PAPERS AND ORIGINALS

Kidney Transplantation: Analysis of 200 Cases

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Summary

The first 200 renal allograft operations performed at Addenbrooke's Hospital, Cambridge, have been analysed. At the time of writing the fractional graft survivals at one, two, and three years were 53%, 49%, and 39% respectively, and these showed no observable change through the seven years of the programme. On the other hand, the survival of patients undergoing renal transplantation steadily improved, the most recent survival rates at one, two, and three years being 83%, 78%, and 67%, whereas the overall rates were 74%, 66%, and 54% respectively. The survival of second allografts was similar to that of first allografts. Ninety per cent. of the patients whose allografts functioned for a year or more returned to active and gainful employment. The return of children to school and of housewives to running a household was similarly gratifying. We conclude on both social and economic grounds that renal transplantation is fully justified as a therapeutic procedure.

Introduction

In June 1972 the 200th renal allograft operation was performed in Cambridge. From 1965 to 1972 166 patients were treated; 31 received second transplants and three a third. Ten patients received kidneys from living donors—all parent-to-child—and the remaining 190 were from cadavers. In this paper we analyse the results of the 200 operations, particularly the degree of rehabilitation obtained after successes.

Patients and Methods

All the patients were accepted into the programme without any selection whatsoever on social or psychiatric grounds. The only

consideration was whether the patient was fit enough for the operation. Of the 166 patients 67 were female and 99 male. The age range was 13 to 60 years.

Most patients were prepared for transplantation by haemodialysis. In the early years blood transfusion was given fairly freely but in the last three years it was kept to a minimum. Serological tissue typing and direct cross-matching of recipient serum against donor lymphocytes was performed for most patients transplanted after 1968. In general recipients were selected according to the best match when donor kidneys became available. Nevertheless, the number of "full-house," four-antigen matches in this series was only four. Details of the surgical technique and immunosuppressive therapy were reported previously (Calne *et al.*, 1968).

A clinical and biochemical diagnosis of a rejection crisis was normally confirmed by needle biopsy (Millard *et al.*, 1970) and treated with an increased dose of steroids, often supported by actinomycin C. A few patients received cyclophosphamide and seven antilymphocytic serum or globulin (McMillan and Evans, 1970). Information on rehabilitation was obtained by direct inquiry from the patient, by circulation of a questionnaire to all living patients, and from the case notes and social records.

Results

The patient survival times from the dates of the first transplant operation are shown in table I and the expanded results according to the year of transplantation are shown in table II. A functioning allograft was defined as a kidney supporting a patient's life without dialysis. The complete allograft function results are shown in table III and the expanded results according to the year of transplantation are shown in table IV. Results for the 31 second allografts (tables V and VI) were similar to those for the first grafts. Only one of the three third transplants functioned. This was from an HL-A-identical donor, and after three years it continued to provide good function.

Curves of graft survival (fig. 1) and patient survival (fig. 2) were computed according to the actuarial method (Barnes, 1965). This method assumes that factors governing survival are the same in graft operations performed now as they were at different times in the past.

Of the 99 male patients 66 had grafts that functioned for a year or more, whereas of the 67 female patients only 36 had grafts functioning for a year or more.

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TABLE I—Overall Patient Survival from Time of First Transplantation (1965-72)

Years of survival	1	2	3	4	5	6	7
Proportion of patients	123/166 (74%)	91/137 (66%)	52/97 (54%)	36/76 (47%)	20/55 (36%)	9/31 (29%)	2/7 (29%)

TABLE II—Patient Survival in Years from Time of First Transplantation (1965-72)

	1 Year	2 Years	3 Years	4 Years	5 Years	6 Years	7 Years
1965-	6/7 (86%)	6/7 (86%)	3/7 (43%)	3/7 (43%)	3/7 (43%)	2/7 (29%)	2/7 (29%)
1966-	13/24 (54%)	11/24 (46%)	11/24 (46%)	10/24 (42%)	7/24 (29%)	7/24 (29%)	
1967-	15/24 (63%)	14/24 (58%)	13/24 (54%)	12/24 (50%)	10/24 (42%)		
1968-	15/21 (71%)	13/21 (62%)	11/21 (52%)	11/21 (52%)			
1969-	17/21 (81%)	16/21 (76%)	14/21 (67%)				
1970-	33/40 (83%)	31/40 (78%)					
1971-	24/29 (83%)						

TABLE III—Overall Transplant Survival (200 Grafts) during 1965-72

Years of survival	1	2	3	4	5	6	7
Proportion of transplants	106/200 (53%)	77/158 (49%)	43/111 (39%)	29/87 (33%)	15/61 (25%)	6/32 (19%)	1/7 (14%)

TABLE IV—Transplant Survival in Years from Time of Operation (200 Grafts) during 1965-72

	1 Year	2 Years	3 Years	4 Years	5 Years	6 Years	7 Years
1965-	6/7 (86%)	6/7 (86%)	3/7 (43%)	3/7 (43%)	3/7 (43%)	1/7 (14%)	1/7 (14%)
1966-	11/25 (44%)	9/25 (36%)	9/25 (36%)	8/25 (32%)	5/25 (20%)	5/25 (20%)	
1967-	15/29 (52%)	14/29 (48%)	12/29 (41%)	8/29 (28%)	7/29 (24%)		
1968-	13/26 (50%)	12/26 (46%)	10/26 (38%)	10/26 (38%)			
1969-	12/24 (50%)	11/24 (46%)	9/24 (38%)				
1970-	31/47 (66%)	25/47 (53%)					
1971-	18/42 (43%)						

TABLE V—Patient Survival after Second Allograft

Years of survival	1	2	3	4	5
Proportion of patients	23/31 (74%)	13/19 (68%)	8/13 (62%)	7/11 (64%)	4/6 (67%)

TABLE VI—Duration of Function of Second Allografts

Years of function	1	2	3	4	5
Proportion of allografts	16/31 (52%)	9/19 (47%)	5/13 (38%)	3/11 (27%)	2/6 (33%)

FIG. 1—Graft-survival curve. Actuarial method (Barnes, 1965).

FIG. 2—Patient-survival curve. Actuarial method (Barnes, 1965).

TABLE VII—Survival of Transplants and Patients in 10 Cases in which Graft was from Parent

	Survival time:	1 Year	2 Years	3 Years	4 Years
Proportion of transplants		6/10 (60%)	4/9 (44%)	2/4 (50%)	1/3 (33%)
Proportion of patients		7/10 (70%)	5/9 (56%)	2/4 (50%)	1/3 (33%)

Fifteen patients were aged 18 or less at the time of transplantation. Five grafts were from a parent and 10 were from a cadaver. Twelve grafts functioned satisfactorily for more than a year.

The results for the 10 patients receiving a primary transplant from a parent are shown in table VII.

Three out of four patients who received HL-A-identical cadaver kidneys did well. When all patients with first transplants, irrespective of ABO blood groups are considered, there was no evidence that the degree of HL-A matching short of four-antigen matches had any influence on the results. For second and subsequent transplantation positive cross-matches were obviously excluded, as were previous antigenic incompatibilities. Patients who developed cytotoxic antibodies after receiving their first transplant appeared to be at a disadvantage for subsequent grafts unless the HL-A match was close. Terasaki *et al.* (1971) made similar observations.

CAUSE OF LATE TRANSPLANT FAILURE OR DEATH

A total of 102 patients (36 female, 66 male) had one or more transplants which functioned for a year or more. Of these 12 returned to dialysis when their grafts failed. The cause of failure in this group was considered to be rejection. In another patient a functioning graft was removed because it contained multiple staphylococcal abscesses which were the source of numerous distant septic emboli. These 13 patients were male. Subsequently four received another transplant but only one was successful. Six requested home dialysis and three died, two of cardiovascular causes and one of infection.

Out of 22 other patients who died after having had a satisfactorily functioning transplant for a year or more 18 were male and four female. In three rejection was the primary cause of death. Ten had cardiac or cerebrovascular conditions. Two died of tuberculosis, and one of these patients also had leprosy. Other deaths were due to bronchopneumonia, pancreatitis, gastrointestinal haemorrhage, intestinal obstruction, a road-traffic accident, and a subdural haematoma after a fall.

DEGREE OF REHABILITATION

Only patients whose allografts functioned for more than four months were considered. Out of five patients whose transplants functioned between four months and a year two returned to their previous occupations. Out of 60 men whose transplants functioned for a year or more 54 went back to work and five never went back (returned to Northern Ireland, psychiatric illness; single, large service pension; self-employed, family carried on business; returned to Northern Ireland, reason for not going back to work unknown; eyesight failed. There was no information on the remaining patient). Twenty-nine returned to their same positions with the same employers as before the operation. Twenty-three found work with different employers but eight were doing jobs similar to the one they had had before transplantation. Three patients had been self-employed and two returned to the same work. Forty-three other men who had transplants functioning for more than one year were still alive, and more-detailed information on them was obtained by means of a postal questionnaire. Twenty-two returned to their former employers. Two were self-employed. Of those who went to different employers seven found work through the Department of Employment, three taking a retraining course, and one was finally employed in a Remploy factory because he had other severe disabilities. Twelve patients found work through their own efforts with support from the medical social worker; one of these arranged his own retraining in a private scheme. Only 12 patients were registered as disabled. The types of jobs are shown in table VIII.

The average time to return to work after transplantation was 7.5 months, but this figure was influenced by the excessive time

TABLE VIII—Patients' Jobs after Transplantation

Psychiatrist Accountant Textile technologist Physical training instructor Bank clerk Civil servant	Clerks Plasterer Motor mechanics Crane driver Coal merchant Chefs	Headmaster Butcher Cobbler Civil engineer Electronics engineer
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that four patients took to return to work—namely, 14, 15, 18, and 48 months. Of these, one patient went through a process of discharge from the Forces and two had postoperative and further medical complications. The patient out of work for four years was blind and needed time for adjustment, rehabilitation, and retraining. There was no correlation between the length of time off work before transplantation and the time after transplantation before return to work. Nine patients thought their wages suffered because of the transplant operation. Seven reported rises in income. The rest thought their wages had been unaffected.

At the end of the follow-up period (28 June 1973) 23 patients had remained in employment for two years or more. Of those who had been transplanted for less than two years 10 were established in steady work and showed every indication of continuing with it. One man returned to the Army for 18 months but despite the fact that he was fit with a well-functioning transplant he was discharged on medical grounds. After retraining he found work as an electric welder. Of the remaining nine patients five had to give up work under two years because of graft failure and two because of other medical complications though their allografts continued to function. One found difficulty in finding work in his own area that would bring him greater financial return than his allowances and one had a Forces pension and settled into voluntary work at his local hospital.

WORKING WOMEN

Nine previously employed women had transplants which functioned for a year or more. Of these, six returned to work, four to their former jobs and two to different jobs with different employers. One patient married shortly after transplantation and never returned to paid employment.

HOUSEWIVES

Patients who were housewives at the time of transplantation gave the impression that they took an active part in household duties even to a late stage in renal failure and resumed their responsibilities shortly after returning home with functioning kidneys. This was impossible to document statistically. There were 23 housewives in this series with functioning transplants. In addition to their household work five were known to have had full-time employment and six had had part-time jobs since transplantation.

SCHOOLCHILDREN

Eight schoolchildren had transplants which functioned for a year or more and which at the time of writing were still functioning (table IX). Five of the six children returning to school did so within three months of transplantation; two were of school-leaving age and started work six and 10 months after the operation. One child eventually returned to school 16 months after the operation. The delay had been due to the slow recovery of his severe renal osteodystrophy. The rapid return to school of these children was in striking contrast to their pretransplantation school attendance record. Five of the children

TABLE IX—Results of Transplantation in Schoolchildren

Case No.	Sex and Age	Donor	Function of Transplant (Months)	Absence from School (Months)		Return
				Before Transplantation	After Transplantation	
1	M. 14	Live	>49	7	2	School
2	F. 14	Live	>40	4	3	School
3	M. 13	Live	>32	29	2	School
4	F. 13	Cadaver	>30	8	2	School
5	M. 13	Cadaver	>25	18	16	School
6	F. 13	Live	>21	18	1.5	School
7	M. 15	Cadaver	>27	24	6	Work
8	F. 17	Cadaver	<42	18	10	Work

had been absent from school for more than a year before the operation.

Discussion

These results for allograft and patient survival are similar to those of many other series. Whereas patient survival showed a gradual improvement over the seven years of the programme there was no significant improvement in transplant survival, and the introduction of tissue typing in 1968 had no effect. Only four HL-A-identical kidneys, however, were transplanted in this series. Often, because of the shortage of donors for logistic reasons, poorly-matched kidneys were grafted.

Joysey *et al.* (1973) analysed the serological aspects of these patients. They found that survival of first grafts was superior in group O recipients compared with other ABO groups. In recipients other than group O matching at the second segregant series gave improved graft survival.

In this series female recipients were less likely than male recipients to have grafts functioning for a year, but if a graft was functioning at a year the chance of it continuing to do so seemed to be greater than for male recipients.

Fifteen patients aged 13 to 18 years were transplanted, and in 12 the grafts functioned for more than a year. In 10 they continued to do so. Two of these patients were killed in road-traffic accidents with normally functioning allografts. The results for the 10 patients who received parental allografts were worse than the world figures (Barnes *et al.*, 1973). The series was small, and three recipients died with functioning grafts from causes unrelated to transplantation.

The actuarial curves in figs. 1 and 2 show an initial steep fall during the first three months after transplantation. The curves for both graft survival and patient survival approximate to straight lines that may be expected to meet the lower axis at about eight and 10 years respectively. It follows that if survival has not altered during the last seven years, with therapy and donor selection hitherto used grafts are likely to succumb by eight years and patients by 10 years after transplantation. On the other hand these actuarial curves would also be consistent with an asymptotic survival and an improvement in patient survival with changing therapy.

Many studies have shown that renal transplantation is a therapeutic success. The aim of this paper was to investigate the return to useful and financially rewarding work of patients with satisfactory transplants. Patients who become fully independent both physically and financially after transplantation and remain in steady work supporting their dependents provide firm testimony for the hypothesis that transplantation is not only good treatment but also of immense value to the community.

Many factors influence the speed of return to work after operation. Our impression is that the patient's personality, his level of anxiety, and his attitude to his illness together with the attitude of his spouse are of great importance. His determination to find work quickly may depend on the extent of his family obligations, whether he has adequate interests to occupy him at home, and his wife's attitude to having him at home. Occasionally the husband and wife exchange roles during the course of his illness and it may delay a man's return to work if his wife has

taken up full-time employment. Obviously postoperative complications and additional disabilities such as deafness, blindness, and peripheral neuropathy delayed resettlement in this series. It was helpful if the patient's previous employer was able to assure continuity of employment after treatment. This provided security during a period of great anxiety though we have little evidence that it influenced the speed of return to work. Out of 32 patients who returned to work within six months of transplantation 20 returned to their previous employers and 11 to different employers, one man being self-employed. Out of 12 patients who returned to work in three months or less nine returned to their previous jobs, which had been held open for them.

As more became known about transplantation employers became increasingly sympathetic towards rehabilitating patients, who must be given time off work to attend hospital regularly for clinical surveillance.

This leads us to the conclusion that stability over several years with one employer before transplantation with subsequent re-establishment in the same job offers the best hope of a smooth and trouble-free return to work after the operation. Certainly with our experience we would advise future patients with impending renal failure to remain in stable employment and to maintain as good a work record as possible rather than move to another position and employer when in an advanced stage of the illness.

It is not usually necessary to register transplanted patients as disabled; it becomes desirable only when there are additional medical complications. Short-term registration is sometimes found to be helpful in order to enlist the aid of the resettlement officer. Some employers have asked for disabled registration so that the employee can be included in their quota of disabled persons.

We were surprised that there was no correlation between the previous time off work and the period required to return to work after the operation. There was no obvious change in the time taken to return to work over the years, and the geographical area from which the patient came appeared to have no effect, though the figures are small. Self-employed patients were thought to be at a disadvantage in their speed of return to work but the numbers are too small for that to be certain. There was no evidence from our figures that patients who received a pension in addition to statutory allowances were slow to return to work.

The rapid return to school of children after transplantation was gratifying.

Nine patients successfully fathered normal children after kidney transplantation. The policy of the unit has been to discourage further pregnancies in women after transplantation and oral contraception is offered to those at risk.

When one considers that no policy of selection on social or psychiatric grounds has been followed the return to work of 90% of the patients with satisfactory transplants has been most encouraging.

We wish to express our gratitude to Miss G. M. Evans, senior medical social worker, for allowing us to use her records and for her help and advice, and to Dr. J. H. Roger, of Reading University, for statistical advice and for carrying out the actuarial analysis.

Our thanks are due to all the surgeons, physicians, nurses, tissue

typers, and others who contributed to this programme of transplantation between 1965 and 1972.

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Effects of Age, Sex, and Polycystic Disease on Progressive Bone Disease of Renal Failure

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Summary

A study of 150 patients undergoing haemodialysis has shown that age had a striking effect on the radiological presentation of renal bone disease, erosions being common in the young and uncommon in older patients and vascular calcification showing opposite trends to this. Men aged 20 to 59 years had a greater tendency to develop erosions than did women in this age range. Examination of a group of 53 patients over a period of five years showed that the half time for the development of vascular calcification was 4.6 years, erosions 26.7 years, and fractures 6.9 years. Nine out of 16 polycystic patients matched for age and sex with 50 controls did not develop erosions and had consistently less vascular calcification than the controls when examined over a six-year period.

Introduction

In a previous study (Tatler *et al.*, 1973) we described the rate of progress of renal bone disease in 135 haemodialysis patients over a period of 10 years. The results indicated that the disease was progressive, with half times ($t_{1/2}$) for the development of vascular calcification, erosions, and fractures of 3.4, 22.9, and 9.1 years respectively. In the present study subgroup analysis was performed on 150 patients in order to determine the effects of age and sex on these lesions. A cohort of 53 patients was examined over a complete period of five years of treatment. An opportunity was also taken to examine the effect of polycystic disease on the progress of radiological lesions.

Present Study

The 150 patients were all on the haemodialysis programme, and haemodialysis techniques, dietary management, and use

of phosphate binders were as previously described (Moorhead *et al.*, 1969; Tatler *et al.*, 1973).

Cadaveric renal transplantation was performed in some of the patients, who were removed from the study when this was successful. Most patients in whom transplantation was unsuccessful were returned to the study and continued with dialysis. Bilateral nephrectomy was performed in only three patients and total or subtotal parathyroidectomy in four.

Radiological investigations were performed as previously described (Tatler *et al.*, 1973), and in the present study we were concerned principally with vascular calcification, erosions, and fractures. Radiographs were obtained at the start or within a few months of the start of haemodialysis.

Cohort of 53 Patients.—These patients had been on dialysis for five or more years. Their radiographs were examined at six-monthly intervals during the first five years for the presence of vascular calcification, erosions, and fractures.

Age and Sex.—Differences in the incidence of the three lesions in male and female patients were sought. The six age groups examined were 0-9, 10-19, 20-29, 30-39, 40-49, and 50-59 years.

Patients with Polycystic Disease.—As a result of the observation that certain radiological manifestations of renal bone disease seemed less frequent in this group nine of the 16 patients with polycystic disease were separately analysed. Six were excluded because of coexistent pyelonephritis, transplantation, or inadequate data. Of the remaining 10 patients, nine were men, and these were compared with 50 other men in the age group 30-59 years.

Method of Analysis.—The percentage of patients with each lesion at successive years of treatment up to 10 years was calculated. Subgroup analysis of the groups mentioned above inevitably reduced the number of patients, and tests for statistical validity were confined to the larger groups. The results of these analyses are given when they seem to be particularly relevant. Throughout, the analyses include all patients except when individual subgroups contained fewer than five.

Cohort of 53 Patients

The mean age of these patients at the start of haemodialysis was 34.15 years. The proportions with fractures, vascular calcification, and erosions one, two, three, four, and five years later are shown in fig. 1, in which the mean starting age is used as the starting point for each curve. By extrapolating the curves to the point at which 50% of the patients would be expected to develop lesions the number of years for this development to take place can be estimated. The estimates for the development time of vascular calcification, fractures, and erosions were 4.6 years, 6.9 years, and 26.7 years respec-

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