

# Transplantation Proceedings

An Official Publication of

The Transplantation Society

The Japan Society for Transplantation

The British Transplantation Society

The Transplantation Society of Australia and New Zealand

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## CONTENTS

Preface.....	<i>R. van Schilsgaarde, G. G. Persijn, and D. E. R. Sutherland</i>	565
--------------	--	-----

## GENERAL INTRODUCTION

Comprehensive Care Essential to Success in Diabetic Nephropathy .....	<i>E. A. Friedman</i>	569
---	-----------------------	-----

Biological Basis for Organ Transplantation in Diabetics.....	<i>J. S. Najarian and D. E. R. Sutherland</i>	573
--	---	-----

Patient Selection and Risk Factors in Organ Transplantation in Diabetics: Experience With Kidney and Pancreas .....	<i>J. Traeger, J. M. Dubernard, E. Bosi, P. M. Piatti, A. Gelet, S. El Yafi, H. Betuel, A. Secchi, J. L. Touraine, and G. Pozza</i>	577
--	---	-----

The Contribution of Pancreatic Transplantation to Current Concepts in Diabetes	<i>K. F. Federlin and R. G. Bretzel</i>	583
--	---	-----

What to Expect From Pancreas Transplantation.....	<i>P. McMaster</i>	587
---	--------------------	-----

Pancreas and Islet Transplant Registry Statistics.....	<i>D. E. R. Sutherland</i>	593
--	----------------------------	-----

Clinical Results of Renal Transplantation in Diabetic Patients .....	<i>J. Jervell, B. O. Dahl, P. Fauchald, T. Moen, G. Sødal, and A. Flatmark</i>	599
--	--	-----

Coronary Artery Disease in 100 Diabetics With End-Stage Renal Failure		
<i>W. E. Braun, D. F. Phillips, D. G. Vidt, A. C. Novick, S. Nakamoto,     K. L. Popowniak, E. Paganini, M. Magnusson, M. Pohl, D. R. Steinmuller,     D. Protiva, and C. Buszta</i>		603

Natural History of Chronic Renal Failure in Juvenile Diabetes Mellitus		
<i>L. A. Castro, G. Hillebrand, R. Landgraf, W. Land, and H. J. Gurland</i>		608

Selection and Assessment of Diabetic Patients for Dialysis and Transplant Programs		
<i>J. Michael, D. Adu, P. McMaster, J. H. Turney, and O. M. Gibby</i>		611

Does Insulin-Dependent Diabetes Mellitus Still Increase Risk to Cadaveric Kidney Transplantation? .....	<i>L. H. Toledo-Pereyra, J. Whitten, S. Baskin, L. McNichol, W. Lin, and K. Thavarajah</i>	613
--	--	-----

*(Continued)*

## CONTENTS

(continued)

Influence of Selection and Pretransplant Monitoring on Outcome of Renal Grafting in Diabetics..... <i>H. Brynger, O. Larsson, I. Ahlmén, P.-O. Attman, I. Blohmé, B. Frisk, and G. Nyberg</i>	615
Improving Results in Primary Diabetic Renal Transplantation..... <i>H. Zincke, D. E. Engen, S. Sterioff, M. W. McDonald, P. P. Frohnert, and W. J. Johnson</i>	617
Cadaveric Renal Transplantation in Insulin-Dependent Diabetes Mellitus: Experience in the Canadian Multicentre Trial <i>The Canadian Multicentre Transplant Study Group</i>	621
Improved Results of Renal Transplantation in Diabetic Nephropathy <i>H. Wilczek, R. Gunnarsson, G. Lundgren, and L. Öst</i>	623
DR-Matching for Cadaveric Renal Transplants in Insulin-Dependent Diabetic Patients..... <i>B. A. Vanderwerf and L. J. Koep</i>	628
Results of Renal Transplantation in Diabetics at the University of Minnesota Since 1979, Including a Comparison of Outcome in Diabetic and Nondiabetic Recipients Randomized to Cyclosporine Versus Azathioprine for Immunosuppression..... <i>D. E. R. Sutherland, D. S. Fryd, M. Strand, N. Ascher, R. L. Simmons, and J. S. Najarian</i>	629
Diabetic Renal Allograft Recipient Pretreatment With Donor-Specific Blood Products and Concomitant Azathioprine Immunosuppression..... <i>C. B. Anderson, G. A. Sicard, J. D. Tyler, G. E. Rodey, C. K. Anderman, and E. E. Etheredge</i>	633
Cadaveric Kidney Transplantation in Diabetics After Total Lymphoid Irradiation (TLI)..... <i>Y. Vanrenterghem, M. Waer, K. Ang, E. van der Schueren, J. Gruwez, R. Bouillon, and P. Michielsen</i>	636
Conversion From Conventional Immunosuppression to Cyclosporine A Therapy in Diabetic Recipients of Cadaveric Kidney Transplants..... <i>G. Thiel, R. Loertscher, F. P. Brunner, U. Keller, J. Landmann, M. Mihatsch, and F. Harder</i>	640
The Use of Intravenous Insulin in the Treatment of Diabetes During Rejection Episodes..... <i>R. O'Donovan, P. Devlin, D. Bennet-Jones, V. Parsons, M. Bewick, M. Weston, and P. J. Watkins</i>	643
Left Ventricular Function Before and After Renal Transplantation in Diabetics <i>O. Larsson, J. Wikstrand, P.-O. Attman, and I. Wallentin</i>	645
Recurrence of Diabetic Nephropathy in Human Renal Allografts: Preliminary Report of a Biopsy Study..... <i>S. O. Bohman, H. Wilczek, G. Jaremkow, and G. Lundgren</i>	649
Living Related Donors in Kidney Transplantation of Diabetics: A Five- to 12-Year Follow-Up Study..... <i>P. P. Frohnert, C. F. Anderson, D. E. Engen, H. Zincke, and J. P. Vogel</i>	654
The Elderly Living Related Donor in Diabetic Renal Transplantation <i>P.-O. Attman, I. Blohmé, H. Gäbel, H. Herlitz, O. Larsson, and H. Brynger</i>	656

(Continued)

## CONTENTS

(continued)

# PANCREAS TRANSPLANTATION IN THE TREATMENT OF DIABETES

Selected Issues of Importance in Clinical Pancreas Transplantation	<i>D. E. R. Sutherland</i>	661
The Importance of Myocardial Imaging as a Selection Criterion of Patients Prior to Pancreas Transplantation .....	<i>L. H. Toledo-Pereyra</i>	671
Combined Renal and Segmental Pancreatic Transplantation as Part of an Integrated Program for the Treatment of Diabetic Renal Failure.....	<i>J. Michael, J. H. Turney, P. McMaster, D. Adu, and O. M. Gibby</i>	675
The Need for Pretransplant Pathologic Examination in Cadaver Donor Segmental Pancreas Transplantation .....	<i>J. P. Squifflet, J. Rahier, Y. Pirson, B. Vandeeleene, M. Carlier, and G. P. J. Alexandre</i>	677
Procurement and Preservation of Human Pancreatic Grafts .....	<i>G. Lundgren, H. Wilczek, G. Klintmalm, G. Tydén, and C. G. Groth</i>	681
The Technique of Neoprene Injection for Human Pancreatic Transplantation: Experience in 40 Cases.....	<i>J. M. Dubernard, J. Traeger, E. Bosi, A. Gelet, S. El Yafi, A. Secchi, P. M. Piatti, A. M. Ruitton, J. L. Touraine, and G. Pozza</i>	684
Follow-Up of Simultaneous Kidney and Pancreas Transplantation in Type I Diabetes	<i>R. Landgraf, M. M. C. Landgraf-Leurs, D. Burg, A. Kampik, and W. Land</i>	687
Clinical Experience With Segmental Pancreatic Allografts.....	<i>R. Munda, M. R. First, C. Webb, and J. W. Alexander</i>	692
Minnesota Experience With 81 Pancreas Transplants Since 1978	<i>D. E. R. Sutherland, P. L. Chinn, F. C. Goetz, B. A. Elick, and J. S. Najarian</i>	695
Combined Kidney and Pancreas Grafting—Is it Really Safe and Does it Jeopardize the Kidney? .....	<i>P. McMaster, J. Michael, D. Adu, O. M. Gibby, T. Vlassis, and J. Turney</i>	704
Influence of Steroid Administration on the Endocrine Function of Neoprene-Injected Segmental Pancreas Allotransplants .....	<i>G. Pozza, A. Secchi, A. E. Pontiroli, E. Bosi, J. Traeger, J. M. Dubernard, A. Gelet, and J. L. Touraine</i>	707
Deterioration in Glucose Metabolism in Pancreatic Transplant Recipients After Conversion From Azathioprine to Cyclosporine.....	<i>R. Gunnarsson, G. Klintmalm, G. Lundgren, G. Tydén, H. Wilczek, J. Östman, and C. G. Groth</i>	709
Postoperative Management After Simultaneous Segmental Pancreas and Kidney Transplantation ....	<i>F. P. Lenhart, K. Unertl, U. Jensen, R. Landgraf, and W. Land</i>	713
Laboratory Findings During Rejection of Segmental Pancreatic Allografts	<i>G. Tydén, G. Lundgren, R. Gunnarsson, J. Östman, and C. G. Groth</i>	715

(Continued)

## CONTENTS

(continued)

Clinical Aspects of Pancreatic Rejection in Pancreatic and Pancreaticorectal Allotransplants .....	<i>J. Traeger, J. M. Dubernard, P. M. Piatti, E. Bosi, A. Gelet, S. El Yafi, H. Betuel, A. Secchi, J. L. Touraine, and G. Pozza</i>	718
Indium-111 Labeled Platelets in Monitoring Pancreatic Transplants in Humans		
<i>W. A. Jurewicz, J. A. C. Buckels, J. G. A. Dykes, B. K. Gunson, R. J. Hawker, S. T. Chandler, C. N. McCollum, and P. McMaster</i>		720
Segmental Pancreatic Transplantation With Duct Ligature or Enteric Diversion: Technical Aspects.....	<i>C. G. Groth, G. Lundgren, H. Wilczek, G. Klintmalm, G. Tydén, R. Gunnarsson, and J. Östman</i>	724
Experience With 13 Segmental Pancreas Transplants in Cyclosporine-Treated Diabetic Patients Using Ethibloc for Duct Obliteration (Surgical Aspects)	<i>W. Land, W.-D. Illner, D. Abendroth, and R. Landgraf</i>	729
Pathologic Evidence of Chronic Pancreatitis in Polymer Duct-Occluded Segmental Pancreas Allografts .....	<i>L. H. Toledo-Pereyra</i>	733
Intraductal Injection of Neoprene to Suppress Native Pancreatic Exocrine Secretion in Humans: Clinical and Metabolic Evaluation		
<i>V. Di Carlo, R. Chiesa, A. E. Pontiroli, G. Pozza, M. Carlucci, C. Staudacher, A. Secchi, and M. Cristallo</i>		736
Pancreatic Endocrine Function After Duct Occlusion in Humans.....	<i>I. B. Brekke, A. Bergan, L. Heen, and A. Flatmark</i>	739
Insulin, C-Peptide, Glucagon, and Somatostatin Secretion in Segmental Pancreatic Autotransplantation .....	<i>F. Fallucca, R. Tersigni, L. Giangrande, P. del Balzo, D. Zicari, M. Marinelli, G. Pimpinella, G. Ghirlanda, and S. Stipa</i>	741
<h2>EXPERIMENTAL PANCREAS TRANSPLANTATION</h2>		
Advantage of Exocrine Drainage on Long-Term Endocrine Function in the Transplanted Rat Pancreas.....	<i>N. P. Ingram, M. S. Nolan, N. J. Lindsey, P. F. Boyle, A. Herold, S. Beck, D. N. Slater, and M. Fox</i>	747
Clinical and Experimental Experience With Pancreaticocystostomy for Exocrine Pancreatic Drainage in Pancreas Transplantation .....	<i>H. W. Sollinger, K. Cook, D. Kamps, N. R. Glass, and F. O. Belzer</i>	749
Effects of Intraductal Irradiation on the Canine Pancreas .....	<i>J. L. Faure, B. Provencal, J. M. Dubernard, X. Martin, M. Devonec, J. Margonari, and J. Traeger</i>	752
Different Techniques of Duct Occlusion for Experimental Pancreas Transplantation in Dogs .....	<i>H. Lippert, H. Wolff, D. Lorenz, O. Abri, and F. Kühn</i>	755
Duct Management of Segmental Pancreatic Allografts in Pigs		
<i>R. T. Schweizer, B. A. Sutphin, P. F. Pfau, R. D. Calaluce, and M. M. Berman</i>		756

(Continued)

## CONTENTS

(continued)

Somatostatin: Progress in Segmental Pancreas Transplantation? An Experimental Study of Canine Duct-Occluded Grafts..... <i>E. Steiner, R. Landgraf, W. Land, P. Gruner, H. Schneeberger, M. Stangl, W. Steimer, and H. Arnholdt</i>	760
Late Observations on Canine Segmental Pancreatic Autografts..... <i>R. G. Cutfield, G. K. Kyriakides, L. Olson, R. M. Condie, D. H. Mintz, and J. Miller</i>	762
Prognosis of Experimental Pancreatic Transplantation in Relation to Vascular Reconstructive Procedure ..... <i>I. Vaněk, V. Bartoš, and V. Kočandrle</i>	764
Long-Term Endocrine Function of In Situ and Autografted, Duct-Obliterated Canine Left Pancreatic Segments ..... <i>H. G. Gooszen, R. van Schilfgaarde, M. Frölich, G. F. Cramer-Knijnenburg, and M. P. M. van der Burg</i>	766
Effect of Venous Drainage to the Vena Cava and Denervation on Endocrine Function of Pancreatic Segments in Dogs <i>D. Baumgartner, R. Illig, and D. E. R. Sutherland</i>	769
Comparison of Endocrine Function Between Right and Left Pancreas Autografts in Dogs... <i>Y. Motoki, M. Gotoh, M. Monden, O. Sakane, K. Shima, and J. Okamura</i>	773
An Analysis of Long-Term Histologic Changes Leading to Decreased Endocrine Function After Duct Obliteration of the Canine Pancreas <i>H. G. Gooszen, F. T. Bosman, and R. van Schilfgaarde</i>	776
Evidence for a Differential Importance of MHC and Non-MHC Alloantigens in Pancreas and Heart Transplantation in the Rat <i>J. Klempnauer, L. Hoins, B. Steiniger, E. Günter, K. Wonigeit, and R. Pichlmayr</i>	778
Early Detection of Rejection in the Allografted Pancreas <i>M. Gotoh, M. Monden, Y. Motoki, O. Sakane, K. Shima, and J. Okamura</i>	781
Histology of Rejection in Rat Pancreas Allografts With Suppressed or Preserved Exocrine Function ..... <i>B. Steiniger, J. Klempnauer, U. Brüsich, and K. Wonigeit</i>	783
Diagnosis of Early Pancreas Allograft Rejection With Indium-111-Oxine-Labeled Platelets ... <i>H. W. Sollinger, L. M. Lieberman, D. Kamps, T. Warner, and K. Cook</i>	785
Fine Needle Biopsy of Canine Pancreas Graft: An Attempt at Cytologic Diagnosis in Graft Rejection <i>E. Steiner, C. Hammer, W. Land, P. Gruner, H. Schneeberger, M. Stangl, and W. Steimer</i>	789
The Effect of Cyclosporine on the Survival of Pancreatic Allografts in Pancreatectomized Baboons <i>D. F. du Toit, J. J. Heydenrych, G. Louw, T. Zuurmond, I. Laker, D. Els, S. Wolfe-Coote, A. Weidman, and H. Davids</i>	791
The Course of Pancreatic Allografts With Physiologic Secretion Drainage in Rats Temporarily Treated With Cyclosporine A <i>W. Timmermann, T. Schang, and W. Thiede</i>	794

(Continued)

## CONTENTS

(continued)

Infection as a Complication of Roux-En-Y-Loop Jejunal Draining Rat Pancreas Grafts, Including the Effect of Cyclosporine A <i>N. J. Lindsey, N. P. Ingram, M. S. Nolan, P. F. Boyle, A. Herold, S. Beck, A. Clark, D. N. Slater, and M. Fox</i>	797
Effect of Theophylline in Experimental Pancreas Allografting in Rats <i>A. Marni, M. E. Ferrero, and C. Rugarli</i>	799
The Effect of Prednisone and Azathioprine on the Endocrine Function of Canine Segmental Pancreatic Autografts <i>R. van Schilfgaarde, H. G. Gooszen, M. Frölich, G. F. Cramer-Knijnenburg, and M. P. M. van der Burg</i>	802
Segmental Pancreatic Allograft Survival in Pancreatectomized Baboons Treated With Total Body or Lymphoid Irradiation and Perioperative Blood Transfusions <i>D. F. du Toit, J. J. Heydenrych, B. Smit, T. Zuurmond, G. Louw, L. Laker, D. Els, S. Wolfe-Coote, J. A. van der Merwe, and A. W. Groenewald</i>	804
Hypothermic Preservation of the Rat Pancreas With A View to Maintaining Endocrine Function Using Either Cold Storage or Pulsatile Perfusion <i>M. S. Nolan, N. J. Lindsey, N. P. Ingram, A. Herold, D. N. Slater, and M. Fox</i>	807
Effect of 24-Hour Cold Storage on the Histology and Long-Term Endocrine Function of Autografted Canine Left Pancreatic Segments <i>R. van Schilfgaarde, H. G. Gooszen, F. T. Bosman, M. Frölich, G. F. Cramer-Knijnenburg, and M. P. M. van der Burg</i>	809

## TRANSPLANTATION OF PANCREATIC ISLET CELLS

Current Status of Experimental Islet Transplantation <i>K. J. Lafferty, S. J. Prowse, C. J. Simeonovic, O. Hegre, and H. P. Chase</i>	813
Clinical Feasibility of Islet Transplantation..... <i>D. W. Scharp</i>	820
Potential Cases of Normal Islet Autotransplantation in Humans <i>J. J. Altman, D. Houlberg, F. Bruzzo, N. Desplanque, J. Boillot, and F. E. Dazza</i>	826
Islet Cell Autotransplantation: Risks, Complications, and Long-Term Follow-Up <i>L. H. Toledo-Pereyra</i>	829
The Metabolic Effects of Islet Transplantation in the Diabetic Dog <i>D. Alderson and J. R. Farndon</i>	831
Intrasplenic Isografts of Canine Pancreatic Islets: Metabolic Study <i>R. V. Rajotte, G. L. Warnock, A. W. Procyshyn, and K. Wieczorek</i>	834
Effect of Streptozotocin on Composite Graft Survival <i>H. Reece-Smith, B. J. Fairbrother, P. McShane, and P. J. Morris</i>	838

(Continued)

## CONTENTS

(continued)

Islet Transplantation in Rats: Secondary Complications and Pancreatic Insulin Content .....	<i>W. Arendarczyk, C. Wójcikowski, and B. Pankowska</i>	840
Cryopreservation and Transplantation of Organ-Cultured Fetal Islets	<i>T. E. Mandel and W. M. Carter</i>	842
Islet Transplantation in Autoimmune Diabetes Mellitus	<i>C. Weber, W. Ting, K. Rosenkrantz, S. Rivera, B. Pernis, and K. Reemtsma</i>	845
Xenotransplantation of Human Fetal Islets in Nude Mice	<i>T. E. Mandel and H. M. Georgiou</i>	849
Evidence that Major Histocompatibility Complex Restriction is Involved in the Survival of Cultured Endocrine Allografts in Mice	<i>S. T. Bartlett, A. Naji, W. K. Silvers, and C. F. Barker</i>	851
T-Cell Reactions Versus Kidney Cells, Islets of Langerhans, and Non-T Lymphocytes	<i>D. Roth, T. Russell, L. Fuller, G. K. Kyriakides, D. Mintz, and J. Miller</i>	854
Reactivity of Pancreas Islet Cells With Antisera of Known Specificity	<i>K. Ulrichs, T. Schang, R. Keller, and W. Müller-Ruchholtz</i>	857
Effect of Pretreatment of Isolated Adult Islets With Monoclonal Antibody	<i>H. Reece-Smith, P. McShane, and P. J. Morris</i>	861
Islet Allografts in Rats Made Tolerant of Renal Allografts by Whole Blood Transfusion Compared to Islet Allografts After Blood Transfusion Alone	<i>D. W. R. Gray, A. D. Hibberd, P. McShane, and P. J. Morris</i>	863
Prolongation of Rat Islet Allografts With the Use of Ultraviolet Irradiation, Without Immunosuppression.....	<i>M. A. Hardy, H. Lau, and K. Reemtsma</i>	865
The Survival of Isolated Pancreatic Islets in Rats Rendered Immunologically Unresponsive to Renal Allografts	<i>D. W. R. Gray, H. Reece-Smith, B. Fairbrother, P. McShane, and P. J. Morris</i>	870
Combined Liver and Pancreatic Islet Allografts	<i>H. Reece-Smith, G. Muller, P. McShane, and P. J. Morris</i>	872

## THIRD INTERNATIONAL SYMPOSIUM ON HEART SUBSTITUTION

Perspectives On Heart Substitution.....	<i>R. Cortesini</i>	877
Future of Cardiac Transplantation.....	<i>D. A. Cooley</i>	880
Clinical Trials of Two-Staged Cardiac Transplantation Using an Orthotopic Mechanical Heart .....	<i>D. A. Cooley</i>	882
Heterotopic Versus Orthotopic Heart Transplantation	<i>C. N. Barnard and D. K. C. Cooper</i>	886

(Continued)

## CONTENTS

*(continued)*

### Approaches to the Artificial Heart

*G. Jacobs, H. Harasaki, R. Kiraly, L. Golding, and Y. Nose* 893

Artificial Heart Substitution: The Total or Auxiliary Artificial Heart ..... *J. Kolf* 898

Current Status of Research and Development of Artificial Hearts in Japan .. *K. Atsumi* 908

Past, Present, and Future of Mechanical Circulatory Support..... *J. T. Watson* 918

# Experience With 13 Segmental Pancreas Transplants in Cyclosporine-Treated Diabetic Patients Using Ethibloc for Duct Obliteration (Surgical Aspects)

W. Land, W.-D. Illner, D. Abendroth, and R. Landgraf

**S**INCE August 1979, 18 segmental pancreas transplantations in 17 diabetic recipients with end-stage renal failure have been performed at our institution (17 combined pancreatic and renal allotransplantations, one pancreatic retransplantation). The course and outcome of simultaneous pancreatic and renal transplantations in the first three patients receiving conventional immunosuppressive therapy have been published elsewhere.<sup>1-3</sup> This article presents our experience with 13 segmental pancreatic allotransplantations in 12 patients treated with the new immunosuppressive agent cyclosporine (Sandimmune, Sandoz Ltd., Basel, Switzerland). As details of patient selection, postoperative management, and long-term follow-up are presented by our group elsewhere in this issue,<sup>4,5</sup> we will mainly concentrate on surgical aspects in this report.

## MATERIALS AND METHODS

Twelve type I diabetic patients in end-stage renal failure (aged 25 to 49 years) have been accepted for treatment. Combined pancreatic and renal allotransplantation was performed in all 12 patients, pancreatic retransplantation alone in one patient.

### Donor Pancreatectomy

The technique of pancreas harvesting has been described previously.<sup>2</sup> Recently, we modified our technique slightly: (1) Hypothermic *in situ* perfusion of the pancreas with Euro-Collins' solution was provided by an intraaortally situated catheter via the celiac axis. (2) The celiac axis, including an aortal patch and the portal vein, respectively, were used for anastomosis exclusively. Harvesting of the pancreas was combined with the removal of the kidneys (all cases), the removal of the heart (three cases), and the removal of heart/lung (one case). Organ harvesting was performed either at our own clinic or at external hospitals. Transportation of the organs was provided by helicopters or emergency cars. Cold ischemia time never exceeded five and one half hours.

### Special Donor Criteria

Special donor criteria for pancreas harvesting were used at our institution: age, 15 to 40 years; stable circulation; blood sugar and serum amylase, normal/subnormal; no obesity; negative crossmatch; and blood group compatibility.

### Duct Obliteration

The duct obliteration procedure was started immediately before transplantation; under hypothermic *in vitro* conditions, the duct was cannulated (Abbotocath cannula). Between 3.5 and 6 mL of Ethibloc (prolamine, alcoholic amino acid solution) were injected throughout the ductal system under x-ray control. Duct obliteration was considered to be efficient when first signs of overinjection appeared as revealed by x-ray. After occlusion, the ductal orifice, as well as the parenchyma near the cut surface, were ligated.

### Recipient Operation

Our technique of pancreatic transplantation has been slightly modified recently. The segmental pancreas graft was situated (in an upside-down position) extraperitoneally in the right iliac fossa by positioning the distal 2/3 intraperitoneally. Circulation was established by end-to-side anastomosis of the portal vein to the right external iliac vein and the celiac axis (plus patch) to the right external iliac artery. The wound was drained for two to four days either by a silicon rubber drain or Penrose drain (Fig. 1). Following closure of this wound, a renal graft from the same donor was placed in the left iliac fossa using the standard technique.

### Immunosuppressive Protocol

Basic immunosuppression consisted of intravenous (IV) cyclosporine 3.5 to 5 mg/kg/d over the first ten days posttransplant. Cyclosporine was administered orally (15 mg/kg) until the end of one month, when it was decreased

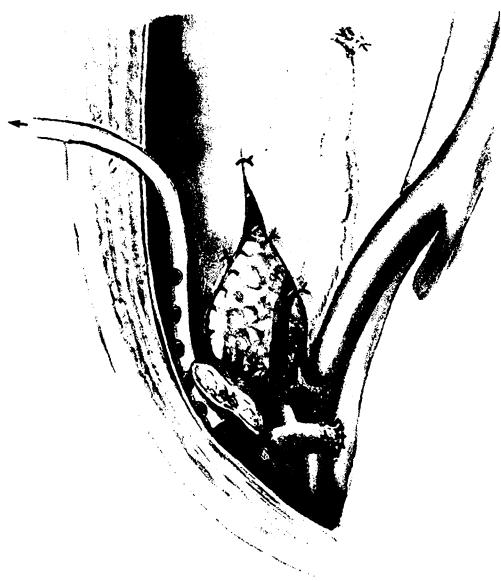
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**Fig. 1.** Technique recently used in segmental pancreatic transplantation: partially extra/interperitoneal position of the graft. For anastomosis, the portal vein as well as the celiac axis (plus an aortal patch) are used. The operation is done at the right iliac fossa.

by 2 mg/kg monthly to a maintenance level of 6 to 8 mg/kg monthly to a maintenance level of 6 to 8 mg/kg body wt.

Steroids (methylprednisolone) were begun at 500 mg IV intraoperatively by decreasing the daily dose to 30 mg

**Table 1. Results of Simultaneous Pancreatic and Renal Transplantation Under Cyclosporine Therapy**

(12 Patients)

Patients in the Consecutive Series (age)	Survival Time (mo)		
	Pancreas	Kidney	Patient
4. H. S.* (36 yr)	(Venous thrombosis)	27	27
5. P. K. (41 yr)	26	26	26
6. A. B. (33 yr)	16	16	16
7. G. L. (26 yr)	6	6	6
8. K. F. (49 yr)	1	1	1†
9. R. J. (25 yr)	2	2	6
	(Rejection)	(Rejection)	
10. H. K. (42 yr)	6	6	6
11. F. S. (40 yr)	5	5	5
12. U. S. (33 yr)	2	2	2
13. S. K. (27 yr)	(No function)	2	2
14. M. S. (36 yr)	1.5	1.5	1.5
15. G. S. (33 yr)	1	1	1

\*Retransplantation: second occurrence of venous thrombosis.

†See Table 2, same patient.

during the first two weeks posttransplant. During the next two months, methylprednisolone was slowly decreased to a daily dose of 8 mg and maintained at that level.

**Antirejection treatment.** Antirejection treatment consisted of three IV bolus injections of 500 mg methylprednisolone during the first rejection episode. The second and third rejection episodes were treated by administration of antithymocyte globulin (ATG, Fresenius, Frankfurt, FRG) in a dose of 4 to 7.5 mg/kg daily over a period of seven days in combination with methylprednisolone in a dose of 120 mg IV daily until reversal.

## RESULTS

The overall results of 12 combined pancreatic and renal transplantations (and one pancreatic retransplantation) are shown in Table 1. One patient died of acute liver failure (acute yellow liver necrosis) posttransplant. The other patients are currently alive. Eight of 13 pancreatic grafts, as well as ten of 12 renal grafts, are currently functioning (August 1983); pancreatic grafts after 26, 16, 6, 6, 5, 2, 1½, and 1 month; renal grafts 27, 26, 16, 6, 6, 5, 2, 2, 1½, and 1 month. Four of 13

**Table 2. Early (Local) Complications Following Simultaneous Organ Transplantation**

Patient	Complications	
	Pancreas	Kidney
4. H. S.	Venous thrombosis (twice)	None
5. P. K.	Transient fistula	Rupture after biopsy (led to operative repair)
6. A. B.	Peripancreatic fluid collection	Wound hematoma (led to evacuation)
7. G. L.	Transient fistula	Wound hematoma (led to evacuation)
8. K. F.	None	None
9. R. J.	Fistula; infection (rejection)	Rejection
10. H. K.	Peripancreatic fluid collection	None
11. F. S.	Peripancreatic fluid collection	Wound hematoma (led to evacuation)
12. U. S.	Transient fistula	None
13. S. K.	No function: infection (led to exploration)	Distal ureter necrosis (led to operative repair)
14. M. S.	Fistula	None
15. G. S.	None	None

pancreatic grafts failed because of acute irreversible vascular rejection,<sup>1</sup> acute posttransplant venous thrombosis,<sup>2</sup> and no primary function.<sup>1</sup> Concerning the last case, an abnormal blood supply of the body and tail of the donor pancreas has to be discussed (only a few nutritive branches arising from the splenic artery without any parenchyma presentation were shown by angiography). We observed a relatively high incidence of early postoperative local complications on both sites of the grafts as shown in Table 2. At the site of the pancreatic graft, peripancreatic fluid collection requiring repeated needle aspiration and transient pancreatic fistula, respectively, were encountered most frequently; at the site of the renal graft, deep wound hematomas requiring surgical evacuation was observed.

Rejection episodes of both organs proved to be almost mild under cyclosporine treatment. There was only one acute vascular-type rejection not responding to antirejection treatment. Normally, all rejection episodes could be reversed either by methylprednisolone (IV bolus) alone or by combined administration of methylprednisolone and ATG.

## DISCUSSION

Our current technique of combined segmental pancreatic and renal grafting using cyclosporine as posttransplant immunosuppressant has been associated with (1) low mortality, (2) an acceptable morbidity, (3) rare immunologic graft loss, (4) a relatively high incidence of early local complications, and (5) a reasonable rate of functioning pancreatic grafts (at the present time, August 1983: 61.5%).

We assume and discuss that this high rate of functioning pancreatic grafts is primarily a result of the strong immunosuppressive potency of the new agent cyclosporine, which reduces the events of irreversible allograft rejection. This observation is in accordance with our results obtained in cadaveric renal transplantation using cyclosporine as basic immunosuppressive therapy; the one-year graft survival rate of renal allografts has

improved by 20% (to 80%) compared with our historic controls using conventional immunosuppressive therapy.<sup>6</sup>

The clinical use of cyclosporine may also have led to the low rate of mortality in our recent series, although other contributing factors, such as better selection and improved management of the patients, and the gaining of experience within the transplant group may play some role.

The morbidity observed in our patients after combined transplantation certainly is higher than in kidney-transplanted patients but it seems acceptable. This morbidity mainly concerns the incidence of early local complications such as peripancreatic fluid collection and transient pancreatic fistula at the site of the pancreatic graft, as well as severe wound hematomas at the site of the renal graft.

Indeed, the incidence of complications from residual function of the exocrine system of the duct-occluded pancreatic graft worries us. We believe that these local complications probably arise from a too-early reabsorption of the occlusion substance Ethibloc (Ethicon, Raritan, NJ) before the acini are completely atrophied (a decisive difference between Ethibloc and neoprene used by the Lyon group and others). It is worthwhile to mention that the administration of somatostatin did not prevent these local complications from arising from residual exocrine secretion. On the other hand, this property of early reabsorption may be the reason for the good long-term function of the pancreatic grafts as discussed by us elsewhere in this issue.<sup>4</sup> If it is suggested that a remaining foreign body causes increased fibrosis in the graft over a longer period of time, then the early reabsorption of ethibloc would imply a beneficial effect (as far as long-term function is concerned) because of a milder fibrosis-inducing effect. A completely intraperitoneal position of Ethibloc-occluded pancreatic grafts might reduce this kind of local complication.

The incidence of wound hematoma at the site of the renal graft is obviously a result of

our aggressive regimen of early postoperative anticoagulation (heparinization). This protocol was applied to prevent venous thrombosis of the splenic vein of the pancreatic graft. In fact, this complication can be prevented completely by aggressive anticoagulation therapy according to our experience. Nevertheless, a

new therapeutic concept of posttransplant anticoagulation is being worked out at the present time.

#### ACKNOWLEDGMENT

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