Pancreatic Transplantation at the University of Pittsburgh

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The field of pancreatic transplantation sustained an important loss with the premature passing of Dr. Robert J. Corry in February 2002. He was a brilliant surgeon, a gifted clinician, and an incredibly generous individual. His legacy of humanity and clinical excellence has served as an inspiration, and this chapter is dedicated to his memory.

Traditionally, single center contributions to <u>Clinical Transplants</u> have tended to focus on a given center's cumulative outcomes over an extended time frame. In this chapter, however, we will juxtapose two very different and relatively novel experiences. The first comprises traditional pancreatic transplantation in Type I diabetics, utilizing a conceptually different approach to immunosuppression, and also describing the implementation of technical refinements designed to improve outcomes. The second includes pancreatic transplantation in the context of multivisceral transplantation. Both experiences offer new insights that may prove to be of interest to the transplant community.

I. Pancreatic Transplantation Under a Regimen of Campath-1H® Preconditioning and Low-Dose Tacrolimus Monotherapy

Dr. Corry's passing came just after the initiation of a new approach to immunosuppression after organ transplantation that was based upon two principles—recipient preconditioning and minimal post-transplant immunosuppression. The initial

experience with pancreatic transplantation under Thymoglobulin preconditioning has been previously published (1). This chapter will focus on a more recent experience, utilizing Campath-1H® preconditioning, that has been utilized for simultaneous pancreas-kidney (SPK), pancreas after kidney (PAK), and pancreas transplantation alone (PTA). The early results with this regimen in have been gratifying.

Campath-1H® is a humanized anti-CD52 monoclonal antibody. A single dose (30 mg) depletes greater than 99% of T-cells, as well as B-cells and monocytes for an extended period of time, and has allowed post-transplant maintenance immunosuppression with tacrolimus monotherapy (2-3). Two doses only of intravenous corticosteroids have been given prior to and during Campath-1H® administration, to prevent cytokine release. This immunosuppressive regimen has resulted in lower rates of rejection and complications in the early post-transplant period, without an increase in infectious complications, and with excellent patient satisfaction.

This section of the chapter will also describe the refinement of the technical aspects of pancreatic transplantation, which have evolved since the re-initiation of whole organ pancreas transplantation described over 20 years ago by Dr. Starzl (4), and refined by Dr. Corry and others (5). These have led to a substantially decreased rate of thrombosis and other technical complications after pancreatic transplantation.

Rationale and Patient Characteristics

The combination of antibody preconditioning and minimal post-transplant immunosuppression, developed by Dr. Starzl, is based upon two principles: 1. T-cell depletion creates the optimal conditions for the promotion of tolerance, and 2. Excessive early post-transplant immunosuppression is potentially antitolerogenic. The induction of a

donor-specific tolerance towards an allograft by T-cell depletion has been demonstrated in a number of animal models (6), and the abrogation of tolerance by calcineurin inhibitors and steroids is also well described (7-8).

Thirty-seven consecutive pancreas transplants (20 SPK, 10 PAK, and seven PTA) were performed utilizing Campath-1H® preconditioning between July 2003 and August 2004. Campath-1H® was given intra-operatively. Two grams of intravenous methylprednisolone were administered, one prior to starting the Campath-1H®, and another at reperfusion. Twice daily oral tacrolimus was started at 12 hours after transplantation, with target 12-hour troughs between 10-15 ng/ml (Table1). Follow up of these patients range from three to 16 months with mean follow up time of 7 months.

Type I diabetics (c-peptide level <0.50) with end-stage renal disease, on dialysis or with a CrCl <20 mg/ml either received a simultaneous kidney-pancreas transplant (SPK) or staged pancreas after living donor kidney transplantation (PAK). Isolated pancreas transplantation (PTA) was performed in patients with hypoglycemic unawareness, keto-acidosis, or difficult-to-control blood glucoses (Table 2). Other than the conventional contraindications of malignancy and infection, there were no absolute contraindications to transplantation, although the most common cause of nonlisting was significant cardiac disease. Pretransplant clearance by dobutamine echo or cardiac catheterization was performed on all recipients. Mean recipient age (Table 2) was 43 ± 7.9 years (range 19-59) with 19% of recipients being over 50 years of age. Mean donor age was 30.3 ± 13 years (range 12-61), with some 11% of donors over age 50. One patient underwent combined kidney-pancreas transplantation from a non-heart beating donor. Donor and recipient selection closely matches guidelines described by Dr. Corry and those published in the

literature (9-10). The most important determinants of pancreas allograft use in Pittsburgh are surgeon visualization, cold ischemia time (goal <24 hrs), and donor lipase levels (peak < 500 IU/dl).

Technical aspects of donor preparation and implantation

The standard technique for pancreas transplantation at the Thomas E. Starzl Transplantation Institute is iliac artery/vein revascularization and enteric drainage using a side-to-side duodenojejunostomy. Separate lateral incisions are made for the pancreas and/or kidney. Pancreas retransplantation is performed through a mid-line incision.

The use of stapling techniques has greatly simplified both the donor back-table preparation as well as graft implantation. On the back table, staples can be used to perform the splenectomy, to ligate the root of the mesentery (both of which are reinforced with locking 4-0 polypropylene) and to ensure hemostasis across the peri-pancreas fat or connective tissue. A Y-graft to the superior mesenteric artery and splenic artery is routinely used, although revascularization of the gastroduodenal artery has been performed in donor organs with a potentially compromised blood supply to the head of the pancreas (11), as in the case of a donor with a replaced right hepatic artery or in a simultaneous pancreas-small bowel harvest.

The head of the pancreas allograft is implanted in a cephalad position with the tail placed in the pelvis. In this position the Y-graft and donor portal vein can be anastomosed to the external iliac vessels, and a loop of recipient jejunum can be mobilized to create a tension-free duodenoenterostomy. A 15-20 degree clock-wise rotation of the portal vein allows for optimal positioning of the pancreas. The duodenoenterostomy is performed with

a circular staple inserted through the lumen of the distal duodenum, and the distal duodenum closed with an endo-GIA stapler (12). The duodeno-enterostomy is reinforced with a row of 4-0 silk Lembert sutures. This technique is equally effective on the left or right side of the recipient.

Outcomes

Patient survival. The overall one-year actuarial patient survival for all patients in this series was 100 % (Figure 1).

Pancreas survival. The actuarial pancreas survival at one year was 94% (35/37; Figure 1). Two pancreata were lost, both of which were in SPK transplants. One pancreas was emergently removed nine months after transplant because of a bleeding pseudoaneurysm, although the allograft was functioning normally. The other pancreas came from a donor with pancreatitis (lipase 900s), which promptly thrombosed on POD 1 day.

Kidney survival. The actuarial kidney survival in the SPK group at one year was 90% (18/20; Figure 1). A single kidney was lost to combined cellular and humoral rejection unresponsive to further Campath-1H® treatment and plasmapheresis with intravenous immunoglobulin. The other kidney thrombosed six weeks after simultaneous kidney and pancreas transplantation. Both pancreases are functioning well. No kidney allograft was lost in the PAK group.

Rejection. Routine monitoring of amylase, lipase and creatinine were performed to monitor the pancreas and renal allografts. Suspicion of rejection was usually confirmed by an ultrasound-guided percutaneous biopsy and histological examination.

The overall rate of rejection was 22% (8/37; Figure 2). Six of seven responded to a methylprednisolone bolus (1 gm) and increased tacrolimus doseages. One kidney was lost

as described above.   Interestingly, all rejection episodes were preceded by tacrolimus trough levels <9.0 for an extended period of time (five-seven days).   Allograft rejection was not observed in pancreases or kidneys if the tacrolimus was >10 ng/ml.

Complications.   The overall complication rate in the pancreas transplants (Figure 3) was 22% (8 of 37) and included thrombosis--5% (1 kidney and 1 pancreas in 2 SPK recipients); anastomotic fistula--5% (1 SPK, 1 PTA); pancreatitis--3%(1 SPK); bleeding requiring re-exploration--8% (2 SPK, 1 PAK).   The thrombosis and anastomotic leak occurred prior to the implementation of the technique described above.   In 30 subsequent patients (not all are included in this report because of <3 month follow-up), no thrombosis and no fistulas have been seen.

Discussion

One of the major advantages of both the immunosuppressive regimen described here and the technical refinements that have been developed is their great simplicity.   This is a safe and straightforward immunosuppressive regimen, with a low rate of rejection, a low rate of infectious complications, and a low rate of technical complications.   In contrast to kidney transplantation alone, weaning to spaced dosing has proceeded much more slowly, given the consequences associated with late rejection.   This approach is very well tolerated. While more follow up will be required to assess the long-term outcomes, this regimen appears to have substantial potential in the care of patients undergoing pancreatic transplantation.

II.   Pancreatic Transplantation En-Bloc with Visceral Grafts

With the recent evolution of intestinal transplantation, the pancreas has frequently been transplanted en-bloc with the intestine, liver and other abdominal viscera. In contrast to combined pancreas-kidney and solitary pancreas transplantation, the pancreas is generally included in the multivisceral graft for non-diabetic indications. The objective of this report is to identify the indications for the procedure and its potential impact on the current United Network of Organ Sharing (UNOS) pancreatic transplant coding system and database. The immunogenicity and functional survival of the pancreas transplanted en-bloc with the other abdominal visceral organs will also be addressed.

Technical Evolution

Because of the embryonic origin of the pancreas, the gland shares its blood supply with the liver and intestine (Figure 2) (13). Accordingly, a few technical challenges were faced with the development of intestinal, liver-intestinal, and multivisceral transplantation. The successful simultaneous recovery of intestinal, pancreatic, and hepatic grafts from the same donor for transplantation to different recipients has been recently described and published (13). In the same article, the technique of en-bloc intestinal and pancreas transplantation was described for the first time with an illustration of the back table procedure (Figure 3) (13). The procedure of combined liver and intestinal transplantation has evolved over the last decade to preserve the duodenum and pancreas en-bloc with the liver and intestine. The rationale of maintaining continuity of the hepatobiliary system with the gut was to avoid the potential risks of biliary reconstruction and maximize the absorptive functions of the transplanted intestine (Figure 4). The pancreas has also been

part of the modified (Figure 5A) (13) and full multivisceral transplantation (Figure 5B) (13) since the development of the procedure. However, a recent modification has been introduced to patients who have a benign disease of their foregut organs (Figure 6) (14).

Recipient Operation

Most of the patients who require intestinal and multivisceral transplantation with inclusion of the pancreas are critically ill and have multiple complex medical issues. The mean number of abdominal surgeries prior to transplantation was 4 ± 4 with a range of 0 to 25. In addition, these patients can lose their abdominal domain and frequently require reconstruction of their abdominal wall.

The arterial reconstruction of the intestinal and multivisceral grafts is uniformly established through placement of an infrarenal aortic graft. The venous drainage of the combined intestinal/pancreatic and modified (without liver) multivisceral transplantation is commonly into the native portal system. However, in 2 recipients, the drainage was into the recipient vena cava. When the pancreas is part of a liver/intestinal and full multivisceral graft, continuity of the portomesenteric venous system is maintained as shown in Figure 4, 5, and 6. Obviously, all pancreatic grafts were drained enterically and orthotopically.

Indications

The whole pancreas was transplanted en-bloc in 78 (32%) out of a total of 246 consecutive primary cadaveric abdominal visceral transplantations that were performed at our institution over the last 13 years. Of these, 43 were adults and 35 were children with a mean age of 40.5 ± 10.1 years, and 4.8 ± 5.8 years, respectively. Included with the

pancreas was the intestine in 4 (5%) grafts, stomach and intestine in 14 (18%) grafts, liver and intestine in 28 (36%) grafts, and stomach, intestine and liver in the remaining 32 (41%) grafts. The primary indications for inclusion of the pancreas were technical in 32 (41%), vascular thrombosis in 18 (23%), gastrointestinal dysmotility in 13 (17%), gut neoplasm in 10 (13%), trauma in 3 (4%), and diabetes in the remaining 2 (2%) recipients. Insulin dependent diabetes was also an associated disorder in another 2 patients, giving a total of 4 (5%) recipients who were diabetic prior to transplantation. Most of the recipients were non-diabetic, and the indications for inclusion of the pancreas were mainly technical and vascular insufficiency.

Donor Characteristics

All donors were deceased and hemodynamically stable. The mean age was 15.7 $\pm$ 13.8 with a range of 3 days to 50 years. All but 2 allografts were ABO identical. Human leukocyte antigen (HLA) matching was random, with no cases of zero –A, –B, –DR mismatches. T and B lymphocytotoxic cross-matches were positive after dithiothreitol (DTT) treatment in 13 (17%) patients. Because of the reported adverse effects of positive donor CMV serology on outcome, attempts were made in the recent cases to avoid using CMV seropositive intestinal donors for CMV seronegative recipients, particularly those who did not need replacement of the native liver (15). Management policies and retrieval operations have been described previously (16,17,18). No attempts were made to treat the donor with anti-lymphocyte preparations. However, the intestinal component of 17 (22%) grafts were irradiated ex-vivo with a single dose of 7.5 Gy. In addition, donor bone marrow cells were given intravenously to 25 (32%) recipients within the first 24 hours after allograft reperfusion at $2.4 - 9 \times 10^{8}$/kg BW. The University of Wisconsin (UW) solution was used

for graft preservation in all but the first case, with a mean cold ischemia time (CIT) of 8.9 $\pm$ 1.7 hours.

Immunosuppression

Immunosuppression has evolved since the beginning of the program because of the high risk of intestinal allograft rejection. Tacrolimus-based immunosuppression was the underpinning of intestinal and mulitivisceral transplantation, and was used for all 78 recipients. With the initial 14 (18%) patients, prednisone was added from the outset as a second agent. Induction therapy was utilized between 1995 and 2001 in 23 (29%) patients with cyclophosphamide in 3 and daclizumab in 20 cases. A tolerogenic protocol was initiated in July of 2001 with recipient pretreatment and post-transplant tacrolimus monotherapy. In 41 pretreated recipients, Thymoglobulin was used in 40 patients and Campath 1H was used in the remaining case. Azathioprine, mycophenolate mofetil, or sirolimus were added as adjunct maintanence immunosuppression agents in selected cases at different time periods. In all patients but the first 8 recipients, prostaglandin E_1 was infused intravenously during the early postoperative period. Episodes of rejection were initially treated with steroids and adjustments of tacrolimus dosing. OKT3, Thymoglobulin, or Campath 1H were used to treat steroid-resistant or severe rejection episodes. Details of the immunosuppressive protocols and drug dosage are described elsewhere (15, 19).

Survival Outcome

With a mean follow up of 30 $\pm$ 26 months (0.3 – 116) and as of August 2004, 52 pancreatic recipients with intestinal and multivisceral transplantations are alive, for an overall survival

rate of 67%. The causes of death were infection (n=11), PTLD (n=5), rejection (n=4), technical (n=3), GVHD (n=1) and others (n=2). Another 5 grafts were lost due to primary non-function in 2, arterial thrombosis in 2, and mycotic pseudoaneurysm in the remaining one. The actuarial patient survival was 81% at 1 year and 77% at 5 years with pancreatic functional survival rates of 76% and 62%, respectively. Despite patient complexity, one-year survival has recently improved to 91%. The recent improvement in outlook may be related to technical innovations, early viral detection, allograft immune-modulation, and recipient pretreatment.

Pancreatic Rejection

Despite the high immunogenicity of the concomitantly transplanted intestine, high degree of HLA mismatch, and transplanting the pancreas across a positive cytotoxic cross-match, only 6 (8%) pancreatic glands experienced mild to moderate acute rejection simultaneously with the intestine and/or liver allograft. The diagnosis was made based on clinical and biochemical data, and all episodes were successfully treated with steroids and/or anti-lymphocytic agents. Chronic rejection was diagnosed on histopathologic examination of an explanted graft or an autopsy specimen on 3 (4%) occasions. These rates of acute and chronic pancreatic rejection are significantly lower than those observed in the simultaneously transplanted intestine.

Preconditioning and Successful Weaning

With recipient pretreatment, patient and graft survival have significantly improved, with a one-year patient survival of 94% and a graft survival of 90%. There has been no significant increase in morbidity, with a low risk of opportunistic infections, including viral infections. Attempts of weaning with spaced doses of tacrolimus monotherapy were successful in 49% (n=20) of the pretreated recipients. With a mean follow up of 19 ± 7 (range: 10 –35) months, 9 patients are on a single daily dose of tacrolimus, 3 on every other day, 2 on three times per week, and 6 on two times per week. There is no single example of graft loss to acute or chronic rejection because of weaning.

Discussion

En-bloc pancreas transplantation is common with intestinal and multivisceral transplantation. Diabetes is a rare indication for inclusion of the pancreatic gland. The lower risk of graft thrombosis is mainly related to the establishment of a large size infrarenal aortic graft and the common use of a Carrel patch during the back table arterial reconstruction. The gland is immunologically protected by the concomitantly transplanted organs, particularly the liver, despite the co-existence of high immunologic risk factors, including a high degree of HLA mismatching and pre-existing antibodies.

Summary:

1. Campath-1H® preconditioning with tacrolimus monotherapy is an effective immunosuppressive regimen for pancreas transplantation, with acceptable patient and graft survival rates early after post-transplantation.

2. Rejection rates are low under this protocol if the tacrolimus level is kept consistently >10 ng/ml.

3. This immunosuppressive protocol, combined with recent technical refinements, has resulted in lower rates of thrombosis and overall complications.

4. Pancreatic transplantation en bloc with visceral grafts has the following unique features:

    A. Diabetes is a rare indication, and HLA matching is not required.

    B. The gland is immunologically protected by the simultaneously transplanted visceral organs.

    C. Disease gravity, surgical complexity and gut alloimmunity influence the overall pancreatic allograft survival.

    D. The current UNOS listing criteria and data registry should be modified for obvious logistic and scientific reasons.
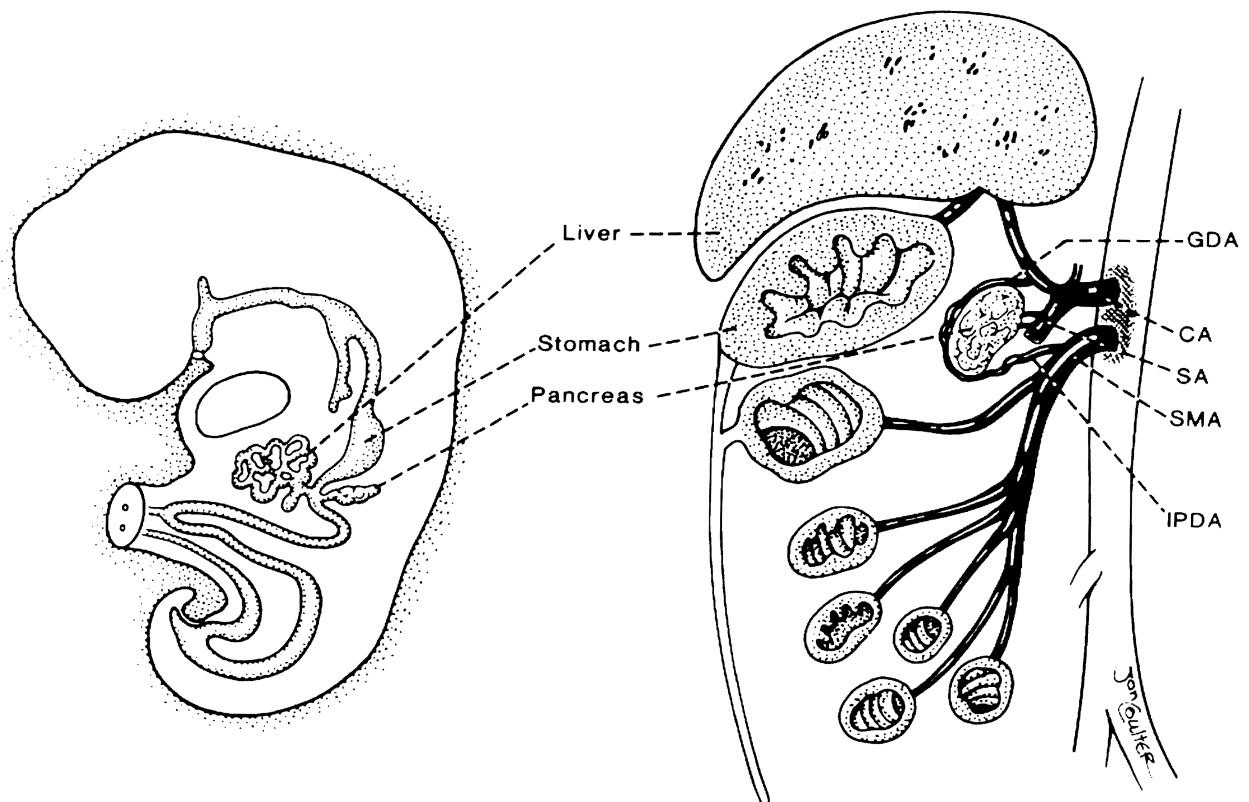
REFERENCES

1. Starzl TE, Murase N, Abu-Almagd K, et al. Tolerogenic immunosuppression for organ transplantation. *Lancet* 2003;361(9368):1502.

2. Marcos A, Eghtesad B, Fung JJ, et al. Use of aletuzumab and tacrolimus monotherapy for cadaveric liver transplantation: with particular reference to hepatitis C virus. Transplantation 2004;77(6):926.

3. Shapiro R, Tan H, Basu A, et al. Campath 1-H preconditioning and tacrolimus monotherapy with subsequent weaning in renal transplant recipients. *Am J Trans* 2004;4(8):405.

4. Starzl TE, Iwatsuki S, Shaw BW Jr, et al. Pancreaticoduodenal transplantation in humans. *Surg Gynecol Obstet* 1984;159:265.

5. Nghiem DD, Corry RJ. Techniques of simultaneous pancreaticoduodenal transplantation with urinary drainage of pancreatic secretion. *Am J Surg* 1987;153;405.

6. Fehr T, Sykes M. Tolerance induction in clinical transplantation. Transplant Immunol 2004 Sept-Oct;117.

7. Smiley ST, Csizmadia V, Gao W, et al. Differential effects of cyclosporine A, methylprednisolone, mycophenolate, and rapamycin on CD154 induction and requirement of NFkB: implications for tolerance induction. *Transplantation* 2000;10:415.

8. Kirk AD, Burkly LC, Batty DS, et al. Treatment with humanized monoclonal antibody against CD154 prevents acute renal allograft rejection in nonhuman primates. *Nat Med* 1999;4:686.

9. Kapur S, Bonham CA, Dodson SF, et al. Strategies to expand the donor pool for pancreas transplantation. *Transplantation* 1999:67(2):284.

10. Krieger NR, Odorico JS, Heisey DM, et al. Underutilization of pancreas donors. *Transplantation* 2003:75(8):1271.

11. Thai NL, Khan A, Tom K, et al. Revascularization of the gastroduodenal artery in a pancreas allograft from a donor with a replaced right hepatic artery. *Transplantation* (in press).

12. Fridell JA, Milgrom ML, Henson S, et al. Use of the end-to-end anastomotic circular stapler for creation of the duodenoenterostomy for enteric drainage of the pancreas allograft. *J Am Coll Surg* 2004;198(3):495.

13. Abu-Elmagd K, Fung J, Bueno J, Martin D. Madariaga J, Mazariegos G, Bond G, Molmenti E, Corry R, Starzl T E, Reyes J. Logistics and technique for procurement of intestinal, pancreatic, and hepatic grafts from the same donor. Ann of Surg 232(5):680-687,2000.

14. Abu-Elmagd K, reyes J, Bond G, Mazariegos G, Wu T, Murase N, Sindhi R, Martin D, Colangelo J, Zak M, Janson D, Ezzelarab M, Dvorchik I, Parizhskaya M, Deutsch M, Demetria A, Fung J, Starzl T. clinical intestinal transplantation: A decade of a single center experience. Ann of Surg 234(3):404-417, 2001.

15. Abu-Elmagd K, Reyes J, Todo S, Rao A, Lee R, Irish W, Furukawa H, Bueno J, McMichael J, Fawzy A, Murase N, Demetris J, Rakela J, Fung J, Starzl T E. Clinical intestinal transplantation: New propectives and immunologic considerations. J Am Coll Surg 186:512-527,1998.

16. Starzl TE, Todo S, Tzakis A, et al. The many faces of multivisceral transplantation. Surg Gynecol Obstet 1991;172:335-344.
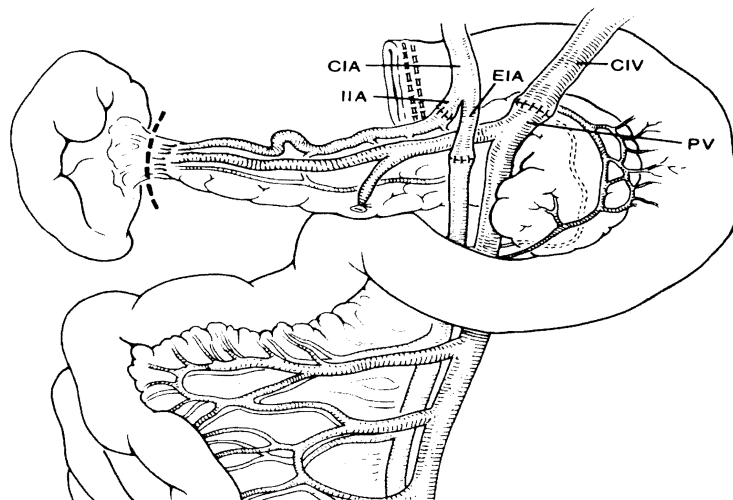
17.   Casavilla A, Selby r, Abu-Elmagd K, et al. Logistics and technique for combinedhepatic-intestinal retrieval. Arch Surg 216 (5):605-609, 1992.

18.   Furukawa H, Abu-Elmagd K, reyes J, Nour B, Tzakis A, Todo S, Starzl TE, Technical aspects of intestinal transplantation. In: Surgical Technology International II (MH Braverman, RL Tawes, eds) Surgical Technology International, pp 165-170, 1994.

19.   Abu-Elmagd KM, bond G, Reyes J, Fung J. Intestinal transplantation: A coming of age. Advances in Surgery, 36:65-101, 2002.

Figure 2

The embryonic origin of the liver, pancreas and alimentary canal. Note the shared axial blood supply and its segmental distribution, CA, celiac axis; GDA, gastroduodenal artery; IPDA, inferior pancreaticduodenal artery; SA, splenic artery; SMA, superior mesenteric artery.

Figure 3   Back table vascular reconstruction of the composite intestinal-pancreatic allograft. Note continuity of the pancreas, duodenum, and small intestine with intact vascular pedicle, CIA, common iliac artery, CIV, common iliac vein; EIA, external iliac artery; IIA, internal iliac artery; PV, portal vein.
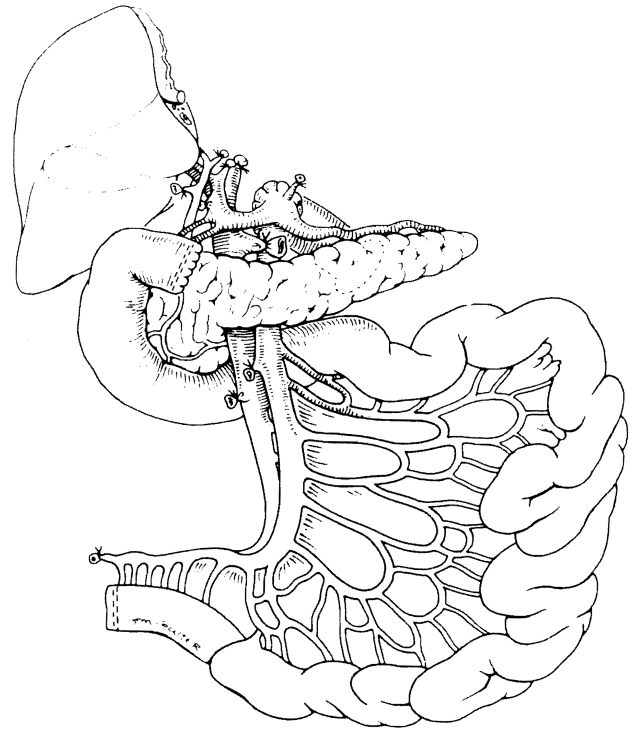
Figure 4

A. Combined liver and intestine without the duodenum and pancreas.
B. Combined liver and intestine en-bloc with duodenum and pancreas. Note continuity of the hepatobiliary system with the duodenum. Resection of the left lobe of the liver was performed because of loss of the abdominal domain of the recipient.

A.

B.

Figure 5

. Modified multivisceral graft that contains stomach,
Duodenum, pancreas, and small intestine. Note preservation of
The gastroepiploic arcade and left gastric pedicle including the
Left gastric vein (LGV). Inset: Venous drainage of the composite
Visceral graft to the side of the recipient superior mesenteric vein
(SMV) stump by using the donor common iliac vein as an extension
graft without compromising the recipient portal venous flow during
graft implantation. PV, portal vein; SV splenic vein.
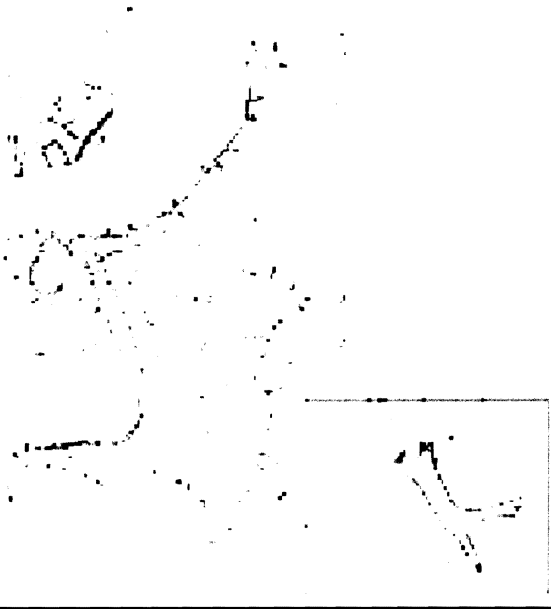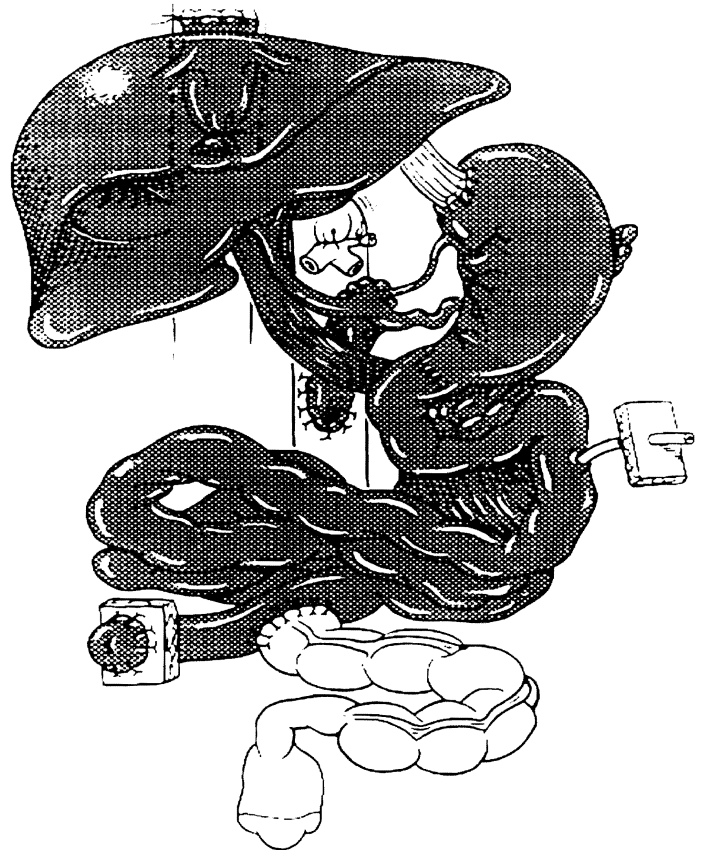
B. Full multivisceral transplant

ig. 7. Modified multivisceral graft that contains stomach,
duodenum, pancreas, and small intestine. Note preservation
of the gastroepiploic arcade and left gastric pedicle with
venous drainage to the side of the recipient superior mes-
enteric vein stump. (Reproduced from Abu-Elmagd K, et al.[15].

Figure 6

A. Transplantation of a modified multivisceral graft (unshaded organs) containing the pancreas and all of the hollow intraabdominal viscera in continuity from the esophagogastric junction to the terminal ileum. The native liver, spleen, pancreas, and a C loop of duodenum have been retained.Biliary drainage from the native liver as well as from both pancreases was accomplished with a side-to-side host-to-graft duodenal anastomosis. The insert shows preservation of the donor splenic (DSA) and left gastric (DLGA) arteries (with Carrel patch) with ligation of the donor hepatic artery (DHA) stump. Note that an interposition arterial graft was initially anastomosed to the recipient infrarenal aorta and before allograft implantation. RSA, recipient splenic artery; RSV, recipient splenic vein; RBD, recipient bile duct; RPV, recipient portal vein; DSMV, donor superior mesenteric vein; DSMA, donor superior mesenteric artery.

B. The use of a modified multivisceral graft (stomach, duodenum, pancreas, and small bowel) after abdominal visceral exenteration with preservation of the host liver and spleen (shaded organs). The portosplenic circulation is maintained intact during graft insertion and the preserved spleen protects the patient from the risk of posttransplant lymphoproliferative disease. This modified multivisceral transplantation has been used to treat recipients with massive gstrointestinl polyposis and extensive Crohn's disease. Note the duct-to-duct biliary reconstruction, RSA, recipient splenic artery; RSV, recipient splenic vein; RBD, recipient bile duct; DSA, donor splenic artery: DLGA, donor left gastric artery; DBD, donor bile duct.

Fig. 19. Transplantation of a modified multivisceral graft (unshaded organs) containing the pancreas and all of the hollow intraabdominal viscera. A: Native liver, spleen, pancreas, and a C loop of duodenum have been retained and drained through a side-to-side host-to-graft duodenal anastomosis. B: Native spleen is preserved with maintenance of the

Table 1: Immunosuppression

Steroids (methylprednisolone)
1 gm premedication 30 min prior to Campath 1H infusion
1 gm at reperfusion of allograft (500 mg each with SPKs)

Campath 1H
30 mg IV over 2 hrs intraoperatively

Tacrolimus
Target 12-hour trough: 10-15 ng/ml
First dose approx. 12 hrs post-operation

Table 2: Donor-Recipient Demographics

Recipient Age	43 ± 7.9 yrs	(range 19-59)
Donor Age	30.3 ± 13 yrs	(range 12-61)
Pancreas CIT	14 ± 3.3 hrs	(range 7-20)
Kidney CIT (total) SPK + PAK*	11 ± 8.2 hrs	(range 2-28)
SPK	15.1 ± 6 hrs	(range 6-28)

*living-related kidneys

Table: 3 Patient and graft survivals

	N	3-6 mos	6-12 mos	>12 mos
Total patients	37	18	12	7
Pt. Survival (100%)	37	18	12	7
Pancreas (94%) Survival	35/37	18/18	11/12	6/7
Kidney (90%)* Survival	18/20	7/8	7/7	4/5

*Only SPKs. No loss of kidney allografts in PAKs (N=11)

Table: 4 Complications

Total patients	Total	3-6 mos	6-12 mos	>12 mos
	37	18	12	7
Complications (22%)	8/37	3/18	4/12	1/7
thrombosis (panc)	1	1	0	0
thrombosis (kid)	1	0	0	1
bleeding	3	2	1	0
fistula	2	0	2	0
pseudoaneurysm*	1	0	1	0

*pancreas allograft

Table: 5 Rejection of allografts

	Total	3-6 mos	6-12 mos	>12 mos
Total patients	37	18	12	7
Rejection (22%)	8/37	1/18	3/12	4/7
Graft loss (3%)*	1/37	0	0	0

*Kidney allograft with humoral rejection

Figure: 1

Tacrolimus
ng/ml

Days

20

10

0