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CONGRESS REPORTS

First Annual Meeting of the American Society of Transplant Surgeons Chicago, May 23, 1975

The newly founded Society of American Transplant Surgeons under its President, Dr. Thomas E. Starzl, had its first meeting at the Hyatt Regency Hotel in Chicago USA on May 23, 1975. A total of 24 papers were presented.

Dr. J. S. Najarian and his group from the University of Minnesota reported on "Renal transplantation in patients with insulin dependent diabetes". Since June, 1969, 94 patients with insulin dependent diabetes mellitus and end stage renal failure underwent renal transplantation. Patient survival at three years was 70% and 45% with kidneys from living related and cadaveric donors respectively. This compares with a 30% three year survival on haemodialysis as reported by Shapiro. The death rate is approximately twice as high as that of a matched non-diabetic control population. Infections and myocardial infarction were the principal causes of death. Age at onset of diabetes, duration of diabetes, electrocardiogram changes and severity of retinopathy were unreliable prognostic indicators. Rehabilitation of patients with viable grafts was good. Visual acuity which had rapidly deteriorated prior to transplantation remained stable after transplantation. Since there is a sharp drop in eyesight during dialysis, early transplantation is recommended. The Minneapolis surgeons prefer to transplant diabetic patients wich chronic renal failure before the creatinine value reaches a value of 5 mg. %. Since bilateral nephrectomy and splenectomy prior to transplantation is associated with an almost 10% mortality in these patients, this procedure is no longer performed; splenectomy is done at the time of transplantation.

A most interesting paper was presented by Dr. C. B. Anderson and his colleagues from Washington University School in St. Louis who reported on "Serum lactic dehydrogenase (SLDH) and irreversable renal allograft rejection." The rationale was that SLDH elevation has been correlated with renal infarction. The hypothesis that measurements of SLDH might be helpful in early prediction of renal allograft rejection was studied in the animal model and confirmed. SLDH was studied in 47 patients who underwent renal allografting. The authors observed that when SLDH levels had reached 500 international units/L and more, only one rejection episode was reversible in 21 patients. On the other hand, if SLDH remained below 500 international units/L, only 2 out of 47 patients had irreversible rejection episodes. SLDH levels were within the normal range when acute tubular necrosis was present and were of no value in slow irreversible rejection. These results have been confirmed in over 30 patients whose SLDH were monitored at the Mayo Clinic.

Dr. Salvatierra from the University of California, San Francisco reported an "Improved patient survival in renal transplantation." The authors philosophy is that graft survival is not jeopardised by accepting a policy of low immuno-suppressive therapy. They were able to show that patient survival with this management is significantly improved. Their present regimen after transplantation is 1) No therapy after the second rejection 2) No further therapy after the first rejection, if renal function does not return to normal 3) No therapy for chronic rejection. They compared the results from 1968 to 1972 when aggressive immunosuppressive treatment was the rule and their results since the new regimen treatment was started. Of the 198 patients who received cadaveric kidneys during the first period, 79% survived for longer than one year, compared to 91% of 205 patients in the second group. Graft survival in these two groups was 49% and 55% respectively. Of 117 patients who received kidneys from living related donors before 1972, 85% survived for one year and longer, compared to 100% of 24 patients in the second group. Graft survival was 73% and 87%, respectively. These results compare to a one year patient survival of 85% on chronic haemodialysis. Dr. Salvatierra and his colleagues could demonstrate that

57% of the patients in the early group died of sepsis, whereas only 11% died of sepsis in the second group. These are certainly excellent results and are superior to hemodialysis, even in patients who receive cadaveric renal allografts.

H. F. Seigler from the Duke University Medical Center, Durham, N. Carolina talked about "Renal transplantation between HLA haplo-identical donor recipient pairs: functional and morphological evaluation." In a prospective study of 62 donor-recipient pairs of renal allograft from an HLA haplo-identical family member the authors tried to measure immunogenicity by exchanging skin grafts. Two groups were established depending on the skin graft survival time. Group A > 15 days, and Group B < 15 days. There was no difference in renal function or in kidney and patient survival in both groups. Mixed lymphocyte stimulation was comparable. However, Group A patients required lower doses of steroids to prevent rejection. This study indicated that the prognosis of HLA haplo-identical renal allograft recipients cannot be prospectively determined by survival of skin grafts.

Dr. James Cerilli gave a most interesting survey on "Renal transplantation in patients with urinary tract abnormalities". Most authors in the past have stated that patients with lower urinary tract abnormalities who need renal transplantation are poor candidates and if transplantation needs to be performed, the ileal conduit is the preferred procedure. Out of a total of 9 patients with bladder and ureteric abnormalities who underwent renal transplantation, 7 patients had a supravesical urinary diversion six months to 12 years prior to the transplant procedure. Adequate bladder emptying could be demonstrated in 7 of the 9 patients after bilateral nephrectomy and ureterectomy. All seven patients had renal allografts with implantation of the donor ureter into their own bladders. Six of the seven patients are alive with normal renal function four years after transplantation with sterile urine and no ureteral reflux and minimal bladder residuals. The authors believe that pre-transplant urinary diversion is rarely indicated even though pre-transplant urinary diversion had been performed. Pre-transplant diagnostic errors probably account for the excellent results obtained.

Dr. F. K. Merkel discussed the importance of microvascular techniques for polar artery reconstruction in kidney transplants. Reconstruction of small polar arteries is extremely important in order to prevent ureteral ischaemia, hypertension, and urinary fistulae. Small polar arteries were reconstructed in 22 renal allografts. Post-transplant arteriography confirmed patency in 14 cases after operation. Long term patency of the small polar arteries of these patients was 94%. It is stressed that small arteries to the upper pole may be sacrificed if they are small and do not cause major ischaemic defects which might result in caliceal fistulae. Lower pole arteries always should be preserved because they supply pelvis and upper ureter.

T. P. J. Schröter and colleagues from the University of Colorado Medical Center, Denver discussed "Cryptococcosis after renal transplantation with a report of nine cases." Nine cryptococcal infections in the large renal transplant series of the Denver group were reported. The most common symptoms were headaches, signs of increase of intracranial pressure, and impaired thinking. A very prominent symptom is the presence of seizures. The initial diagnosis was usually established by demonstrating a space-occupying brain lesion. The diagnosis was confirmed by identifying cryptococcus neoformans in cultures of the cerebrospinal fluid. Untreated infections were usually insidious in onset, slowly progressive and usually without a fever. Therapy with low doses of intravenous Amphotericin B and/or 5-Fluocytosine orally over a prolonged period of time, controlled the infection while immunosuppressive therapy was continued. No patient died of cryptococcosis and no graft has been lost. The authors discussed the possibility of retransplantation in these patients two years after they have been free of antigens suspicious of cryptococcosis. Experience at the Mayo Clinic confirms the authors' report that systemic cryptococcosis in renal transplant patients is usually insidious and, in the early period, associated with minimal symptoms. Combination therapy of i. v. Amphotericin B and oral 5-Fluorocytosine over a period of three months or more is recommended. Cultures of sputum, serum, urine, and cerebro-spinal fluid should be negative before the therapy is discontinued.

Dr. D. T. Uehling and colleagues from the University of Wisconsin Medical Center in Madison discussed the details of the "Effect of cessation of immunosuppression after renal transplantation." They reported on their experience with 5 recipients of successful living related donor kidney transplants who stopped their immunosuppressive therapy against medical advice. The two recipients, who were non-identical by tissue typing and mixed lymphocyte culture (MLC), became uraemic after cessation of immunosuppression for periods of 5 and 6 months. Both patients died in uraemia by refusing to re-institute immuno-

suppression. Three recipients of MLC and HLA identical kidneys were without immunosuppressive therapy for periods of 7, 12, and 30 months, respectively. None of these patients developed significant changes in renal function and none was biopsied. One of these patients demonstrated a plasma blocking factor in indirect CML. Two patients are currently back on immunosuppression. The third patient has remained stable and off immunosuppression for 35 months. In subsequent discussion it was stressed that even recipients of MLC and HLA identical kidneys will eventually lose their grafts. Dr. Belzer commented on a patient he had seen who had been off immunosuppressive therapy for five years and who presented eventually with an irreversible rejection resulting in graft loss.

Dr. G. Mendez-Picon from the Medical College of Virginia in Richmond and his colleagues discussed the use of "Plasma protein fractions in preservation of cadaver kidneys". Two groups of 23 cadaver kidneys each were preserved with cryoprecipitated plasma (CPP) or with plasma protein fractions (PPF). Both groups were preserved with pulsatile perfusion. PPF does not contain any fibrinogen or gamma globulin. Harvesting characteristics and perfusion time in both groups were comparable. 85% of the kidneys in the PPF group achieved immediate function compared to 75% of the kidneys in the CPP group. One kidney of the PPF group never worked, compared to 4 in the CPP group. It is concluded that PPF is as effective as CPP for the preservation of kidneys up to 48 hours prior to transplant. The use of PPF in renal transplantation seems to be advantageous since it is simple to prepare, hepatitis risk free and has no antibodies, whereas CPP takes longer to prepare and might cause immunological changes as reported recently by Filo and his colleagues.

Dr. J. A. Treman and his colleagues from the University of Washington Medical School in Seattle discussed the "Adverse effect of high doses of steroids on renal allografts and homografts." The authors could demonstrate severe glomerular changes in canine renal homografts which were preserved for five hours with hypothermic pulsatile perfusion when increased doses of methylprednisolone were added. In contrast, a control group of kidneys which were not exposed to methylprednisolone did not show any changes. Changes were most severe in the group where 3 grams of methylprednisolone had been added. They compared these results with their experience in human renal allografting where 94% of grafts from living related donors were functioning at one month and 82% at one year when rejection had been treated with less than 1 gram of methylprednisolone i.v. This compares to only 69% and 59% graft survival at one month and one year, respectively, when higher doses were used. The authors concluded that excessive doses of methylprednisolone are therefore not advisable in renal transplantation. This presentation caused considerable controversy since it was stressed by several people that the half-life of methylprednisolone is extremely short in the renal transplant patient and can therefore not be compared with high doses of methylprednisolone added to the perfusate where it is not metabolized. These comments support the experience at the Mayo Clinic where high doses of methylprednisolone are used for rejection crises. No adverse effect on renal function has been observed in human volunteers receiving 1 gram of methylprednisolone i.v. In addition, in the animal and in the human model high doses of i.v. methylprednisolone 50 mg/kg or more given before harvesting did not result in renal damage as seen on histopathological examination.

Dr. L. H. Toledo-Pereyra and his colleagues from the University of Minnesota Medical School, Minneapolis discussed the controversial subject of "Long term function of perfused cadaver kidney transplants." The question whether pulsatile perfusion or simple cold storage is the preferred management of the harvested renal allograft prior to transplantation has become more and more controversial. Clark and his associates were able to demonstrate in a large series that pulsatile perfusion was associated with a higher rate of transplant failure at one month and at one year than when simple cold storage of kidneys was utilized. Toledo-Pereyra and his colleagues examined the effect of perfusion on the long term function of 226 cadaver kidneys. The actual survival function of non-perfused kidneys (79) was compared at three years with the survival of perfused kidneys (147) by analyzing renal function, tissue match, kidney loss, warm and cold ischemia time, recipient's age and acute tubular necrosis. There was a 20% better overall three year functional survival of perfused kidneys (70%) than those preserved by the storage method (50%). In a prospective randomized comparative study which was performed in 37 kidneys, they observed a 20% better function of perfused kidneys than non-perfused kidneys at one month, one year, and three years. It is concluded that pulsatile perfusion for 24-48 hours does not adversely effect long term renal allotransplant function and does not result in an increased antigenicity. Increased antigenicity has been reported by Filo and also by

Manick, as well as the possibility of demasking antigens by mechanical damage as suggested by Anderson are probably rarely seen and do not justify discontinuation of the pulsatile hypothermic perfusion method. More studies in regard to simple cold storage with an intracellular type of solution are needed. It is believed that the kidney which has suffered some ischaemic damage will do better when conserved by the perfusion method rather than the storage method, since flow and pressure studies are possibly good indicators of the viability of the graft. This also points to the bias that very often kidneys which have suffered ischaemic damage are preferably preserved with pulsatile perfusion rather than cold storage to obtain these parameters.

Dr. A. P. Monaco and his colleagues from the Harvard Medical School in Boston reported on the "Active enhancement of the human cadaver renal allograft with ALS and donor bone marrow: case report of an initial attempt." Doctor Monaco has achieved excellent results in graft survival in rodents and in dogs with bone marrow given to the recipient between days +5 and +9. It seems that from his animal experience timing and dosage were extremely important. A clinical application of this system was undertaken in a 30 year old female who received a cadaveric renal transplant and who had 30 % preformed circulating HLA antibodies. The patient received a cross-match negative, no common antigen cadaver kidney. At the time of harvesting donor marrow was obtained and stored in DMSO at -180° C. The standard protocol of prednisone azathioprine, and anti-lymphocyte globulin for 14 days, was used. On the 25th post-operative day the patient received 11×10^9 donor marrow cells (90 % viable), i.v. No signs of GVH disease occurred. Several studies showed persistence of donor erythrocytes for two months post infusion, but no evidence of the presence of donor white cells, one, two or three months post infusion. Six months after the bone marrow infusion, the recipient was negative for CMI and SBF to donor HLA antigens. During the entire post-operative course the patients creatinine was within normal limits and the patient did not experience any rejection episodes. Eight months after transplant the patient died of a perforated sigmoid diverticulitis; the renal allograft was essentially normal. It is concluded that preservation of human donor specific marrow is feasible at the time of cadaver kidney harvesting, that bone marrow can be administered without serious complication, particularly without any overt GVH disease and without precipitating graft rejection. No definite conclusions can be drawn in regard to the effectiveness of this treatment, but it is of interest that the patient who received a multiple antigen mis-matched kidney had no episodes of rejection. It seems that the use of donor marrow injection after grafting makes the system suitable for application to clinical cadaveric transplantation.

Horst Zincke, M. D.
Consultant in Urology and
Transplantation Surgery
Mayo Clinic
Rochester, MN 55901
U. S. A.