The liver allocation committee is joined by the following members, who are open to further suggestions:

Dr. F. Mühlbacher	-	Vienna
Dr. P. Neuhaus	-	Berlin
Dr. B. Ringe	-	Hannover
Dr. M. Slooff	-	Groningen
Dr. J.B. Otte	-	Brussels UCL
Dr. U. Jost	-	Hannover
Dr. G. Persijn	-	Eurotransplant (head of the committee)
Dr. J. de Boer	-	Eurotransplant
Ms. E. van Duin	-	Eurotransplant
Student	-	Eurotransplant

Pancreas transplantation

The last issue was pancreas transplantation. Different opinions about the role of tissue typing were discussed. Because of the low number of these transplantations it was finally agreed to try to HLA type donor and recipient beforchand whenever possible.

Those centers who give away a kidney together with a pancreas will be compensated with a kidney from the Eurotransplant pool to facilitate the exchange in this program.

Conclusion

The fifth Eurotransplant Users Meeting revealed many similar problems to those in former meetings. Again it was apparent how useful the open discussion on all these subjects was, to all participants. However, improvement should be pursued continuously by all users with the help of Eurotransplant. Furthermore, the growing field of heart, heart/lung(s), liver and pancreas transplantation gives rise to new questions of allocation and tissue typing, which again may best be faced by close co-operation of all users. Continuing efforts within the community of Eurotransplant will help to attain successful organ transplantation all over Europe.

Last but not least, a sincere "thank you" should once more be given to Guido Persijn and Bernard Cohen together with their co-workers who provided all the relevant data and made the meeting so successful.

9. Pancreas transplantation at the University of Louvain: results of 2 successive techniques*

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Introduction

Pancreas transplantation aims at providing physiological insulin replacement therapy in type I diabetes mellitus, a disease in which the beta-cells within the islets of Langerhans are destroyed by an auto-immune process[1].
It is important to realize that in transplanting a vascularized pancreas, it is also implanting more than 99% of cells - mostly exocrine cells - which are not useful in the recipient and can have detrimental effects leading to graft pancreatitis, leaks and other technical complications.
Thus, a variety of pancreas transplantation techniques[2,3,4] have been described for the management of the exocrine secretion, indirectly proving that none of them are well designed.

The pancreatic duct can be occluded or provision can be made for drainage of the pancreatic juice, externally or into the peritoneal cavity, but usually into a hollow viscus.
We report herein our results using two different successive techniques for human pancreas transplantation i.e. enteric and urinary drainage of the exocrine secretion.

Population and method

Until now, our selection criteria were uniform: all type I diabetic recipients with pre or end-stage renal failure (creatinine clearance less than 30-50 ml/min) with severe retinopathy and neuropathy, without a living (un)related kidney donor have been

considered as potential candidates for cadaver pancreas and kidney transplantation. Several options were followed: negative T-cell crossmatch with a compatible ABO-donor; no HLA-matching; segmental graft (tail and body) in the first series and whole vascularized graft in the second one along with a segment of duodenum; cold storage of the graft using either Eurocollins solution or Silica Gel Filtered plasma (SGF, University of Minnesota) or U.W. solution (University of Wisconsin); intraperitoneal implantation; exocrine secretion drained into either a jejunum loop for the segmental grafts (pancreaticojejunostomy on a Roux-en-Y loop) or the bladder for the whole pancreas (pancreatico-duodeno-systonomy); simultaneous kidney graft from the same donor; cyclosporine A plus prednisone as the basic immunosuppressive therapy along with azathioprine, antithymocytic or antilymphocytic globulins, monoclonal antibodies (OKT3) for rejection treatment.

Results

Series I

Between November 1982 and December 1986, ten patients (mean age ± SD: 36.4 ± 6.9 years) with the previous criteria, underwent a simultaneous kidney and pancreas transplantation with enteric diversion of the segmental pancreas graft. Seven were on chronic hemodialysis and the last three in pre-end-stage renal failure at the time of transplantation.

Three patients died from the following reasons: the first one, 38 years old, twelve days after the second pancreas transplantation due to metabolic disorders after ischemic bowel problems; the second one, 51 years old, 38 days after grafting from a gram negative septic shock; the last one, 56 days after transplantation, from a CMV encephalitis.

All renal and pancreatic grafts were functioning at the time of death. The other patients are currently alive. Acute rejection at 2 months of both transplanted organs led to a double transplantectomy in one of them. The renal graft is functioning in 5 recipients. Four of them are currently (December 1990) insulin-independent (follow-up: 86, 70, 60 and 59 months).

One of them underwent two successful pregnancies and delivered two normal babies. Another recipient remained without exogenous insulin therapy during 2 years; progressive deterioration of the pancreatic endocrine function necessitated the resumption of insulin therapy (20 units per day) while the renal function was excellent and stable (follow-up: 97 months).

Finally, the last patient was never off insulin therapy after transplantation (follow-up: 82 months).

At 1 year, the actuarial survival rates are 64% for the patients, 60% for renal and 45% for pancreatic grafts (fig. 1-ABC).

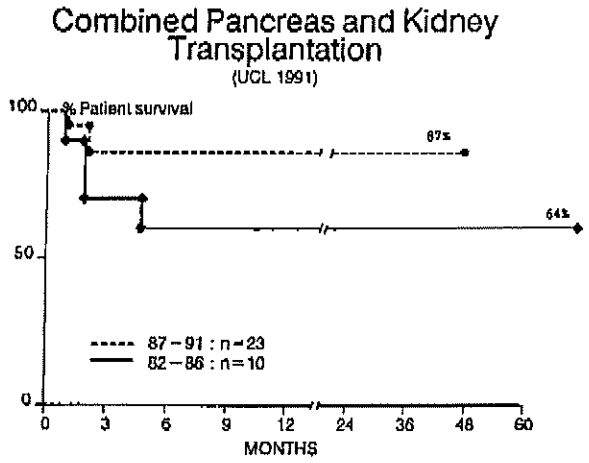

Fig. 1A: Actuarial survival curves of patients (fig. 1A), within 2 consecutive series of pancreas transplantations at the University of Louvain. First era (1982-1986): 10 patients, 11 pancreases, 10 kidneys. Second era (1987-1990): 23 patients, 24 pancreases, 23 kidneys, 1 liver.

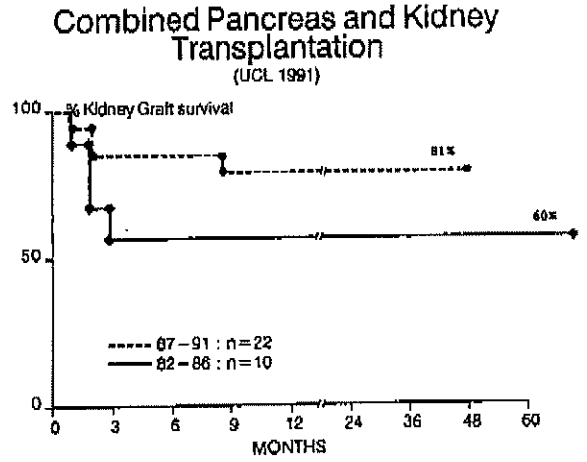

Fig. 1B: Actuarial survival curves of pancreatic grafts (fig. 1C) within 2 consecutive series of pancreas transplantation at the University of Louvain. First era (1982-1986): 10 patients, 11 pancreases, 10 kidneys. Second era (1987-1990): 23 patients, 24 pancreases, 23 kidneys, 1 liver.

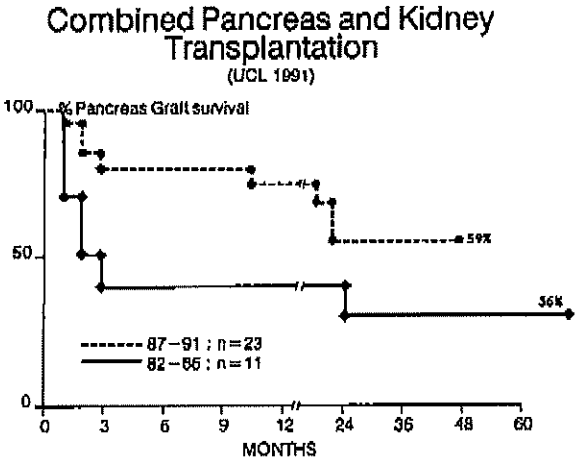

Fig. 1C: Actuarial survival curves of pancreatic grafts (fig. 1C) within 2 consecutive series of pancreas transplantation at the University of Louvain. First era (1982-1986): 10 patients, 11 pancreases, 10 kidneys. Second era (1987-1990): 23 patients, 24 pancreases, 23 kidneys, 1 liver.

Series II

In January 1987, the technique for pancreas grafting was modified: today (December 1990), twenty-three diabetic patients (mean age ± SD: 36.9 ± 6.2 years) underwent a whole pancreas transplantation (24 grafts, one recipient receiving 2 successive combined procedures) along with a duodenal segment. The exocrine secretion was drained into the bladder using a latero-lateral pancreatico-duodeno-cystostomy; the anastomosis was performed using the stappler device in the last 10 recipients.

Fourteen were on chronic haemodialysis and nine in pre-end-stage renal failure at the time of transplantation. Twenty-two patients received simultaneously a kidney graft from the same donor while the 23rd recipient underwent a combined pancreas liver transplantation, the cause of liver failure being an auto-immune hepatitis. Unfortunately, three patients died during the post-operative course: the first one at day 52 from a pulmonary CMV infection, the second one at day 41 from aspergillosis and the last one at day 27 from A.R.D.S. (Acute Respiratory Distress Syndrom) following the first OKT3 injection in order to treat a renal graft rejection. All three patients had both functioning grafts at the time of death. Finally, the recipient who underwent two successive combined pancreas and kidney grafts

(first kidney graft lost at month 9 and first pancreas graft lost at month 11) lost the second renal graft at day 24 and the second pancreatic graft at day 37; eventually, the recipient died at day 79 from infectious and metabolic causes.
Five pancreatic grafts were lost (resumption of insulin therapy) by chronic rejection (17, 17, 12, 11 and three months after transplantation) and one renal graft at month 9. Currently (December 1990), nineteen patients are alive (follow-up from 2 to 43 months): 15 over 19 pancreases are well-functioning as are 18 kidneys and one liver. Noteworthy is the course of one patient presenting an isolated pancreas graft rejection based upon a drop in the urine amylase content without any sign of renal graft rejection[4].
At one year, the actuarial survival rates are 87% for patients, 81% for renal and 77% for pancreatic grafts (fig. 1-ABC).

Comments

The functional survival rate of pancreas transplantation has significantly increased during the last years mostly due to technical modifications but also to improved experience in that field. That is clearly reflected by the analysis of our own data using two different and successive surgical techniques i.e. the enteric and the urinary drainage of the exocrine secretion of the pancreas graft. The improvement is obvious in the second series of 23 patients; these results are similar to those reported to the International Pancreas Registry for the corresponding periods[5]. That experience provides us with additional information. Firstly, if enteric drainage of the exocrine function is the physiological way to preserve the architectural integrity of the graft, monitoring of the exocrine function is difficult except in the immediate post-operative period when duct catheterization is operational. For long-term monitoring of pancreatic graft function, only endocrine responses can be assessed. In these conditions, the only possibility to detect pancreas rejection would be to detect rejection in a simultaneously transplanted kidney from the same donor.

Secondly, the bladder drainage of the exocrine secretion used during the 2nd period avoids numerous disadvantages of the pancreaticojejunostomy. Our experience with that technique in the last 23 patients emphasizes that fact: the technique is simpler and safer at least for the recipient compared to the donor procedure. The obvious advantage is the possible detection of rejection by the urinary amylase dosage. A significant drop in the amylase content (more than 50%) means that rejection therapy should be started as soon as possible. That type of rejection monitoring also means that single pancreas transplantation should be considered for non uremic diabetic recipients in whom extra renal secondary complications seem to be rapidly evaluating. Thirdly, the one year pancreas graft functional survival is satisfactory in combined kidney and pancreas recipients, but median term results should be improved (fig. 1C).

Indeed, in our series, five pancreatic grafts were lost during the second era, four between 11 and 17 months after transplantation. If the presumed cause was a chronic rejection in each case, no objective proof can be proposed as pancreas biopsy even through a cystoscope is not an easy tool. Other hypothesis should be taken into consideration such as the recurrence of the original disease[6]. Moreover, some recipients with failing graft behave like type II diabetic patients: c-peptide secretion is present (even in large amount) but there is a peripheral insulin resistance due to an increased weight, CsA and steroïd diabetogenic effects. Hyperinsulinemia is also common due to the peripheral venous drainage of the graft. In conclusion, further improvements should be expected in pancreas transplantation for preventing long-term graft losses. These could come from the increased experience with the pancreatic biopsies and their interpretation, the consideration of HLA-compatibilities for exchanging pancreas grafts and the use of more potent immunosuppressive regimens and new drugs such as FK-506, Rapamycin and Deoxyspergualin, etc.

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