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Small Bowel Transplantation

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Introduction

Permanent intestinal failure was a challenging clinical entity for decades. The introduction of total parenteral nutrition (TPN) by Dudrick in 1968 opened a new horizon of life support for patients once considered to have terminal prognoses. Unfortunately, chronic, prolonged TPN is not without hazards; eventually the majority of TPN-dependent patients lose their liver secondary to TPN-induced cholestasis and subsequent irreversible liver damage. Isolated orthotopic liver transplantation is not indicated, since the need for TPN will persist, with subsequent damage to the new liver. Venous access for delivery of TPN can be a serious problem, especially in children, in terms of both line sepsis and venous site availability. Long-term expenses for lifetime home/hospital TPN is an added limitation.

Although the small bowel was part of the composite of organs to be experimentally transplanted early in the 1960s, it is the last transplantation to be clinically successful. Rejection, infections, and technical complications were the main obstacles to earlier success. Thirty years of experimental and clinical research preceded the successful series of small bowel transplantations at the University of Pittsburgh (39 patients through March 1993). Technical refinement, innovative immunosuppression, and better postoperative management will help achieve a reproducible, consistent cure. Small bowel can be transplanted alone, combined with a liver transplant, or transplanted as part of multivisceral graft. The cecum, ileocecal valve, and colon can also be included.

Indications for Small Bowel Transplantation

Failure to support bodily needs through water and caloric intake by enteral route alone mandates small bowel transplantation. Causes include short gut syndrome, dysfunctional small bowel, and some non–short gut/nondysfunctional conditions.

SHORT GUT SYNDROME

The minimum length of small bowel necessary to maintain adequate enteral absorption of water and nutrients is not well established. It varies between 10 and 20 cm in presence of ileocecal valve and colon and 40 cm without them.

DYSFUNCTIONAL SMALL BOWEL

Dysfunction in the small bowel may be due to either absorptive insufficiency (e.g., microvillous inclusion enteropathy) or motility disorders, including total intestinal aganglionosis (total Hirschsprung's disease), defective ganglionosis, and intestinal pseudo-obstruction (microcolon, megacystis syndrome, holovisceral myopathy or Sieber syndrome).

NON–SHORT GUT/ NONDYSFUNCTIONAL INDICATIONS

There are other situations in which enteral nutrition would fail: (1) diffuse splanchnic vessel thrombosis without short gut, making isolated orthotopic liver transplantation impossible because of the lack of portal inflow; and (2) pancreatic tumors with lymph node involvement around the celiac trunk or the superior mesenteric artery (SMA), with an otherwise negative metastatic work-up. The latter is usually a part of an extended upper abdominal exenteration and multivisceral transplantation.

CAUSES OF SHORT GUT

Multiple intestinal atresias

Gangrenous bowel complicating

- Gastroschisis
- Omphalocele
- Malrotation and midgut volvulus
- Necrotizing enterocolitis (NEC)
- Mesenteric vascular occlusion (arterial/venous) with or without celiac trunk thrombosis (may be secondary to hypercoagulable state or to advanced atherosclerosis)

Uncontrolled regional ileitis (Crohn's disease) with subsequent irreversible intestinal damage

Multiple polyposis syndromes

Massive intestinal trauma

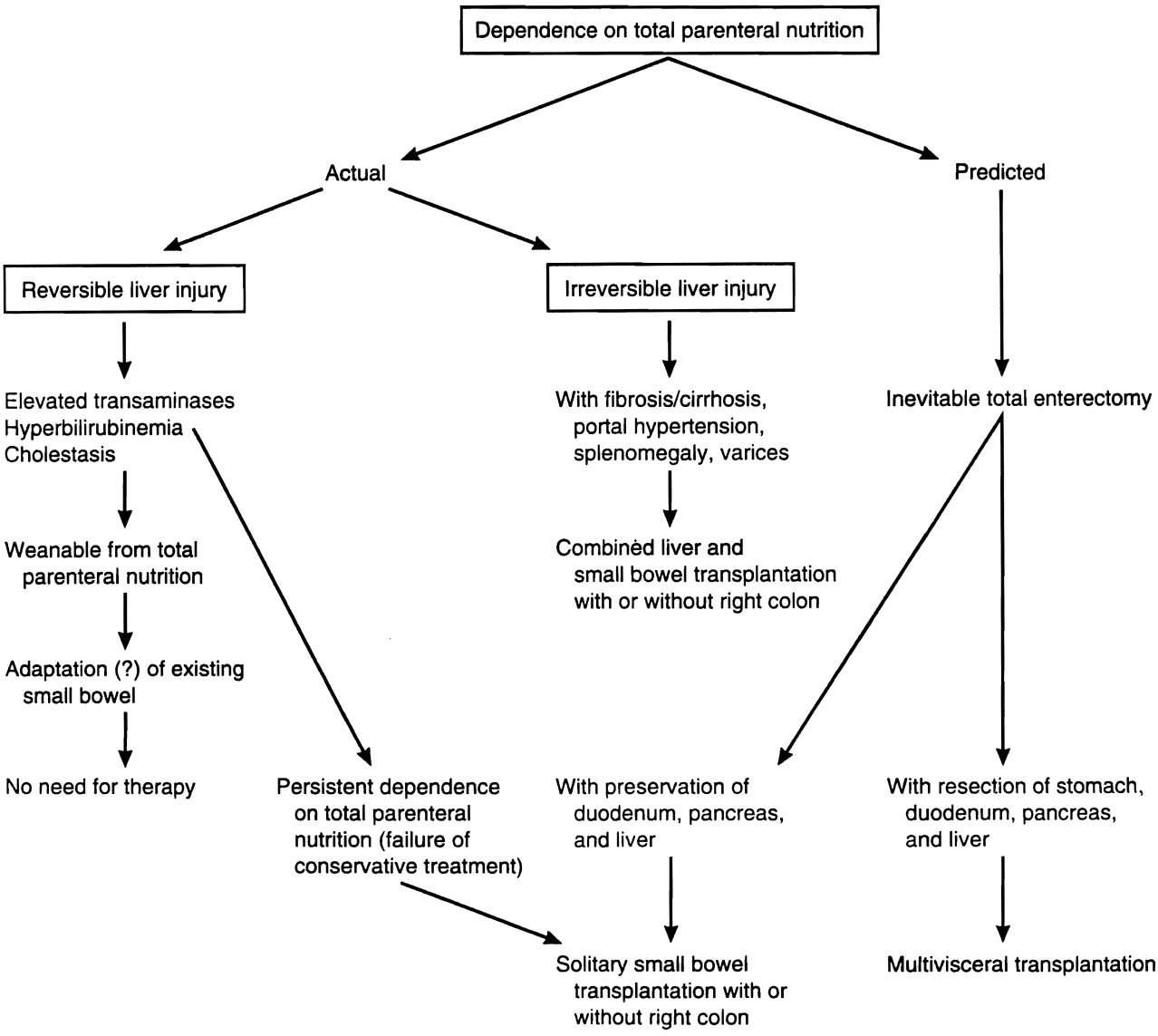
Pretransplantation Evaluation

The patient selection process begins with a detailed history, including previous surgical procedures, and a thorough physical examination for signs of portal hypertension or endstage liver disease, with ancillary work-up as needed.

In patients with vascular occlusive syndromes (chronic mesenteric vascular occlusion, superior mesenteric vein (SMV) thrombosis, portal vein thrombosis, Budd-Chiari syndrome), Doppler ultrasonography, magnetic resonance imaging (MRI), angiography, and venous phase portography are necessary so as to be able to tailor the procedure according to the pre-existing vascular condition. Portal vein or even SMV occlusion are not contraindications for transplantation, since a multivisceral transplant can be performed after resection of the native intra-abdominal organs.

Notably, the neck and upper- and lower-extremity vessels should be evaluated, especially in patients

Management of Patient Selection



ANCILLARY WORK-UP IN PATIENT SELECTION FOR SMALL BOWEL TRANSPLANTATION

Anatomic evaluation of gastrointestinal (GI) tract

- Barium studies
- Angiography (if indicated)

Physiologic evaluation of GI tract

- Absorption studies (D-xylose, 72-hour fecal fat analysis)
- Motility study (in motility disorder patients)
- Endoscopic GI tract biopsy for documentation of the presence and the extent of the disease (e.g., microvillous inclusion enteropathy and Hirschsprung's disease)

Evaluation of liver function

- Biochemical (liver injury enzymes [serum glutamic pyruvic transaminase, serum glutamic oxalate transaminase, α-glutamyl transpeptidase], detoxification function [bilirubin ammonia], synthetic function, albumin, prothrombin time/partial thromboplastin time)
- Histologic (if irreversible liver damage cannot be proven clinically or biochemically, to rule out signs of irreversible liver damage, bridging fibrosis, or cirrhosis)
- Endoscopic (to document presence of esophageal varices or to perform sclerotherapy in bleeding varices)
- Imaging (Doppler ultrasonography to verify patency of hepatic vessels and inferior vena cava, computed tomography or magnetic resonance imaging when indicated)

Cardiopulmonary evaluation (in adults or when there is suspicion of possible involvement)

- Electrocardiogram
- Echocardiogram
- Thallium stress test
- Multiple gated acquisition analysis
- pulmonary function tests

Renal evaluation if indicated (e.g., intestinal pseudo-obstruction or hepatorenal syndrome)

- Ultrasonography
- Intravenous pyelography
- Voiding cystourethrography
- Blood urea nitrogen, serum creatine, urine creatimne clearance

Evaluation in special situations

- Evaluation for possible malignancy when indicated (imaging and appropriate biopsy to document presence of malignancy and rule out widespread metastasis)
- Evaluation of immune system if immune deficiency is suspected (quantitative immunoglobulin, T-cell function tests to rule out congenital immune deficiency syndromes known to accompany multiple intestinal atresias)
- Evaluation for causes of hypercoagulable states (deficiencies of natural anticoagulants, such as protein C, protein S, and antithrombin III; presence of anticardiolipin phospholipids; polycythemia vera)

with a history of multiple central lines or vascular thrombosis, to ensure adequate vascular access for intraoperative management and monitoring.

In addition, the following evaluations are required:

Nutritional assessment: Necessary baseline information regarding the pretransplantation nutritional status of the patient includes a complete dietary and weight history and a growth curve. Use of TPN and any oral/enteral supplements is recorded; serum levels of vitamin, minerals, and trace elements are checked.

Blood typing: Tissue typing (human lymphocyte antibody [HLA]) is done, as is testing for panel reactive antibodies (PRA).

Virologic evaluation: This includes cultures and titers (IgG, IgM) for cytomegalovirus, Epstein-Barr virus, herpes, varicella, and mumps, and screening for human immunodeficiency virus (HIV) and hepatitis.

Psychiatric/social service evaluation: Patient/family emotional stability and the existence of support systems should be determined to ensure postoperative patient compliance.

Preoperative Management

Preoperative management is based upon 6 main goals, as follows:

1. Maintainance of adequate nutrition with adequate vitamin, electrolyte, and trace element levels
2. Maintainance of pre-existing oral feeding if applicable or establish oral use if possible, even if nutritional value of intake is doubtful or nil. Patients—especially children—who do not develop oral intake habits face significant post-transplantation difficulty in starting oral feeding
3. Prevention (if possible) of progression of liver damage that is due to TPN dependence from reversible to irreversible. Cyclic TPN, low-dextrose-content TPN, and simultaneous enteral feeding are among measures that lower the risk of TPN-induced endstage liver disease
4. Prevention and treatment of central line–associated sepsis by adopting a strict aseptic technique of handling home/hospital TPN and by performing surveillance quantitative stool cultures to monitor signs of bacterial/fungal translocation. Selective decontamination of the digestive tract is advisable under these circumstances to prevent systemic and fulminant bacterial/fungal lethal infections
5. Management of hepatic dysfunction as necessary. Methods include control of encephalopathy by regulation of ammonia levels through lowering of the amino acid content in TPN; the use of enteral lactulose, if applicable); the use of plasmapheresis (the value of which has been limited, with a moderate rate of success); administration of clotting factors (fresh-frozen plasma or cryoprecipitate) to correct prolonged prothrombin time; and counteracting the hematologic effect of hypersplenism with blood and platelet transfusion
6. Management of variceal (esophageal, gastric, or stomal) bleeding by sclerotherapy, continuous infusions of vasopression, or continuous infusion of somatostatin.

Cadaveric Organ Procurement

Organ donors are matched by ABO grouping and size match. There is no minimum age limit. An absence of liver disease (determined by history and biochemical testing), as well as freedom from infection, are mandatory. In the presence of a normal liver, no functional or anatomic assessment of the intestine is required. The HLA matching is random. Attempts to mechanically cleanse the bowel are not performed unless the colon is to be included in the graft; however, if this is necessary, a tap-water enema is performed prior to harvesting. A solution containing amphotericin B, tobramycin, and polymyxin E is administered via a nasogastric tube. Ablation of the gut-associated lymphoid tissue (GALT) is not performed. Systemic antibiotics and selective decontamination of the gut prior to the harvesting procedures, using the regimen outlined in Table 1, is started once the donor is identified and repeated every 6 hours if time permits.

The success of the harvesting procedure depends on the presence of one or two central stems: the superior mesenteric artery in harvesting for an isolated small bowel transplant, or the celiac axis and superior mesenteric artery in harvesting for the en-block liver and small bowel or multivisceral transplant.

Perfusion of the graft using University of Wisconsin (UW) solution is performed through the infrarenal aorta and portal vein. The venous outflow is

TABLE 1

INTESTINAL DECONTAMINATION FOR DONOR AND RECIPIENT

ANTIBIOTIC[a]	DOSAGE		
	<5 Yrs (mg)	5–12 Yrs (mg)	>12 Yrs (mg)
Amphotericin B	100	250	500
Tobramycin	10	40	80
Polymyxin E	25	50	100

[a] Systemic antibiotics: cefotaxime, 25 mg/kg/dose tid IV; ampicillin, 25 mg/kg/dose qid IV.

drained through the inferior vena cava either in the chest (most common) or in the abdomen (less common). Figs. 1A, 2A, and 3A show different possibilities of harvesting; Figs. 1B, 2B, and 3B depict recipient operations (discussed below).

Small bowel can be harvested with the liver in continuity to be used as a combined liver and small bowel transplant graft or to be separated for use in two separate recipients (i.e., an orthotopic liver transplantation and an isolated small bowel transplantation).

If the extent of the final transplant is still in question (requiring intraoperative evaluation), it is advisable to harvest the graft as multivisceral organs (i.e., stomach, duodenum, liver, pancreas, small bowel, and colon in continuity). Recently, we have included the colon in the graft to help overcome defective water absorption with subsequent high ileostomy output.

Operative Decisions and Techniques

The extent and the degree of liver disease is usually established preoperatively. When doubts about the status of the liver exist, a needle biopsy and a frozen section obtained during the operation is helpful. The presence of cirrhosis mandates hepatectomy. In functional small bowel failure (absorption/motility), the operative evaluation, in addition to preoperative findings, will help the surgeon reach a decision regarding the extent of resection/replacement. Also, frozen-section biopsy of the mesenteric/pancreatic lymph nodes helps establish the operatibility of tumors.

The recipient procedure entails arterialization of the graft via an end-to-side arterial graft anastomosis to the infrarenal aorta. The SMV of an isolated small bowel graft can be anastomosed end-to-end to the superior mesenteric vein of the recipient or can be anastomosed end-to-side to the recipient portal vein (piggyback).

In combined liver and small bowel grafts, no portal or SMV anastomosis is required, as the graft is harvested en-bloc. The recipient portal vein draining the native pancreas and duodenum can be anastomosed either to the inferior vena cava (IVC) (portacaval shunt) permanently or temporarily. It can also be drained to the graft portal vein in end-to-side fashion.

The outflow of the liver drains through the suprahepatic vena cava to the recipient's hepatic veins, which are fashioned into a single stoma (piggyback). Notably, the recipient IVC is left uninterrupted through a meticulous hepatectomy sparing the retrohepatic inferior vena cava (piggyback technique). (See Figs. 1B, 2B, and 3B for the various surgical options.)

Postoperative Management

REJECTION PREVENTION

The introduction of the immunosuppressive agent FK-506 in 1989 facilitated dramatic improvement in the success of clinical small bowel transplantation. This is due to not only to the greater potency of FK-506 versus Cyclosporin A, but also because the absorption characteristics of FK-506 after oral administration are less influenced by the presence or absence of bile and bile acids than by the motility and function of the intestine itself. Immunosuppression is induced by the administration of 0.1 to 0.15 mg/kg/d of FK-506, continuous intravenous (IV) infusion, starting as soon as graft revascularization is complete, until an FK-506 plasma level of between 2 and 3 ng/ml is reached. Adults require one-third of the dose to achieve similar levels. Once intestinal motility is regained, oral FK-506 is started at 0.3 mg/kg/d in two divided doses. A 24- to 48-hour overlap period is usually required before adjuvant steroid therapy can be discontinued under one of two regimens:

1. 1 g IV hydrocortisone is given during the operation, followed by 100 mg IV methyl prednisone, tapered over a 5-day course to 20 mg/d IV. This baseline dose is then tapered slowly to weaning, which averages 4.6 weeks.

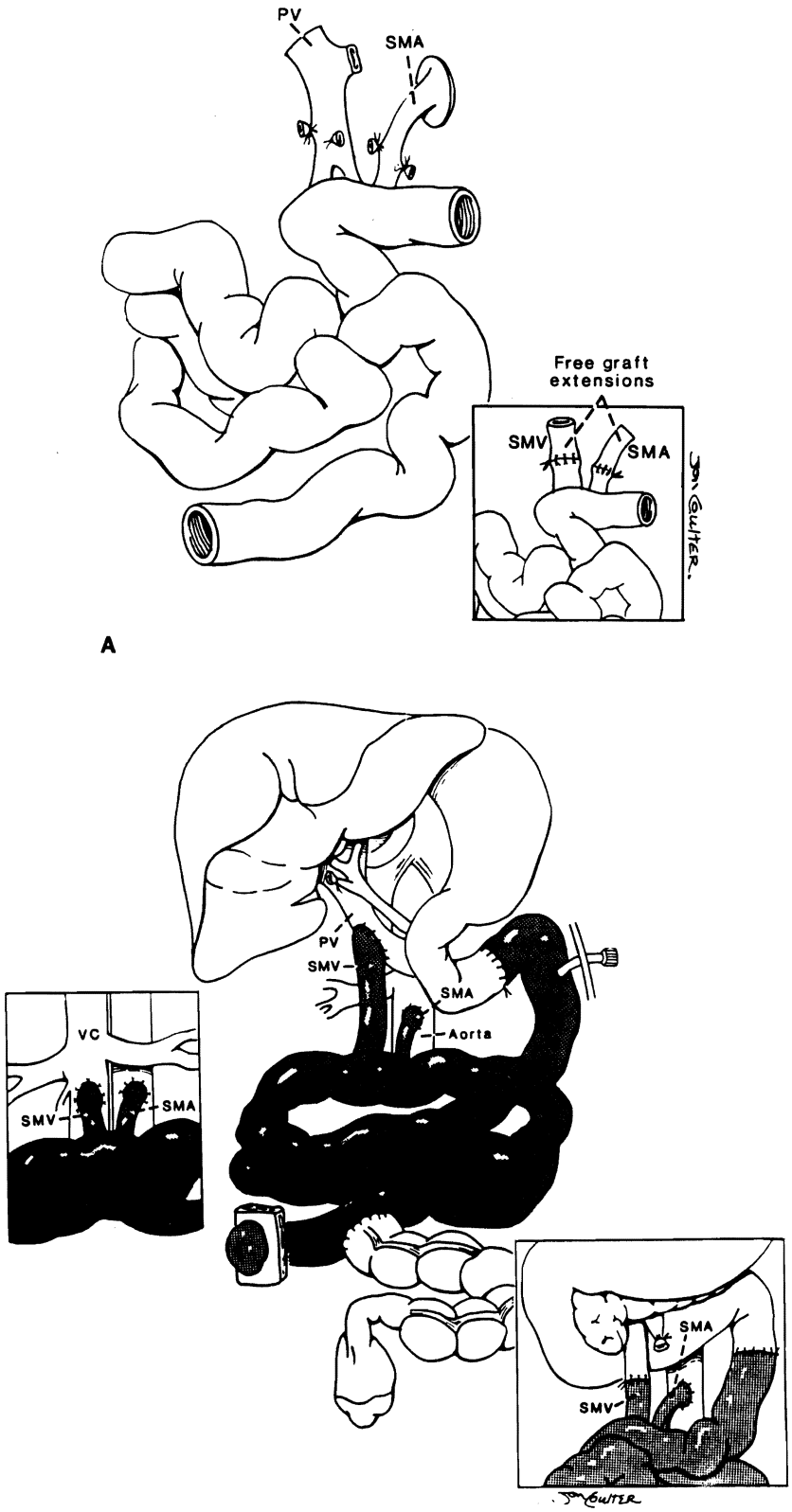


Figure 1. Isolated small bowel transplantation. **(A)** Donor operation with full-length vascular pedicle of the superior mesenteric artery (SMA) (with Carrel patch) and the superior mesenteric vein (SMV). If both vessels are divided more distally, they can be lengthened on the back table with arterial and venous grafts *(inset).* **(B)** Recipient operations: anastomosis of full-length SMA to the aorta and the angled end of the SMV to the portal vein (PV); alternative method, in which the SMV is anastomosed to the recipient SMV inferior to the pancreas *(lower inset);* option of SMV drainage into the inferior vena cava (VC) *(upper inset).* (From Todo S, Tzakis AG, Abu-Elmagd K et al: Intestinal transplantation in composite visceral grafts or alone. Ann Surg 216:223, 1992, with permission.)

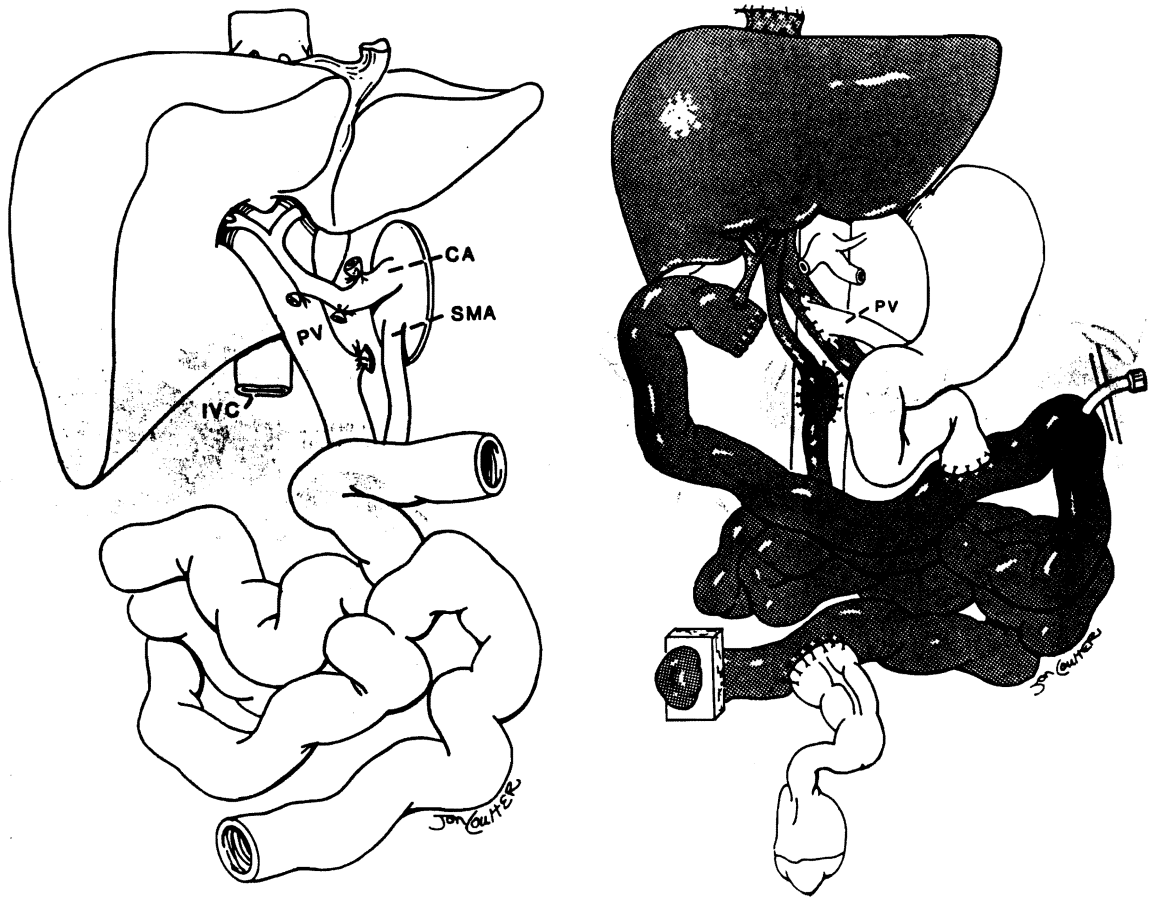


Figure 2. Small bowel–liver allograft. **(A)** Donor operation. Note the continuity of donor portal vein. (*Abbreviations:* CA, celiac axis; IVC, inferior vena cava; PV, portal vein; SMA, superior mesenteric artery.) **(B)** Recipient operation. Carrel patch containing the origin of the superior mesenteric artery and the celiac axis is anastomosed to the aorta. Ideally, the venous return from residual splanchnic viscera of the recipient is routed by vascular anastomosis into the graft portal vein. Numerous options of graft rearterialization and venous drainage have been described in other texts. (From Todo S, Tzakis AG, Abu-Elmagd K et al: Intestinal transplantation in composite visceral grafts or alone. Ann Surg 216:223, 1992, with permission.)

2. A baseline dose of methylprednisone, 20 mg/d IV, is given for patients weighing more than 10 kg; the baseline dose for those less than 10 kg is 10 mg/d. The steroid is then tapered slowly to weaning over 4 to 6 weeks.

When enteral/oral feeding is achieved, methylprednisone is replaced by oral prednisone. The first regimen (above) is always used for isolated small bowel transplantation and for grafts including the right colon, while the second regimen (above) is used in combined liver and small bowel transplants.

In addition to FK-506 and steroids, prostaglandin E_1 (PGE_1) is administered at 0.003 to 0.009 μg/kg/min IV continuous infusion for a minimum of 5 days to reduce FK-506 nephrotoxicity and to aid in immunosuppression.

REJECTION MONITORING

Liver function tests and liver biopsies, in addition to clinical physical examination, help monitor liver rejection. Rejection of the small bowel and colon are detected by monitoring the patient's clinical picture, stoma output, and stoma color. Stomal endoscopy and biopsy can be performed as frequently as twice a week if the index suspicion for rejection is high.

Table 2 shows the correlation of clinical, endoscopic, and histologic findings in different stages of small bowel rejection.

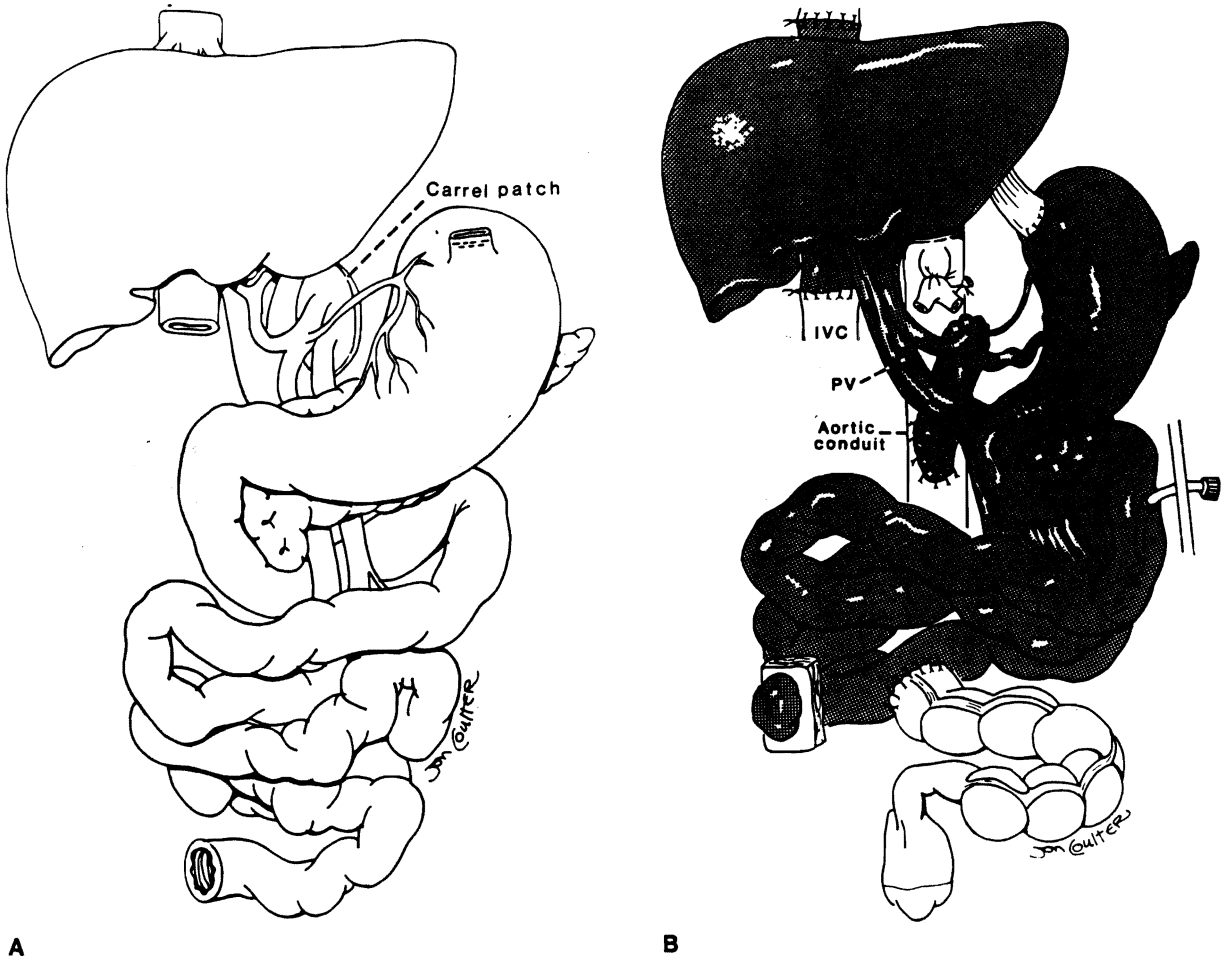


Figure 3. Multivisceral allograft **(A)** before and **(B)** after transplantation. Splenectomy is performed on the back table. In this case the Carrel patch, with the superior mesenteric artery and celiac axis origins, has been used to cap a free graft of donor thoracic aorta that has been used as a conduit. This is only one of several options that the operator should be prepared to exercise. (*Abbreviations:* IVC, inferior vena cava; PV, portal vein.) (From Todo S, Tzakis AG, Abu-Elmagd K et al: Intestinal transplantation in composite visceral grafts or alone. Ann Surg 216:223, 1992, with permission.)

REJECTION CONTROL

Mild to moderate acute cellular rejection is treated with an increased FK-506 dosage, a bolus of steroids, or a steroid-tapering recycle. OKT3 may be used in severe acute cellular rejection. Multiple episodes of moderate acute cellular rejection, especially in the presence of renal dysfunction, may warrant the addition of azathioprine to augment baseline immunosuppression.

Documentation of chronic rejection by angiographic and histologic changes showing arteritis obliterans and mucosal microabscesses mandates resection of the graft and retransplantation, if possible.

INFECTION PREVENTION AND TREATMENT

The key to successful small bowel transplantation is infection control. The bowel is the nutrient-transporting organ, and also acts as a barrier against entry of pathogens into the body, which is achieved by the fundamental structure of the gut and GALT, comprising $CD4^+$ and $CD8^+$ T cells, B cells, macrophages, M cells, and natural killer (NK) cells.

Normally, pathogens (bacterial and fungal) living inside the gut lumen pass through the epithelial mucosa into the lamina propria and then to the mesenteric lymph nodes and possibly other tissues with the

TABLE 2

MONITORING OF INTESTINAL GRAFT REJECTION

REJECTION	CLINICAL FINDINGS	ENDOSCOPIC FINDINGS	MUCOSAL BIOPSY FINDINGS
Acute (mild to moderate)	Fever Abdominal pain Vomiting Increase of stomal output Watery diarrhea Ileus	Ischemic/dusky mucosa Mucosal edema Hyperemia Loss of fine mucosal pattern Decrease of peristalsis	Cell infiltration Villus blunting Cryptitis Epithelial cell damage and regeneration Mucus/Paneth cell reduction
Severe	Severe diarrhea Abdominal pain Abdominal distension Metabolic acidosis Positive blood culture Adult respiratory distress syndrome	Ulceration Mucosal sloughing Bleeding Loss of peristalsis	Mucosal hemorrhage Mucosal sloughing Microabscess
Chronic	Chronic diarrhea Malabsorption Progressive weight loss	Pseudomembrane Hypoperistalsis Loss of mucosal fold Oily intestinal contents	Fewer inflammatory cells Evident cryptitis Regenerative epithelium Submucosal fibrosis (suggestive but not conclusive)[a]

[a] Histologic diagnosis of chronic rejection is made with the resected graft, which shows arteritis obliterans and mucosal abscess.

(Modified from Todo S, Tzakis AG, Abu-Elmagd K et al: Intestinal transplantation in composite visceral grafts or alone. Ann Surg 216:223, 1992, with permission.)

help of macrophages. This is an active process, used for sampling purposes as part of immunologic surveillance. In transplanted bowel, the combination of (1) immunosuppression, (2) repopulation of GALT with recipient cells, (3) bacterial and fungal overgrowth, and (4) cryptitis associated with acute cellular rejection enhances bacterial translocation beyond the physiologic mission intended.

Monitoring of post-transplant quantitative stool cultures allows prediction of the organisms that will be associated with translocation. Growth of a single or minimal number of organisms greater than 10^9 colonies/g of stools is associated with a higher incidence of translocation. This rationale lies behind the policy of application of selective decontamination of the digestive tract. Modification of the constituents of the antibacterial/antifungal regimen is required according to the culture and sensitivity results of gut bacteria. We administer selective decontamination of the digestive tract four times a day enterally for 6 to 8 weeks post-transplant and 2 weeks thereafter whenever acute cellular rejection of the bowel is documented. Intravenous broad-spectrum antibiotics are given for 5 days after transplantation and whenever positive blood, urinary tract, or respiratory tract infections are documented. Central lines and catheters are changed as per routine infection control guidelines.

NUTRITIONAL SUPPORT

Total parenteral nutrition is continued postoperatively as soon as these patients are hemodynamically stable (24 to 48 hours) and continued as long as their enteral nutrition is inadequate (19 to 210 days—mean, 65 days). Weaning from TPN is started when enteral intake reaches 50 percent of the caloric requirement or when fluid status requires it. Reciprocal increase of enteral feeding and decrease of TPN is progressed gradually until freedom from TPN is achieved. A transitional period, when low-calorie or noncaloric intravenous fluids may still be needed to compensate for high stomal output, is dealt with on individual basis. One to 2 weeks of close monitoring of fluid and electrolyte balance is usually required before all intravenous fluids are discontinued and the patient is totally dependent on enteral intake of water, electrolytes, and calories. Enteral feeding is started when peristalsis of the transplanted bowel is regained and a radiologic contrast study documents patency of

the bowel with integrity of the intestinal anastomosis. Attaining this status usually takes 7 to 10 days. Enteral feeding is established via a nasogastric, nasoduodenal, gastrostomy, or jejunostomy tube, depending on the availability of the route. Continuous, gradually increasing feeds are preferred to bolus feeds.

The ideal formula should have a low osmolality to prevent hyperosmolar diarrhea. The protein source should be in small peptide form to ensure rapid absorption. Extensive animal research has indicated that glutamine is a conditionally essential amino acid. It plays a role in acid–base balance; is an important precursor of nucleic acids, nucleotides, and amino sugars; and is considered to be the preferred respiratory fuel for enterocytes. The major proportion of fat contents of the ideal formula should be in the form of medium-chain triglycerides (MCT), so that it is absorbed directly without the need for lacteals and lymphalics. Standard commercial formulas, such as Vivonex TEN, Peptamen, Modified Compleat, and Alitraq, are used. Once the enteral feeding is established, efforts are made to establish and encourage the oral route. It has been observed that patients, particularly children, who have not been eating before transplantation face difficult clinical problems in accepting oral feeding, possibly due to a hyperactive, unsuppressed gag reflex; difficulty in swallowing; or psychologic factors. Cycling of tube feeding betters the chance of improvement of oral intake.

Close observation of the stoma output, regarding volume, pH, presence of reducing substance (glucose), and quantity of bacterial/fungal overgrowth, is important. Abnormalities in urine output, blood urea nitrogen (BUN), serum creatinine, electrolytes, and acid–base balance are treated promptly intravenously while the patient is still on intravenous fluids or enterally when weaned from intravenous fluids. In the absence of colon, there is usually a tendency to lose water, sodium, magnesium, and bicarbonate, warranting excess supplementation with sodium citrate or bicarbonate and magnesium gluconate. Antidiarrheal drugs (e.g., loperamide and diphenoxylate) are useful for controlling rapid transit and increasing stomal output. Our experience with somatostatin analogues has not been encouraging. Pectin can also be used as a stool-thickening agent, with limited success.

Monitoring of nutritional status once these patients are weaned from TPN and intravenous therapy can be achieved through monitoring of small bowel graft function, as shown in Table 3.

TABLE 3

MONITORING OF SMALL BOWL GRAFT FUNCTION[a]

FUNCTIONAL ASPECT	TEST
Carbohydrate absorption	Testing of reducing substance in stoma output D-xylose absorption test Blood sugar level[a]
Fat absorption	72-hour stool fat excretion Serum levels of vitamins A, D, E[a]
Protein absorption	Serum albumin and prealbumin[a] Anthropometric measurements[a]
General absorption	Urine output[a] Serum zinc, magnesium, iron[a] FK-506 levels[a] Schilling tests

[a] After weaning from total parenteral nutrition and intravenous therapy.

Management of Postoperative Complications

Postoperative complications can be classified as technical, immunologic, infectious, renal, respiratory, or recurrence of primary disease. Although efforts are made to prevent complications, they can occur, and should be treated promptly.

TECHNICAL COMPLICATIONS

Bleeding and gastrointestinal anastomotic leaks are the main possible technical problems, requiring exploration and appropriate management. Vascular thrombosis in pediatric patients is prevented by administration of anticoagulants (aspirin, heparin, Persantin) once the prothrombin time is less than 17. Vascular strictures can be managed by transluminal balloon angioplasty.

IMMUNOLOGIC COMPLICATIONS

Rejection and graft-versus-host disease are prevented and treated with augmentation of immunosuppression.

INFECTIONS

Immunosuppression is to be dramatically reduced or even discontinued in presence of viral infections. Gancyclovir is used in the prevention, treatment of initial infection, and treatment of reactivation of cytomegalovirus (CMV). Acyclovir is the drug of choice for treatment of Epstein-Barr virus (EBV), chickenpox, and viral herpes infections. The value of acyclovir oral chronic prophylactic therapy is still in question. Post-transplantation lymphoproliferative disease has been shown to be EBV-related. It almost always responds to discontinuation of immunosuppression and intravenous administration of acyclovir. Adenovirus and influenza viruses can be lethal, especially when they occur early postoperatively. The lack of specific treatment may play a role in their development. Intravenous immunoglobulin, Ribavirin, or Amantadine may be used when appropriate. Bacterial and fungal infections are dealt with as usual, using the drugs indicated by sensitivity studies. Selective decontamination of the digestive system (SDD) is administered to reduce the chances of translocation as the source of these infections.

RENAL COMPLICATIONS

Renal impairment is prevented by adequate monitoring of the fluid balance and of nephrotoxic drug levels (e.g., antibiotics and antifungal and antirejection agents). Prostaglandin E (PGE) and dopamine may be helpful at a renal dose. Short-term hemodialysis can be used.

RESPIRATORY COMPLICATIONS

Infections such as *Pneumocystis carinii* pneumonia are prevented by prophylactic administration of trimethoprim sulfa. Pentamidine can be used in the presence of an allergy to trimethoprim sulfa; dapsone can be used in those allergic to trimethoprim sulfa who cannot tolerate pentamidine inhalation. Intravenous trimethoprim sulfa or pentamidine are the drugs of choice for the treatment of this fatal infection.

Mechanical ventilation, and respiratory physiotherapy are crucial in the management of postoperative infection or mechanical respiratory problems. When medical management by diuretics and albumin fails, drainage of pleural effusion can be achievd by insertion of a pigtail catheter.

RECURRENCE OF THE PRIMARY DISEASE

So far we have not seen recurrence of intestinal pseudo-obstruction or microvillous inclusion enteropathy. A recipient of an isolated small bowel for advanced Crohn's disease lost his graft 12 months post-transplant because of chronic rejection, rather than recurrence of Crohn's disease.

Results

Between May 1990 and March 1993, 39 patients underwent small bowel transplantation at the University of Pittsburgh Medical Center. Twenty were adults and 19 were children. Tables 4 and 5 show the demographic breakdown, type of operation, follow-up period, and results of both the mediatric and adult groups.

Conclusions

The Pittsburgh experience in small bowel transplantation shows that the results of this procedure are now more reproducible than before. This may be due to the availability of the potent immunosuppression agent FK-506, and to a better understanding of the two-way traffic of dendritic cells and lymphocytes that happens immediately following small bowel transplantation. This allows donor lymphocytes to be replaced by recipient ones in the GALT, forming a mixed chimerism. Alteration of the balance between these two components leads to the development of graft-versus-host disease. The Pittsburgh experience also shows that solitary small bowel transplantation is feasible, and that the relative simplicity and safety of this procedure outweighs the potential immunologic advantage provided by the liver in combined liver and small bowel transplantation. The addition of the liver is reserved for endstage liver disease or in presence of an inborn malfunction in the liver, such as protein C deficiency.

Lastly, a longer follow-up period is required to evaluate and plan prevention measures and a strategy for treating the infections and handling the technical complications associated with small bowel transplantation.

TABLE 4

SMALL BOWEL TRANSPLANTS: PEDIATRIC EXPERIENCE AS OF MARCH 15, 1993

AGE	SEX	NATIVE DISEASE	GRAFT	PATIENT SURVIVAL (DAYS)	GRAFT SURVIVAL (DAYS)	TPN STATUS
3.2	F	NEC	SB + L	>965	>965	Free
4.3	M	Gastroschisis	SB + L	>842	>842	Free
2.8	M	Intestinal atresia	SB + L	385	385	Died (PTLD)
0.6	F	Intestinal atresia	SB + L	23	23	Died (GVHD)
1.1	F	Volvulus	SB + L	>583	>583	Free
1.7	F	Volvulus	SB + L	>581	>581	Free
2.5	F	Microvillous inclusion enteropathy	SB	>491	>491	Free
1.3	M	Intestinal atresia	SB	>446	>446	Free
10.2	F	Intestinal pseudo-obstruction	SB	>374	>374	Free
1.5	M	NEC	SB + L	70	70	Died (MSOF)
4.2	F	Gastroschisis	SB + L	>278	>278	Free
1.4	M	Gastroschisis	SB + L	29	29	Died (sepsis)
0.9	M	Microvillous inclusion enteropathy*	SB + L	>237	>237	Free
0.5	M	Gastroschisis	SB + L	>231	>231	Free
4.5	F	Intestinal pseudo-obstruction	MV + C	>133	>133	Free
3.6	M	NEC	SB + C + L	>96 >36	60 Retransplanted	Free (rejection)
0.9	F	Gastroschisis	SB + C + L	>91	>91	Partial
15.5	M	Volvulus	SB + C + L	>70	>70	Free
3.0	F	NEC	SB + C + L	>7	>7	Early

(*Abbreviations:* GVHD, graft-versus-host disease; MV, multivisceral; NEC, necrotizing enterocolitis; MSOF, multisystem organ failure; PTLD, post-transplant lymphoproliferative disease; SB, small bowel; SB + L, small bowel + liver; SB + C + L, small bowel + colon + liver; TPN, total parenteral nutrition.)

TABLE 5

SMALL BOWEL TRANSPLANTS: ADULT EXPERIENCE AS OF MARCH 15, 1993

AGE	SEX	NATIVE DISEASE	GRAFT	PATIENT SURVIVAL (DAYS)	GRAFT SURVIVAL (DAYS)	TPN STATUS
31.1	M	Gunshot wound	SB SB	776	667 71	Retransplant Died (sepsis)
26.7	F	SMA thrombosis	SB + L	>955	>955	Free
21.0	M	Traffic accident	SB + L	>572	>584	Partial
32.0	M	CA + SMA thrombosis	MV	>518	>518	Partial
50.0	F	Crohn's disease	SB	>423	>423	Free
34.0	F	Desmoid tumor	SB	>406	239	Graft removed
38.0	M	Crohn's disease	SB	376	370	Graft removed Died (sepsis)
22.0	F	Crohn's disease	SB	>368	>368	Free
25.0	M	Desmoid tumor	SB + L	>294	>294	Free
29.0	F	Traffic accident	SB	>281	>281	Free
24.0	M	CA + SMA thrombosis	MV	>291	>291	Free
20.0	F	Traffic accident	SB	>281	>281	Free
31.0	F	CA + SMA thrombosis	SB + L	>216	>216	Free
19.1	M	Traffic accident	SB + L	>213	>213	Free
44.0	F	SMA thrombosis	SB + L	>189	>189	Free
37.0	F	Familial polyposis	SB	>108	>108	Free
44.0	M	Gastrinoma	MV	49	49	Died (sepsis)
39.0	M	Crohn's disease	SB + C	>28	>28	Partial
35.5	M	Crohn's disease	SB + C	>22	>22	Early
58.0	F	Multiple intestinal resection	SB + C	>12	>12	Early

(*Abbreviations:* CA, celiac axis; MV, multivisceral; SB, small bowel; SB + L, small bowel + liver; SB + C + L, small bowel + colon + liver; SMA, superior mesenteric artery; TPN, total parenteral nutrition.)

Suggested Readings

Starzl TE, Todo S, Tzakis AG et al: The many faces of multivisceral transplantation. Surg Gynecol Obstet 172:335, 1991

Todo S, Tzakis AG, Abu-Elmagd K et al: Intestinal transplantation in composite visceral grafts or alone. Ann Surg 216:223, 1992