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PANCREATICODUODENAL TRANSPLANTATION IN HUMANS

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IN THE FIRST CLINICAL TRIALS of pancreatic transplantation (1, 2), the graft consisted of the whole pancreas, duodenum and a short segment of jejunum. The duodenal component of the transplant apparently was responsible for a high incidence of infection and other lethal complications, probably because intestinal rejection was difficult to control with the immunosuppressive therapy then available. In one study (3), it was documented how total pancreatic transplantation with the duodenal segment was abandoned in favor of transplantation of the pancreatic body and tail. With these "segmental" transplants, the transfer of suboptimal amounts of pancreatic tissue, imperfect techniques for management of the graft exocrine secretions, vascular thromboses, other technical complications and difficulties with the control of rejection have contributed to the unsatisfactory results throughout the world (4).

During the last year, four patients with diabetes have been given composite splanchnic organ grafts which included the entire pancreas, spleen and variable amounts of duodenum. For two of the recipients, enough jejunum was included to allow its anastomosis as a graft Roux-en-Y to the gastrointestinal tract of the recipient. Observations of the four patients have defined both the causes and management of complication specific to the intestinal and splenic components of the graft. They also have convinced us that our final version of a composite organ graft or variations of its principle, will come to be the preferred methods of pancreatic transplantation in human beings.

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METHODS

The donor operation. Except for avoidance of blood type ABO incompatibilities and positive cytotoxic antibody cross matches, tissue typing was done at random (Table I). The D,3 and 4 antigens which are strongly associated with juvenile-onset diabetes (5) were identified in three of the four recipients but none of the donors (Table I). The donor age and sex patterns were variable (Table I). The grafts were taken from multiple organ donors, using the same approach as for combined donor hepatectomy and nephrectomy (6). The proximal portion of the celiac axis was dissected free. The left gastric branch of the celiac axis was ligated at its origin. The hepatic artery was dissected free and ligated beyond the gastroduodenal arterial branch (Fig. 1). When the superior mesenteric artery was adherent to the pancreas, it was ligated proximally and distally and left with the graft (Fig. 1).

The spleen and the tail of the pancreas were gently mobilized. The first part of the duodenum was transected and the distal end was closed in two layers (Fig. 1), after stapling or suturing the proximal end to prevent contamination. Preparations were made for *in situ* perfusion of the kidneys and pancreas by placement of cannulas into the distal part of the aorta and inferior vena cava (6).

When both the pancreas and nephrectomy teams were ready, the aorta was cross clamped above the celiac axis and cold lactated Ringer's or Collins solution was infused through the aortic cannula while vena caval blood was removed and while the transected portal vein was bled out. After completion of the aortic infusion, an aortic patch was removed in continuity with the celiac axis and the graft. A variable amount of jejunum was kept with the pancreaticoduodenal and splenic specimen (Fig. 1). The chilled composite graft, was placed in a cold bath of Collins solution

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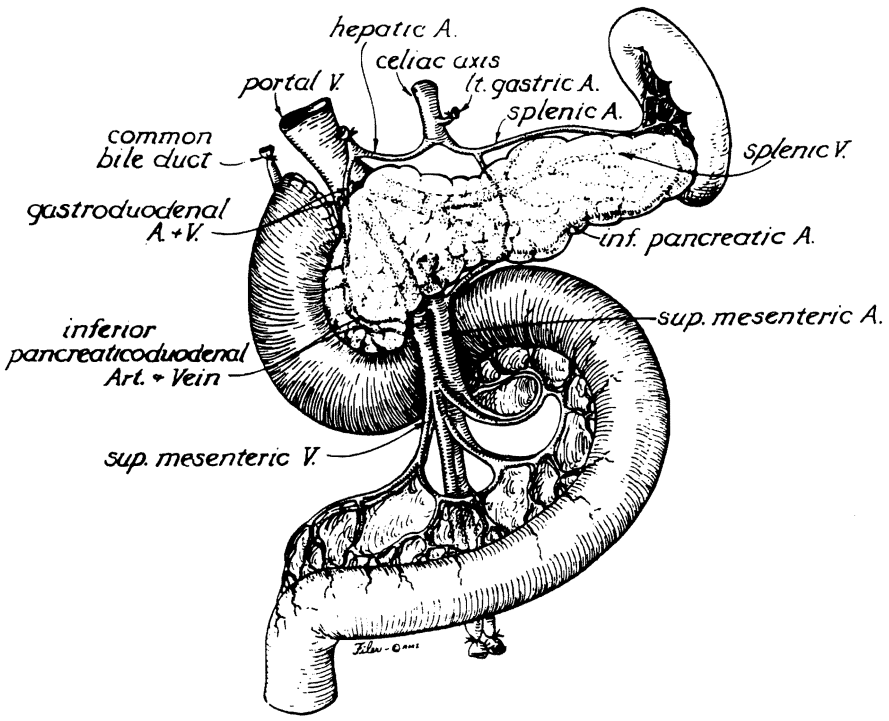

FIG. 1. Composite graft removed from donors in preparation for pancreaticoduodenal transplantation. The long jejunal segment was kept in Patients 1 and 2 but removed at the backtable along with the distal part of the duodenum in Patients 3 and 4. The spleen was retained in all except Patient 3.

until it could be revascularized in the recipient. The cold ischemia times before revascularization in the recipients ranged from 45 to 140 minutes.

Recipient selection. Three men and one woman, between 30 and 42 years of age (Table I) who had been insulin dependent (Type I) diabetics for 23 to 29 years, were selected. End-stage diabetic nephropathy necessitating dialysis or transplantation was an obligatory condition of candidacy imposed by the Institutional Review Board of the Univeristy of Pittsburgh. Consequently, the four recipients had undergone dialysis for long periods followed by a successful cadaveric renal transplantation from three weeks to seven months before pancreatic grafting (Table II). Insulin requirements before pancreatic grafting are noted in Table III).

Patients 1, 2 and 4 had severe sensory and motor neuropathy of the legs as well as autonomic neuropathy characterized by poor motility of the gastrointestinal tract and by a fixed heart rate that was nonresponsive to exercise (7, 8). All four patients had undergone multiple ophthalmologic procedures, including laser treatments for retinopathy. Patient 1 was completely blind in one eye and Patient 2 was legally blind.

The recipient operation. The organs transplanted in addition to the entire pancreas are summarized in Table II for each patient. The spleen was excluded only in Patient 3. In Patients 1 and 2, the entire duodenum and about 2 feet of jejunum were retained initially (Fig. 2), but later, it was necessary to remove most of the intestinal graft (Fig. 3). In Patients 3 and 4, only the segment of duodenum into which the ampulla of Vater emptied was kept (Fig. 4).

It was simplest to place the composite organ grafts on the left side of the recipient through an extraperitoneal lower abdominal incision, keeping the transplanted viscera in the same spatial orientation as in the donor. This was possible in two patients. The celiac axis and portal vein were anastomosed end-to-side to the external or com-

TABLE I.—DONOR/RECIPIENT COMPARISON IN INSTANCES OF PANCREATIC TRANSPLANTATION

Patient No., Age, yrs., Sex	*ABO type*	*D_R type*	*Antigens of possible 4 matched at A, B loci*
1 35 M	0—> A	2,4—> 3	1
2 33 F	0—> 0	2—> 3,4	0
3 30 M	0—> 0	5,7—> 3,4	0
4 42 M	A—> A	5—> 3,4	0

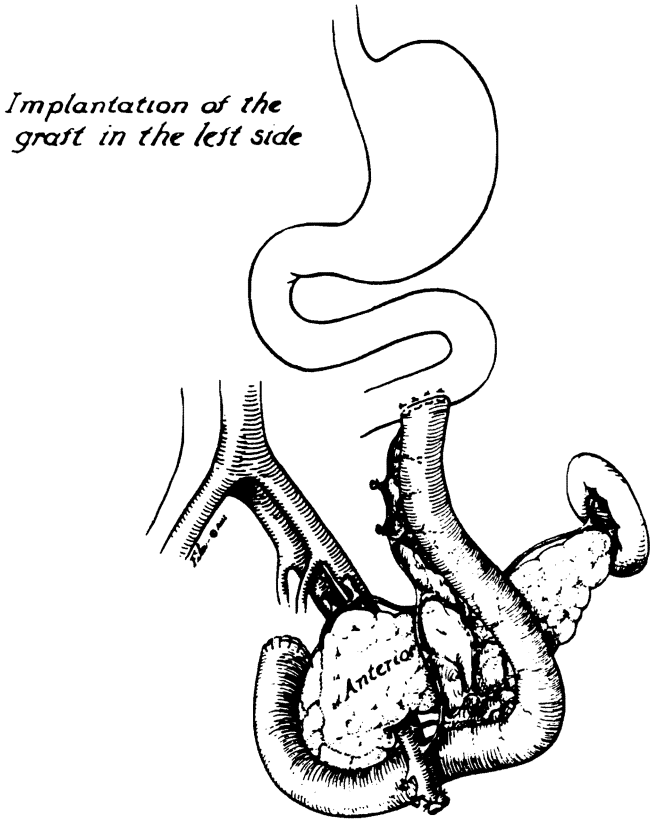

FIG. 2. Technique of implantation into the left side used in Patient 1. The graft jejunum which provided an exit for the pancreatic exocrine secretions became a major source of morbidity, and eventually, it was removed (Fig. 3.).

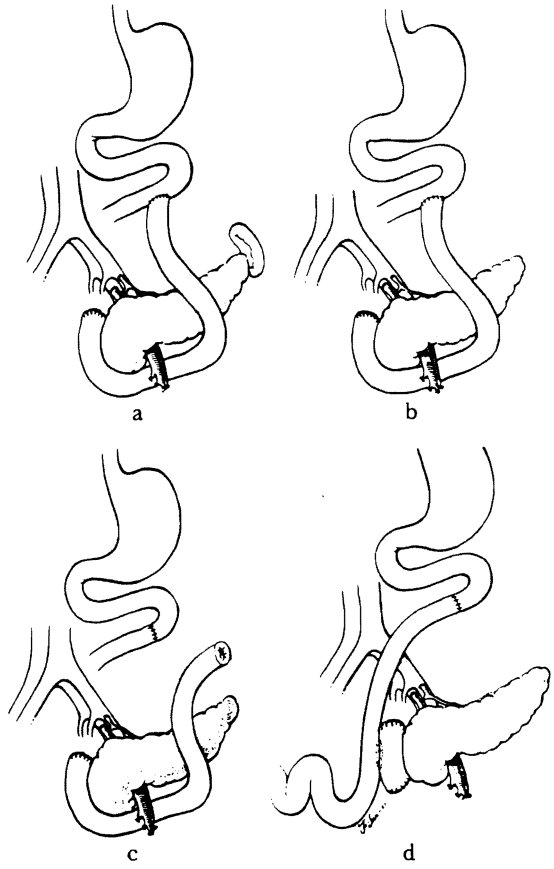

FIG. 3. Operative revisions in Patient 1. a, The entire specimen shown in Figure 1 was transplanted. b, Splenectomy was performed after six and one-half days. c, The graft jejunum was detached from its anastomosis to recipient jejunum and brought to the skin of the left lower quadrant. d, The graft jejunum and distal part of the duodenum were resected and a "bubble" of duodenum retained for anastomosis to the recipient jejunum. (See text for details).

mon iliac vessels (Fig. 2). The pancreas and the spleen were placed in the extraperitoneal space. A window was made in the peritoneum through which an intestinal anastomsis could be performed. Identification of the site of the anastomosis to the recipient jejunum was facilitated by a short middle midline incision. Details of the intestinal connections and their revisions are described under the heading Results.

In two patients, the grafts were placed on the right side because a renal graft already occupied the lower left part of the extraperitoneal space (Fig. 4). With this variation, the specimen was rotated 180 degrees so that the spleen was at the right (Fig. 4) and the portal vein was inferior. The vascular anastomoses were to the iliac vessels of the recipient. Provision for an intestinal anastomosis through a peritoneal window was the same as on the left side.

Postoperative immunosuppression. When the four patients were given cadaveric kidneys three weeks to seven months previously (Table II), they were treated with cyclosporine and steroids as previously described (9). At the time of the pancreatic transplantation, the cyclosporine doses were approximately 10 milligrams per kilogram per day and the prednisone doses were 20 milli-

TABLE II.—FEATURES OF PANCREATIC TRANSPLANTATION

Patient No.	*Previous cadaver kidney TX*	*Date pancreas TX*	*Spleen included in graft*	*Spleen later removed*	*Intestine in orginal graft*
1	3 mos.	3/06/83	Yes	6½ Days	Duodenum, jejunum
2	3 wks.	4/09/83	Yes	Never	Duodenum, jejunum
3	5 mos.	10/24/83	No		Bubble of duodenum
4	5½ mos.	12/23/83	Yes	18 Days	Bubble of duodenum

TX, Transplantation.

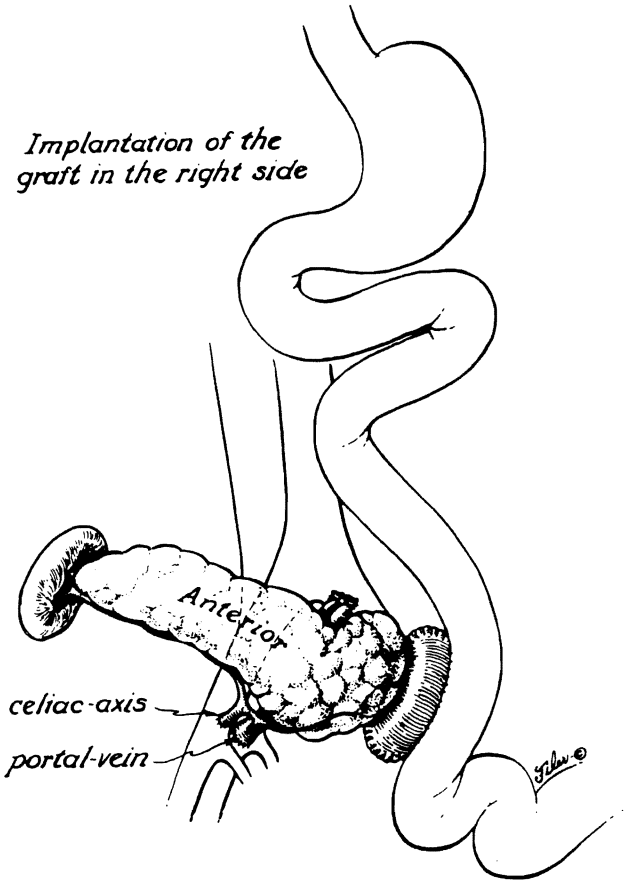

FIG. 4. Pancreaticoduodenal and splenic transplantation to the right side of the pelvis in Patient 4. Note that all of the jejunum and most of the duodenum were removed, leaving a short segment of duodenum closed at both ends which was anastomosed side-to-side to the recipient jejunum.

grams per day. After pancreatic transplantations, a five day burst of steroid therapy was given, beginning at 200 milligrams per day with decrements of 40 milligrams per day until the base line dose of 20 milligrams per day had been reached. For patients who could not eat during the one or two days postoperatively, 6 milligrams per kilogram per day of cyclosporine given intravenously were substituted for the oral dosage, and the intravenous route was overlapped with resumption of the oral dosage for another day or two. Subsequently, the cyclosporine and steroid dosages were reduced further. Cyclosporine therapy was monitored by frequently measuring the venous blood concentration of the drug.

RESULTS

All of the four patients are alive with observation periods of two and a half months to one year. The renal function from the previously transplanted cadaver kidneys has remained good in all four.

Pancreatic graft function. The graft in Patient 3 underwent venous infarction a few hours postoperatively due to thrombosis of the splenic and portal veins. It was removed one day after its insertion, and insulin therapy was resumed. The other three patients have not required insulin in the two and a half, 11 and 12 months since operation. After revascularization of the pancreatic grafts, the plasma glucose concentrations fell at the rate of about 50 milligrams per cent every one-half hour until a euglycemic level was reached. Fasting plasma glucose levels have been in the normal range, and the results of glucose tolerance tests consistently have been normal (Fig. 5). A detailed account of the metabolic and endocrine changes in these patients will be published separately.

The peripheral neuropathy in the three patients with functioning grafts has reversed or is reversing (Table III). Reversal of autonomic neuropathy was also noted and was particularly striking in Patient 1 who resumed sexual function within six months after five years of impotence and who took up jogging and hand ball as cardiovascular responsiveness improved. These three patients have had stabilization of visual complications (Table III).

Splenic complications. In Patient 3, the spleen was removed before transplantation because of space limitations. Thrombosis of the venous outflow necessitated graft removal one day later. Patient 1 who was of A blood type was given a composite graft from an O donor. The estimated blood loss at operation was 100 milliliters. During the next six days, the hematocrit level fell from 41 to 21 per cent. After five days, the serum haptoglobin level was 35 milligrams per cent, the reticulocyte count was 5.5 per cent, the direct and indirect bilirubin value had increased to 1.0 and 2.9 milligrams per cent, respectively, and the urine was positive for urobilinogen. The results of the direct Coomb's test was positive. Type A blood could not be matched with the patient because of anti-A isoagglutinins which had appeared in the serum. Anti-A isoagglutinins also were eluted from the circulating red blood cells. Six transfusions of washed group O red blood cells were given over the next three days to stabilize the hematocrit level of the patient.

After six and a half days, the transplanted spleen was removed. It weighed 190 grams. Histopathologically, there was red pulp congestion, immunoblast proliferation and intimal swelling. Although karyotyping studies were not done, the fact that lymphoid expansion oc-

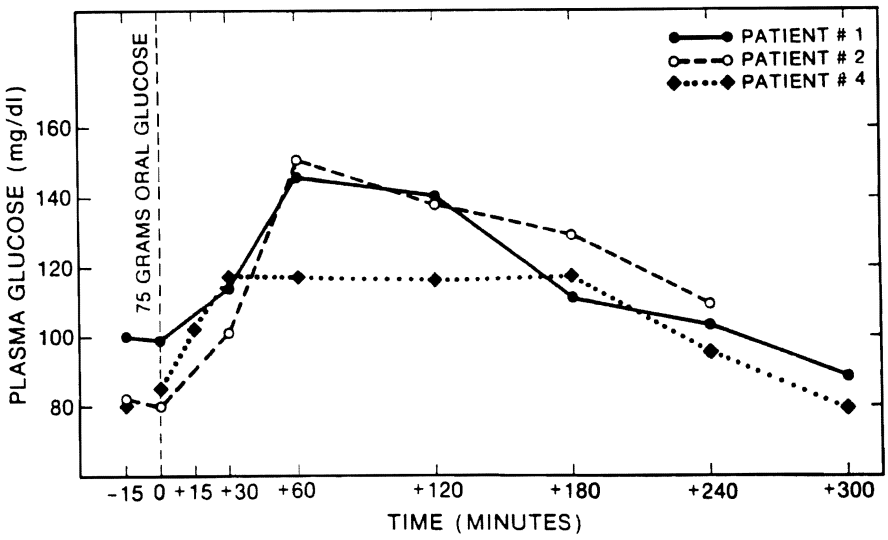

FIG. 5. The most recent glucose tolerance tests of the three patients with functioning grafts, performed after an overnight fast as recommended by the Diabetes Data Group (28), using an glucose challenge of 75 grams taken orally. Impaired glucose tolerance is defined as two-hour plasma glucose values between 140 and 200 milligrams per cent with an intervening value above 200 milligrams per cent. Fasting plasma glucose values exceeding 140 milligrams per cent or two-hour plasma glucose values above 200 milligrams per cent accompanied by an intervening value above 200 milligrams per cent are diagnostic of diabetes mellitus. All tests are within normal limits by these definitions.

curred predominantly in the marginal zones suggested that the proliferating cells were of donor origin. Cells populating the marginal zones do not recirculate (10), and in addition, this site is directly bathed in host blood and is thought to be the major site at which antigen presents to this organ (10, 11). Of note, germinal centers were absent and no changes were seen in the periarteriolar lymphoid sheath.

Postoperatively, the hematocrit level stabilized. The anti-A isoagglutinins disappeared from the serum over the next nine weeks.

Patient 1 also had a reduction in platelet count from 230,000 per cubic millimeter preoperatively to 140,000 before graft splenectomy. The change did not cause concern, but in Patient 4, who received a graft from a donor with the same ABO blood type, the decline was from 200,000 to 22,000 during an 18 day period. After graft splenectomy in both Patients 1 and 4, the thrombocyte counts were restored to the pre-existing level within a few days. In contrast with the histopathologic findings in Patient 1, the grafted spleen removed from Patient 4 did not show marginal zone expansion.

After 11 months, Patient 2 still has a splenic homograft which has been visualized with radionuclide scans. She has not had hematologic complications.

Intestinal complications. In Patient 1, a 2 foot length of graft jejunum was anastomosed to the recipient jejunum (Fig. 3 a and b). After a few weeks, the patient had cramps, watery diarrhea and hypoalbuminemia in the 2 gram per cent range. By gastrointestinal tract series and computerized axial tomography, the luminal aspect of the graft jejunum was irregular and thickened. At reoperation, three months after the original procedure, the graft jejunum was detached from the recipient intestine and anastomosed to the skin of the abdominal wall (Fig. 3c). Although the intestine looked almost normal from the

TABLE III.—ENDOCRINE GRAFT FUNCTION

Patient No.	*Preop. daily insulin units*	*Postop. daily insulin units*	*Neuropathy*	*Eyesight*
1	80 NPH, 10 Reg.	0	Reversed	Stabilized (one eye blind)
2	100 Lente	0	Reversed	Stabilized (legally blind)
3	70 Reg.	70 Reg.	Unchanged	Unchanged
4	20 NPH, 10 Reg.	0	Reversing	Stabilized

Reg., Regular.

TABLE IV.—PROTEIN CONCENTRATION OF FLUID EXCRETED BY PANCREATICODUODENOJEJUNAL GRAFT*

	Basal, (mgm. per cent)	*Postsecretin (mgm. per cent)*†
Complement 3	22	22
Complement 4	3	3
IgG	50	56
IgA	26	27
Albumin	1,790	1,280
α_1 antitrypsin .	97	94

*Patient 1, see Figure 3c.
†Samples were obtained at 15 minutes after an intravenous dose of 1 clinical unit per kilogram of secretin.
IgG, Immunoglobulin G; IgA, immunoglobulin A.

outside, extensive mucosal damage was evident both grossly and microscopically. Epithelial destruction was accompanied by prominent acute and chronic inflammation, the latter composed chiefly of T-lymphocytes. The muscularis mucosae and deeper layers of intestine were unaffected despite the severity of the mucosal granulation. Damage was confined to the donor intestine and the results of biopsies of adjacent host intestine showed intact epithelium. After a week, the jejunum and duodenum were examined and biopsies taken by insertion of an endoscope through the skin stoma. Continued granulation of the mucosa was observed. Patchy areas of epithelium overlying this process suggested some degree of regeneration. Both processes were seen in second biopsies taken 15 days later.

During the 42 days when the skin jejunostomy was in place, its daily output ranged between 2 to 3 liters, a volume greater than expected from an otherwise normal pancreas. The protein concentration of the collected luminal content was almost 2 grams per cent, a figure that did not change greatly with secretin stimulation (Table IV). It was concluded that a protein losing enteropathy of the 2 or 3 foot duodenojejunal homograft segment was responsible for the loss of 40 to 60 grams of endogenous protein per day and accounted for the hypoalbuminemia that had occurred. At a third operation, the jejunum and distal part of the duodenum were removed, leaving a bubble of duodenum which was anastomosed side-to-side with the jejunum of the recipient (Fig. 3d). Histologically, continued inflammation and granulation tissue were seen in the mucosal layer. Epithelial regeneration was patchy and was present in a minority of sections. Vascular ectasia was now prominent in the submucosa. Within a few days, the serum albumin concentration of the recipient rose to normal, and all of the intestinal symptoms were relieved. Further hospitalization has not been necessary.

Patient 2, with an original graft that included the duodenojejunal segment, also had abdominal cramps, diarrhea and hypoalbuminemia. At a second operation six months post-transplantation, the jejunum and distal part of the duodenum were removed, leaving a proximal duodenal bubble that was anastomosed to the jejunum of the recipient. The resected portion of intestine bore a striking histologic resemblance to that from Patient 1. Within a week, the symptoms were relieved and the serum albumin level rose from 2.0 to 3.5 grams per cent. The final enteric reconstruction reached by stages in Patients 1 and 2 (Fig. 3d) was used at the time of transplantation for Patients 3 and 4 (Fig. 4).

DISCUSSION

The slowly evolving but cumulatively dramatic benefits of successful pancreatic transplantation were epitomized by the patients we studied. The three who retained the grafts have never required insulin after operation. They have had multiple normal glucose tolerance tests and fasting blood glucose concentrations during the subsequent two and one-half, 11 and 12 months. The reversal of neuropathy and the stabilization of small vessel disease and eye complaints have been striking. Although other workers have noted the same things in isolated instances, attempts at pancreatic transplantation usually have failed (1–4). The poor results can be explained partly by conceptual flaws, including the use of too little pancreas or ineffective strategies for dealing with exocrine secretions in many of the transplant procedures used until now.

The logic of transplanting the entire pancreas as part of a composite organ graft is evident from the most casual inspection of the upper abdominal viscera in both human beings and animals. The duodenum and spleen share the blood supply of the pancreas to which they are intimately adherent, and in addition, the duodenum receives the exocrine pancreatic secretions.

Thus, it was not surprising that pancreaticoduodenal grafts were used in the acute experiments performed upon animals reported long ago (12) and many years later (13). The pancreas, duodenum, jejunum and spleen were part of the complex visceral grafts studied by us more than 20 years ago from which pancreatic function was demonstrated during the five and a half to nine day postoperative lives of five dogs (14). Although immunosuppression was not used, these were the first examples of sustained pancreatic homograft function.

Most of the grafts transplanted under immu-

nosuppression in the pioneering work done by Lillehei and co-workers in dogs (2, 15) and eventually in humans (1, 2, 16) consisted of all of the pancreas, the duodenum and a short section of jejunum. Poor results both in animals and humans after such procedures caused their abandonment in favor of the suboptimal partial pancreatic grafts from which the exocrine secretions have posed special technical problems (3, 4). Eventually, the issue of pancreaticoduodenal transplantation was reopened by the results of the canine studies of Diliz-Perez and associates using cyclosporine and steroid therapy (17).

Aside from providing a complete pancreas, the advantages of the composite splanchnic organ grafts are principally technical. A large volume of blood flow through the graft is assured, particularly if the spleen is included. Large caliber vascular anastomoses can be directed into the intestinal tract through conventional and generally low-risk enteric anastomoses.

In addition, there may be a subtle immunologic advantage for the pancreas of having the additional antigen mass provided by extrapancreatic tissues. Mitigation or delay of the rejection of individual organs has been described when they were transplanted as part of a multiple organ complex (14, 18) and the spleen has been mentioned frequently as a beneficial companion organ for the kidney (19–21), skin (21, 22) and pancreas (23) in such diverse species as the dog, rat and guinea pig.

Nevertheless, the inclusion of the extrapancreatic organs has been responsible for morbidity, and in this study, the liabilities specific to both the spleen and intestine have been defined. The spleen was responsible for examples of hemolytic anemia and thrombocytopenia, complications of splenic transplantation that were recognized two decades ago in dogs (20, 24) and in humans (20, 25).

The hematologic disorders in the two patients in our study may have been related in part to antibody production by the splenic grafts. Small amounts of lymphoid tissue carried with orthotopic liver grafts have been shown to produce new immunoglobulin phenotypes in hepatic recipients (26). Theoretically, the vastly greater B-lymphoid mass in a splenic graft could jeopardize the recipient by producing large quantities of graft versus host antibodies that could react against formed blood elements and tissues. There was no direct evidence for this in the patient with severe acquired thrombocytopenia, although the complication was promptly relieved by graft splenectomy. However, the hypothesis was particularly tempting in Patient 1, an A blood type recipient who was given a spleen from an O donor. Anti-A isoagglutinins produced by the grafted O type spleen apparently were responsible for a positive Coomb's test result, hemolytic anemia and jaundice. All were relieved by splenectomy.

Notwithstanding these complications, we plan to include the spleen in future total pancreatic grafts providing there is donor-recipient ABO identity. Delayed splenectomy in the two patients with hematologic complications was extraordinarily easy, being accomplished in a few minutes after opening the lateral end of the extraperitoneal wound. By the end of six and a half to 18 days, the rest of the graft had mature revascularization. The only technical accident in the four recipients in our study was venous thrombosis of a graft from which the spleen had been removed prior to implantation.

In contrast, we intend to eliminate as much intestine as possible from future pancreatic grafts, as was done from the outset in Patients 3 and 4, leaving only enough duodenum at the level of the ampulla of Vater for a side-to-side anastomosis to recipient jejunum (Fig. 4). In the first two patients, the duodenum and jejunum in excess of this minumum amount became denuded of epithelium. A major protein losing enteropathy resulted. Whether the intestinal injury was caused by rejection, ischemia or other factors could not be determined, but the disabling consequences have dampened the enthusiasm for a clinical trial of intestinal transplantation under cyclosporine and steroid therapy that had been justified by the results of research done on dogs (27).

SUMMARY

Whole cadaveric pancreata were transplanted to the pelvic extraperitoneal location in four patients with diabetes who previously had undergone successful cadaveric renal transplantation. One graft was lost within a few hours from venous thrombosis but with patient survival. The other three are providing normal endocrine function after two and a half, 11 and 12 months. The exocrine pancreatic secretions were drained into the recipient jejunum through enteric anastomoses. Because mucosal slough of the graft duodenum and jejunum in two patients caused a protein losing enteropathy and necessitated reoperations, we now do the pancreatic transplantation with only a blister of graft duodenum

large enough for side-to-side enteroenterostomy. The spleen has been transplanted with the pancreas mainly for technical reasons, and this technique should have further trials in spite of the fact that delayed graft splenectomy became necessary in two recipients to treat graft induced hematologic complications.

REFERENCES

1. Kelly, W. D., Lillehei, R. C., Merkel, F. K., and others. Allotransplantation of the pancreas and duodenum along with the kidney in diabetic nephropathy. Surgery, 1967, 61: 827-837.
2. Lillehei, R. C., Idezuki, Y., Feemster, J. A., and others. Transplantation of stomach, intestines and pancreas; experimental and clinical observations. Surgery, 1961, 62: 721-741.
3. Sutherland, D. E. R. Current status of clinical pancreas and islet transplantation; registry results. Horm. Metab. Res., 1983, Suppl. 13, 28-36.
4. Land, W., and Landgraf, R. Segmental pancreatic transplantation, international work shop. Horm. Metab. Res, 1983, Suppl. 13, 1-104.
5. Svejgaard, A., and Ryeer, L. P. HLA genotype distribution and genetic models of insulin-dependent diabetes mellitus. Ann. Hum. Genet., 1981, 45: 293-298.
6. Starzl, T. E., Hakala, T. R., Shaw, B. W., Jr., and others. A flexible procedure for multiple cadaveric organ procurement. Surg. Gynecol. Obstet., 1984, 158: 223-230.
7. Rundles, R. W. Diabetic neuropathy; general review with report of 125 cases. Medicine, 1945, 24: 111-160.
8. Mackay, J. D., Page, M. M., Cambridge, J., and Watkins, P. J. Diabetic autonomic neuropathy; the diagnostic value of heart rate monitoring. Diabetologia, 1980, 18: 471-478.
9. Starzl, T. E., Hakala, T. R., Rosenthal, J. T., and others. Variable convalescence and therapy after cadaveric renal transplantation under cyclosporin-A and steroids. Surg. Gynecol. Obstet., 1982, 154: 819-825.
10. Kamararatne, D. S., Bazin, H., and MacLennon, I. C. M. Marginal zones; the major B-cell component of rat spleens. Eur. J. Immunol., 1981, 11: 858-864.
11. Burke, J. S. Surgical pathology of the spleen; an approach to the differential diagnosis of splenic lymphomas and leukemias—Part 1, disease of the white pulp. Am. J. Surg. Pathol., 1981, 6: 551-563.
12. Goussay, B. A. Technique de la greffe pancreaticoduodenale au cou. CR Soc. Biol., 1929, 100: 138-140.
13. DeJode, L. R., and Howard, J. M. Studies in pancreaticoduodenal homotransplantation. Surg. Gynecol. Obstet., 1962, 114: 553-558.
14. Starzl, T. E., Kaupp, H. A., Jr., Brock, D. R., and others. Homotransplantation of multiple visceral organs. Am. J. Surg., 1962, 103: 219-229.
15. Idezuki, Y., Feemster, J. A., Dietzman, R. H., and Lillehei, R. C. Experimental pancreaticoduodenal preservation and transplantation. Surg. Gynecol. Obstet., 1968, 126: 1002-1014.
16. Lillehei, R. C., Simmons, R. L., Najarian, J. S., and others. Pancreaticoduodenal allotransplantation; experimental and clinical experience. Ann. Surg., 1970, 172: 405-436.
17. Diliz-Perez, H. S., Hong, H-Q, de Santibanes, E., and others. Total pancreaticoduodenal homotransplantation in dogs under cyclosporine and steroids. Am. J. Surg., 1984, 147: 677-680.
18. Starzl, T. E. Experience in Hepatic Transplantation. With the assistance of C. W. Putnam. Pp. 182-192. Philadelphia: W. B. Saunders Co., 1969.
19. Kountz, S. L., and Cohn, R. Prolonged survival of a renal homograft by simultaneous splenectomy and splenic homotransplantation. Surg. Forum, 1962, 13: 59-62.
20. Marchioro, T. L., Fudenberg, H., Rowlands, D., and others. Splenic homotransplantation. Ann. N. Y. Acad. Sci., 1964, 120: 626-651.
21. Barmis, J. P., Schanzek, H., Sloane, C., and Taub, R. N. Specific impairment of humoral and cellular immunity after splenic allotransplantation in rats. Transplant. Proc., 1977, 9: 341-346.
22. Bitter-Suermann, H., and Shevach, E. M. Induction of transplantation tolerance in guinea pigs by spleen allografts—I, operative techniques and clinical results. Transplantation, 1982, 33: 45-51.
23. Bitter-Suermann, H., and Saue-Soderbergh, J. The course of pancreas allografts in rats conditioned by spleen allografts. Transplantation, 1978, 26: 28-34.
24. Jorean, G. L., Jr., Fiscus, W. G., Trentin J. J., and others. Splenic transplantation in the dog. Ann. N. Y. Acad. Sci., 1964, 120: 612-625.
25. Starzl, T. E., Marchioro, T. L., Rifkind, D., and others. Clinical experience with organ transplantation. South. Med. J., 1965, 58: 131-147.
26. Kashiwagi, N., Porter, K. A., Penn, I., and others. Studies of homograft sex and of gamma globulin phenotypes after orthotopic homotransplantation of the human liver. Surg. Forum, 1969, 20: 374-376.
27. Diliz-Perez, H. S., McClure, J., Bedetti, C., and others. Successful small bowel allotransplantation in dogs with cyclosporine and prednisone. Transplantation, 1984, 37: 126-129.
28. National Diabetes Data Group. Diabetes, 1979, 28: 1039-1057.