/N.G.:

Mycostatin  
Tobramycin  
Amphotericin  
Polymycin

## HOOK-UP

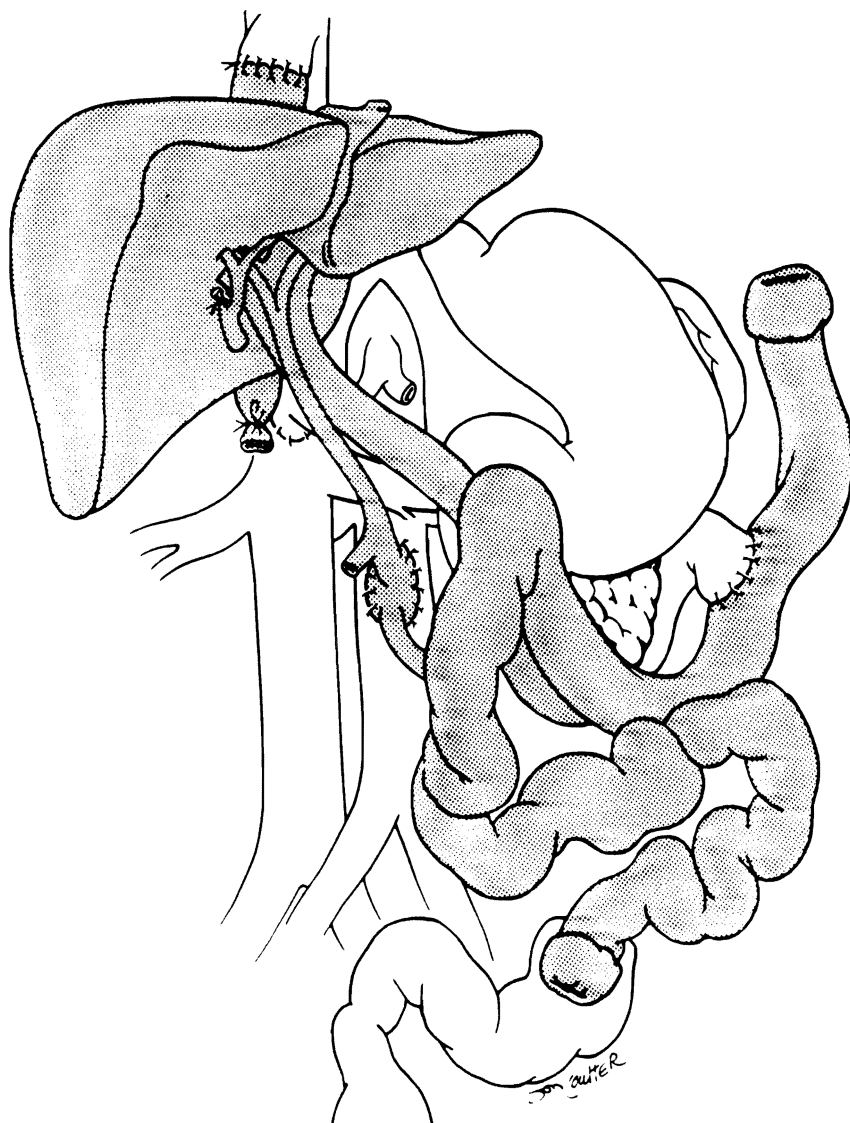


Fig. 3. Anastomosis to the recipient abdominal aorta and vena cava.

postoperative day (POD) and again on PODs 34 and 48 (Fig. 6).

*Prevention and treatment of infection.* Intestinal decontamination was performed for both donor and recipient (Table 2). Only one dose could be given to the donor via a nasogastric tube. The recipient received intestinal decontamination for six months. Intravenous antibiotics used for the treatment of bacteremias, which the patient was found to have pretransplantation, were

continued. The patient developed other bacteremias after transplantation which were also treated with intravenous antibiotics (Table 3). Cytomegalovirus (CMV) viremia and donor enteritis was detected at 3 1/2 months and was treated with a 14 day course of DHPG.

*Biopsies.* A liver biopsy performed at three months showed significant steatosis but no evidence of rejection. The biopsy was repeated at six months and showed evidence of mild rejection but not the previously noted



Fig. 4. UGI series after GI continuity was established. Note a barium cholangiogram from reflux into the Roux Y loop.

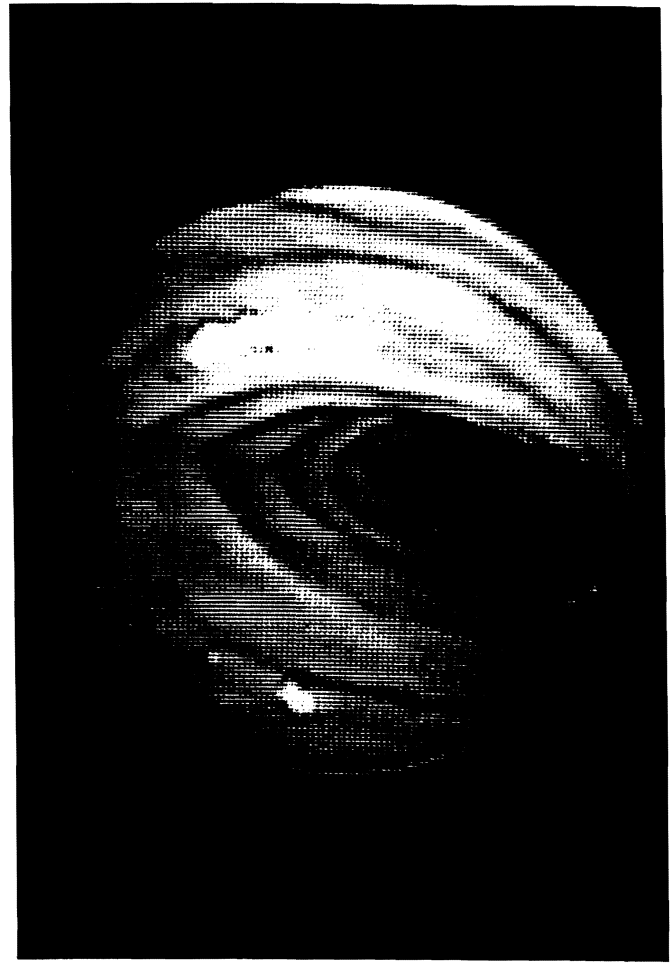


Fig. 5. Endoscopic photograph of donor jejunum.

TABLE 3  
TREATMENT OF INFECTION

<i>INFECTION</i>	<i>ORGANISM</i>	<i>TREATMENT</i>
<b>PRETRANSPLANT</b>		
1. Catheter-associated bacteremia, POD 51	Staphylococcus aureus	Nafcillin IV
2. Polymicrobial bacteremia, POD 5	Staphylococcus aureus	Vancomycin IV
	Eschericia coli	Cefotaxime IV
	Acinetobacter sp.	
<b>POSTTRANSPLANT</b>		
1. Bacteremia, POD 15	Enterococcus sp.	Vancomycin IV*
		Ampicillin IV
		Vancomycin PO
2. Enteritis, POD 30	Cytomegalovirus	Ganciclovir IV
3. Bacteremia, POD 38	Coagulase neg. Staph.	Vancomycin IV
4. Bacteremia, POD 47	Coagulase neg. Staph.	Vancomycin IV#
		Vancomycin PO#
5. Bacteremia, POD 49	Streptococcus pneum.	Vancomycin IV#

\*Patient developed this infection while still on Vancomycin for treatment of pretransplant infection.

#Patient developed both of these episodes of bacteremia while receiving intravenous Vancomycin for treatment of infection number

3. Oral Vancomycin was added when coagulase negative staphylococci were found in her stool.

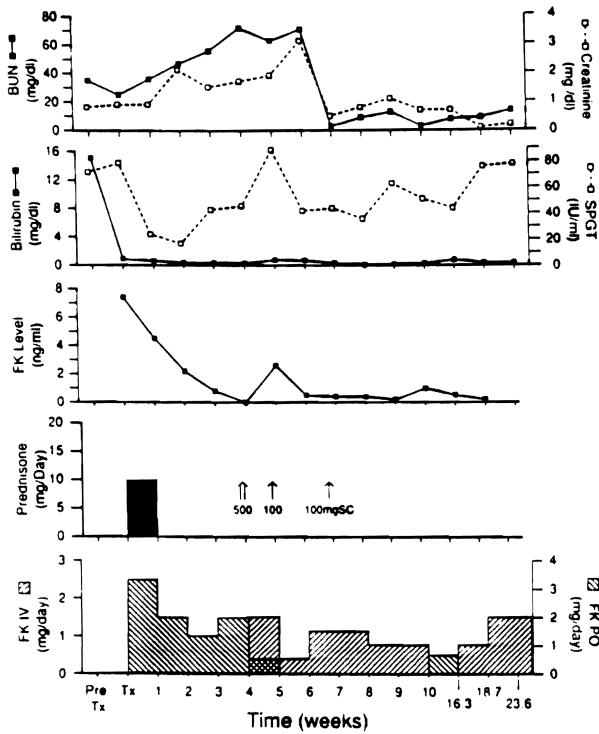


Fig. 6. Liver and kidney function tests and immunosuppression.

steatosis.

Intestinal biopsies were obtained 8 days, 3 weeks and 3 1/2 months after transplantation. The first intestinal biopsy showed a mixed infiltrate at the stroma which consisted of lymphocytes, eosinophils and some plasma cells with a distortion of the villous architecture, but the epithelium was intact. These changes resolved on subsequent biopsies (Fig. 7). The latter biopsy showed CMV inclusion bodies (not shown in figure).



Fig. 7. Intestinal biopsy at 3 1/2 months.

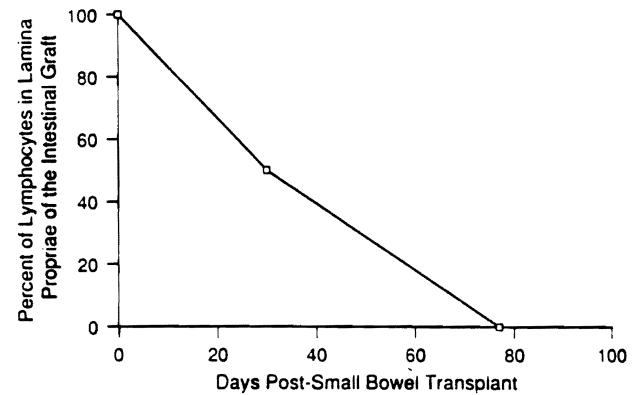
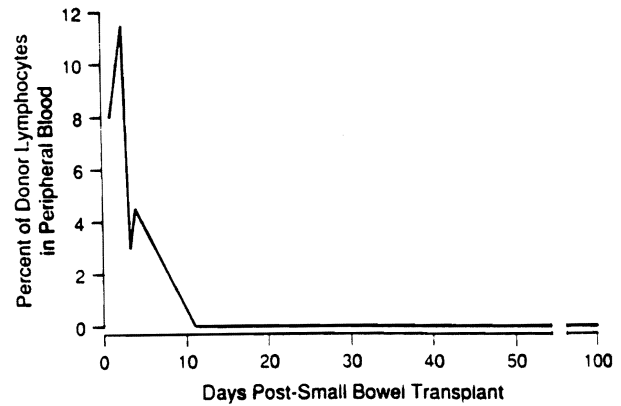


Fig. 8. Percent of donor lymphocytes in A) peripheral blood and B) lamina propriae of the intestinal graft.

**Immune monitoring.** HLA phenotypes of lymphocytes from lamina propriae of the intestinal biopsies as well as peripheral blood smear were identified with immunocytochemical techniques employing monoclonal antibodies. The results of these studies are shown in Figures 8A and 8B (by permission of Iwaki).

Immune monitoring demonstrated a two way traffic of lymphocytes between donor and recipient, which settled with the establishment of recipient lymphocytes in the lamina propriae of the intestinal graft and disappearance of the donor lymphocytes from the peripheral blood of the recipient.

**Other laboratory studies.** CBC, electrolytes, BUN, serum creatinine, total bilirubin, SGOT, SGPT, alkaline phosphatase, serum albumin and globulin were followed daily while the patient was in the hospital and

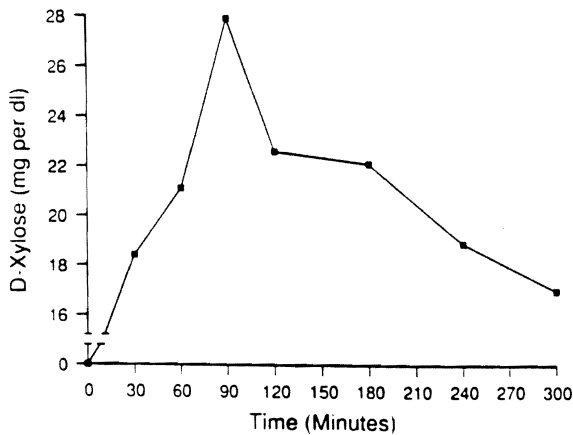


Fig. 9. D-xylose absorption study at three weeks posttransplantation.

once or twice weekly thereafter. Serum FK506 levels were obtained once or twice weekly. Representative values are shown in Fig. 6.

**Nutrition.** Parenteral nutrition was maintained after transplantation. Starting at two weeks after transplantation, enteral feedings were given through the proximal stoma at increasing quantity and concentration. TPN was completely replaced by oral and enteral feedings at two months after transplantation.

The patient's weight, 12.4 kg at the time of the transplantation, is now—six months later—14 kg. Her height, 83 cm initially, is now 93 cm.

A D-xylose absorption study at three weeks after transplantation via the central stoma was normal (Fig. 9). Fecal fat excretion at four months was 8.85 (normal 0-8.8%).

Serum ferritin at 3 1/2 months after transplantation was 135 ng/ml (normal 12-250 ng/ml).

**Technical complications.** Due to the large size of the graft, the fascia could not be safely approximated in the midline. Simple skin closure was performed which resulted in dehiscence. The latter was treated with packing. The wound epithelialized, and the patient currently has a small midline incisional hernia.

**Clinical course.** The postoperative course was complicated by fevers which lasted for 1 1/2 months and for which several causes were either suspected or identified. These included the previously described bacteremias, CMV infection, rejection and perhaps the lymphocytic migration.

The patient was discharged from the hospital three months after transplantation and has remained at home with the exception of short hospital stays for biopsies.

### Commentary

Vivian McAlister and David Grant

This case is a remarkable surgical achievement. It illustrates the potential for small bowel and liver grafting as a treatment of short gut syndrome in patients with or without liver failure. Isolated small bowel transplantation has been unsuccessful due to the inability to control rejection.<sup>1</sup> Only two patients have had prolonged intestinal graft survival and neither is free of parenteral support.<sup>2,3</sup> This is the second report of successful small bowel and liver grafting and the first report of this procedure in a child. Successful combined small bowel and liver transplants were performed in two adults at our institution 18 and 30 months ago.<sup>4</sup> Like the case reported here, these patients are on regular diets and they require no parenteral support. Three questions raised by this experience are reviewed below.

What is the best surgical procedure for transplanting the small bowel and liver together? The abdominal cavity may be very small in patients that have had massive intestinal resections. To avoid problems with size discrepancies as reported in this case, the small intestine/liver graft should probably be obtained from a donor 30-50 percent smaller than the recipient. The piggy-back technique described by Tzakis and colleagues allows transplant surgeons to easily manage large size differences of the donor and recipient vena cava. Creation of a portacaval shunt prior to the transplant maintains venous return from the native gastrointestinal tract during the anhepatic phase of the operation without the need for venovenous bypass. However, this technique deprives the transplanted liver of hepatotrophic substances from the native pancreas. So we have preferred to anastomose the end of the native portal vein to the side of the intact donor portal vein.<sup>4</sup>

Exteriorization of both ends of the intestinal graft as described in this case may be unnecessary. More than 50 small bowel transplants were performed in our laboratory in pigs with no leakage from primary intestinal anastomoses.<sup>5</sup> Anastomosis of the proximal end of the intestinal graft to the native gastrointestinal tract may optimize graft function by exposing the transplanted gut to the nutrient factors in the succus entericus. Creation of a distal stoma provides an easy route to biopsy the graft. However, in our experience, mucosal biopsies are unreliable for the early detection of rejection due to the patchy nature of this process.<sup>6</sup>

Does the liver contribute to small bowel allograft survival by enhancing immunosuppression and tolerance? The immunosuppressive effects of liver trans-

plantation have been demonstrated in both animals and humans. Liver grafting produces clonal deletion of cytotoxic T cells,<sup>7</sup> enhancement of anti-class II MHC antibodies<sup>7</sup> and release of soluble donor immunosuppressive class I antigens.<sup>8</sup> Long term hepatic graft survival without immunosuppression is commonly seen in the pig and in certain inbred rat strains whereas other organs such as skin, heart and kidney are acutely rejected.<sup>7,9</sup> In these animals, simultaneous liver grafting induces a state of donor specific unresponsiveness which permits transplantation of skin, heart and kidney grafts without immunosuppression.<sup>8,10</sup> Similar effects may occur in man. Fung et al have reported that simultaneous liver transplantation permits successful kidney transplantation in patients with preformed cytotoxic antibodies.<sup>11</sup> Gonwa et al have reported a much lower rate of kidney rejection in patients with simultaneous liver grafts.<sup>12</sup>

Whether simultaneous liver grafting protects the intestinal graft from rejection is still unclear. We have recently demonstrated that simultaneous liver transplantation prevents intestinal allograft rejection in a low-responder rat strain combination. However, many of the animals in this study died of graft-versus-host disease.<sup>13</sup> Another study using a high-responder rat strain combination and a multivisceral transplant model showed that simultaneous liver grafting did not protect the intestinal allograft from rejection.<sup>14</sup> Further experiments are needed to clarify the complex immunological responses associated with multivisceral grafting.

Why is sepsis so common after intestinal grafting? This patient had many infections as did the patients that were transplanted at our institution. Small bowel and liver recipients may require less immunosuppression than usual.<sup>15</sup> The reduced need for antirejection therapy may be due to the immunosuppressive effects of simultaneous liver grafting as described above. Alternatively, host immune defenses may be compromised by occult graft-versus-host disease caused by the large numbers of lymphocytes in the combined graft.<sup>16</sup> Finally, bacterial translocation from the rejecting intestinal allograft may contribute to host infections after small bowel transplantation.<sup>17</sup>

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