ONE HUNDRED KIDNEY TRANSPLANTS IN THE BELFAST CITY HOSPITAL *

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IN 1959 an artificial kidney service for Northern Ireland was commenced in the Belfast City Hospital. The original intention was to treat only temporary renal failure, but inevitably patients were referred with other types of kidney disease, and it became necessary to attempt to provide treatment for end-stage renal failure. During the seven year period 1962-1968 seventeen patients were treated by short periods of maintenance haemodialysis, then sent for kidney transplant to the few centres in Great Britain then engaged in kidney transplantation. In 1968 financial provision was made for the treatment of chronic renal failure by hospital haemodialysis and kidney transplantation, two beds being provided for regular dialysis. A ten bed unit for regular dialysis was brought into operation in 1971. The first kidney transplant was carried out in November 1968 and the hundredth transplant in November 1976.

PATIENTS AND METHODS

During the early years when regular dialysis treatment was greatly restricted, patients could be accepted only when a space occurred as the result of a transplant or death, even if they were suitable in all respects. Later when the ten bed unit was ready for use, patients without medical contra-indication were accepted between ages 15 and 50. Patients with a history of myocardial infarction, cerebro-vascular accident, multi-system disease such as diabetes mellitus or systemic lupus, severe disease

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* These results have been briefly reported by McGeown, Mary G., et al (1977), Lancet, 2, 648.
unrelated to the renal disease or known mental instability were excluded. Hypertension, left ventricular failure and pericarditis were considered acceptable complications. Often perfectly suitable young patients could not be accepted because no places were available. Similarly at other times patients somewhat older than 50 were accepted because a space existed at the time they needed it. The age range of patients receiving transplants was 13 to 53; 34 were between the ages of 15 and 34, 24 between the ages of 35 and 40, 25 between the ages of 41 and 49, and 7 aged 50 or over, at the time of the first graft.

Ninety-one patients received the 100 kidney transplants, there being seven second transplants and two third transplants. The commonest primary renal diseases leading to terminal renal failure were glomerulonephritis (48 per cent), chronic pyelonephritis (18 per cent), polycystic disease (16 per cent) and hypoplastic kidneys (5 per cent).

PREPARATION FOR TRANSPLANTATION

Once accepted for the programme, the patients were informed as fully as possible of the details of the treatment planned for them. Whenever possible an arterio-venous fistula was prepared in advance of need, usually when serious restriction of dietary protein was commenced. Patients referred when already in terminal failure were maintained by regular peritoneal dialysis until a fistula could be prepared and developed ready for use. Peritoneal dialysis was also used as a temporary measure for patients already accepted who reached the terminal stage when the programme was full. Patients were transplanted either after hospital haemodialysis or occasionally after hospital peritoneal haemodialysis; only one patient was transplanted following home haemodialysis. One patient, the youngest, aged 13, received a transplant from his mother just in advance of actual terminal renal failure.

The general aim was to restore the patients to a reasonable state of health and nutrition before considering transplantation. A few patients had a kidney transplant while still very unfit and still being treated by peritoneal dialysis, either because the haemodialysis programme was full or because a satisfactory arteriovenous fistula could not be made. Ten patients received peritoneal dialysis only. The median time on dialysis was nine months, 47 patients receiving a kidney graft in nine or more months, and 44 in less than nine months. Nine patients waited longer than two years on dialysis.

The patients received 14 hour haemodialysis twice a week on Kiil kidneys or capillary kidneys, using a single pass system either from a batch tank or a Dylade. For a six month period during an outbreak of HBs Ag hepatitis in 1971, all haemodialysis was on disposable flat plate or capillary kidneys. Dialysers were not reused in hospital dialysis. Patients treated with peritoneal dialysis received 30 one litre exchanges twice weekly.
Dietary restriction of protein and sodium was used until the patients were established on dialysis but after this the diet contained 60 g protein, the sodium intake being prescribed according to the difficulty experienced in the control of hypertension, and the potassium intake, according to pre-dialysis level of plasma potassium varied from 50 to 70 mmol/day.

Orovite tablets were prescribed for all patients. A few patients required methyldopa and/or clonidine for hypertension not controlled by dialysis. Even after bilateral nephrectomy a few continued to require these hypotensive drugs, although in smaller dosage. Since 1973 patients with low plasma iron receive oral iron, and prior to that some received intravenous total dose infusion. Considerable quantities of diazepam (Valium) were prescribed during the earlier years, but the consumption of this became less after the conclusion of a psychiatric study of the patients. Nitrazepam (Mogadon) was taken for night sedation by many of the patients, although flurazepam (Dalmane) displaced it for a short time. Later the patients were advised to avoid flurazepam because of a cerebral syndrome possibly related to its use. Patients with hypocalcaemia were treated with calciferol or dihydrotachysterol, some also received aluminium hydroxide—none developed any evidence of dialysis dementia. Persistent hypercalcaemia unrelated to these drugs was treated by subtotal parathyroidectomy in a few patients.

All the patients had a micturating cystogram to determine adequacy of bladder capacity and bladder emptying and the presence or absence of reflux. All patients had a barium meal but more recently bleeding occurring during dialysis from duodenal ulcers not shown on the barium meal has led us to do a more detailed study of gastric function (Doherty, O'Connor, Buchanan, Douglas, McGeown, 1977). One patient required vagotomy and later a subtotal gastrectomy for bleeding from recurrent ulceration.

Bilateral nephrectomy was carried out almost routinely until the end of 1975, 65 out of 76 patients undergoing removal of their kidneys prior to transplantation. In another patient the kidneys were removed after the transplant because of severe hypertension. In 1976, because of severe hypertension not satisfactorily controlled by dialysis, or because of polycystic disease, seven of 16 patients underwent bilateral nephrectomy.

The bilateral nephrectomy was carried out as a one stage operation through a single incision except in patients with bilateral polycystic kidneys. In one patient with polycystic disease, a very large kidney was removed on one side, the other being left. The thymus was not removed in any patient, and the spleen in only one, when it had been damaged inadvertently during the bilateral nephrectomy.

As the patients were to have a major operation at short notice when a kidney became available, it was thought unwise to allow the packed cell volume to fall below 15 per cent, and a liberal policy as regards blood transfusion was followed compared with most units. Only six patients
did not receive transfusion. The fact that the majority of patients had undergone bilateral nephrectomy no doubt increased the need for blood transfusion.

Tissue typing was carried out, using a standard lymphocyte toxicity method. Seven transplants were carried out before the tissue typing service was established and these grafts were given on the basis of ABC match only. The donor tissue type was known and was used to select the best matched recipient for the other 93 transplants. The direct cross-match was negative in all except one patient where the cross-match was not carried out because the kidney was received without a lymph node. The result of the cross-match was not known until the operation was under way, for the 58 patients who received an imported kidney.

DONORS

Ninety-six cadaver and four live donor grafts were carried out. One patient received a kidney from his identical twin (Nevin and McEvoy, 1973) and three patients received a kidney from a parent. Thirty-eight of the cadaver kidneys were from local donors, the initial warm ischaemia time varying from 15 to 80 minutes, two patients receiving kidneys with a warm ischaemia time of 70 minutes and one of 80 minutes. The warm ischaemia time was generally shorter for kidneys received from other centres but, in all, 18 kidneys with warm ischaemia of 50 minutes or more were used.

The total ischaemia time varied from 159 to 855 minutes. The longest total ischaemia time (805 and 855 minutes) were associated with long-term good function. Drugs were not given to local donors as preparation for transplantation but nine had already received Decadron, one mannitol and seven antibiotics. Some of the donor kidneys from other centres had received pre-treatment with various drugs including heparin, phenoxybenzamine, dibenzyline, rheomacrodex and frusemide.

TECHNIQUE OF REMOVAL OF DONOR KIDNEYS

Ante-mortem assessment of the donor's physiological status was carried out by a senior member of the team in all of our kidney retrieval procedures. Very critical attention was paid to the general vital signs such as peripheral capillary circulation, urinary output, blood urea and creatinine levels and blood pressure in the period before demise. Whilst beating heart donor retrieval was not practised, the timing for retrieval was carefully judged to provide as "vital" tissue as possible.

Depending on the anatomical chest/abdominal configuration, either a total midline exposure or curved upper abdominal incision was used. Meticulous dissection to find polar vessels was performed but no on-block renal removals were carried out. Care was taken to prevent traction on the renal pedicle to avoid circular intimal tears which had been noted in two imported kidneys.
Immediate perfusion gave the first and most reliable sign of having obtained a good organ for transplantation—a five star perfusion being noted as being a solid flow in the drip chamber. The local kidneys were perfused manually and the solutions used were fructose/bicarbonate, Gelin’s solution or Per fus det. The majority of kidneys received from other centres were perfused with Per fus det.

TRANSLANT OPERATION

The transplant operation was a standard iliac fossa extra-peritoneal insertion. After wide and thorough surgical toilet, a urethral catheter was passed and bladder irrigation carried out with 2 per cent Neomycin solution, usually about 150 ml of this solution being left in the bladder to facilitate lateral wall vesical dissection. Peri-vascular lymphatic dissection was carried out with 90 linen ligature of the tissues to avoid lymphoceles.

In the majority of cases the renal vein was anastomosed to the external iliac as end to side, using 5/0 ethiflex. Particular attention was paid in the siting of the venotomy in the recipient vessel to produce a “coned out” open anastomosis at the venostomy. Arterial reconstitution is now practised as end to side anastomosis, using 6/0 ethiflex after a sharp linear arteriotomy is done on the recipient vessel. On two occasions, arterial bench surgery was required to join a large polar vessel to the main renal artery.

At all times very careful attention was paid to haemostasis to avoid post-operative haematomata and infection. Ureteroneocystostomy has been carried out by two techniques. Cystotomy and a Leadbetter-Politano mucosal tunnel was initially used, using 4/0 chromic gut without a splint. Subsequently, vesical myotomy and on-lay direct anastomosis of ureter to vesical mucosa, using 4/0 chromic gut, was found easier and simpler. The anastomosis should be placed well down on the side wall of the bladder. Whilst requiring a meticulous technique, this has the advantage of placing the anastomosis in the relatively non-mobile part of the bladder and at the same time renders future uretogram studies easier if required.

The wound was always drained by two corrugated drains. Postoperatively, six hourly vesical irrigation was continued until the effluent was pink and the risk of clot retention ceased. Urethral catheters were usually removed between the fourth and fifth day.

IMMUNOSUPPRESSION AND POST-TRANSPLANT CARE

The patients given living donor grafts, with the exception of the identical twin, received their first immunosuppression 24 hours before the transplant. The other 87 patients receiving cadaver kidneys were given the first immunosuppression as soon as the intravenous infusion was
commenced in theatre, well before the actual transplant. They were then given azathioprine 5 mg/kg body weight and hydrocortisone 200 mg intravenously. The dose of hydrocortisone 200 mg was repeated at six hour intervals intravenously over the first 24 hours (800 mg in total). During the second 24 hours azathioprine 1.5 mg/kg body weight and prednisolone 20 mg were given orally. This treatment was repeated daily until the creatinine clearance exceeded 20, later 30 ml/min, when the azathioprine was increased to 3 mg/kg body weight and continued at this level unless leucopenia occurred. Maintenance treatment was azathioprine 3 mg/kg body weight and prednisolone 20 mg daily. After six months the dose of prednisolone was reduced gradually to 10 mg daily, this dose being reached some time during the second year. Patients developing a Cushingoid appearance were changed to a double dose of prednisolone given on alternate days.

Rejection episodes were treated by increasing the dose of prednisolone to 200 mg daily in divided doses reducing in two to five day steps through 150, 100, 75, 50 to 20 mg daily. At first the dose of azathioprine was doubled for five days and actinomycin C 400 ug was given once intravenously, but this was discontinued after two patients died of sepsis following treatment of late rejection episodes. Increase in the dose of prednisolone alone appears to be satisfactory for treatment of rejection, without an increase in cytotoxic drugs. In a few patients rejection was treated with an intravenous bolus of methylprednisolone 1 g repeated at 24-48 hour intervals up to a maximum of four doses, but this method did not appear to be superior to the previous method.

Considerable care was taken to exclude other causes of a decline in graft function before making a diagnosis of rejection, especially after finding that a rising plasma urea and creatinine in two patients were associated with severe hyperglycaemia rather than rejection (Hill, Douglas, Rajkumar, McEvoy and McGeown, 1974). Renography has been found valuable in the early post-transplant period to show that the graft blood supply is intact, and later to exclude ureteric obstruction, although care and experience is needed in interpretation (Doherty, Douglas and McGeown, 1977).

Other tests used at times included urinary osmolality, estimation of fibrin degradation products (Lameire, Baele, Hilderson and Rengoir, 1973; Hoq, Anderton, Cunningham and Cash, 1974) in urine, excretion of N-acetyl-beta-D-glucosaminidase (N.A.G.) (Wellwood, Ellis, Hall, Robinson and Thompson, 1973), the rosette inhibition test (Bach, Dormont, Dardenne and Balner, 1969; Bewick, Ogg, Parsons, Snowden and Manuel, 1972), the accumulation of radioactive fibrinogen in the graft (Salaman, 1972; Howard, Sutherland and Najarian, 1973), and evidence of increase in graft size by radiographic measurement of metal clips inserted in the capsule of the graft at both poles. At present rejection is diagnosed by a combination of clinical features and laboratory tests. The
laboratory tests most helpful are the plasma urea, serum creatinine, creatinine clearance, amount of proteinuria, blood sugar level, urinary excretion of N.A.G. and exclusion of virus infection, in particular cytomegalic virus infection.

Other aspects of post-transplant care may be of importance. The transplants were carried out in a theatre within the Renal Unit and the patient was treated throughout the immediate post-operative period in an area receiving filtered air under controlled pressure, the patient’s room being situated between “clean” and “dirty” corridors. All used and waste materials and specimens were disposed of via the “dirty” corridor.

Until the bladder catheter and drains were removed and the wound was completely healed, the patient was isolated as much as possible. Visits by doctors were reduced to the minimum really necessary and visitors were not allowed in the patient’s room although they could visit freely in the “dirty” corridor and chat through a polythene panel in the door. Nursing duties were planned so that the nurses who looked after the patient had as little contact as possible with other patients within the unit—which also includes facilities for treatment of patients with acute renal failure. Daily wound swabs, urine cultures, throat swabs and blood cultures were taken during the period of strict isolation. Prophylactic antibiotics and antifungal agents were not used. The use of antibiotics was sparing, if possible being withheld during episodes of fever until a positive diagnosis was made by culture.

Daily urea, electrolytes and full blood count with film were taken and once urine was produced daily serum creatinine and creatinine clearance were also carried out. Serum alkaline phosphatase was estimated twice weekly. Elevation of plasma potassium within the first 36 hours of operation was treated by intravenous infusion of sodium lactate, glucose and insulin, and later by calcium resonium followed by haemodialysis when necessary. During the diuretic phase, sodium and potassium supplements were given as required.

Furosemide was not given during operation or early in the post-operative period and few patients were given it at any time. Heparin, rheomacrodex and antilymphocyte serum were never used and local irradiation of the graft was used once.

After discharge from hospital, usually about three weeks after operation, the patients were reviewed twice weekly for the first three months, after which the frequency of attendance was reduced according to whether problems had been encountered, and during this time the dose of steroid was reduced as described above. At the beginning of the second year most patients were seen once every four weeks and at the end of that year once every eight weeks. Even the “oldest” transplants are reviewed at 12 week intervals. At each review the patient is weighed, urine is tested for sugar, etc., a mid-stream urine specimen, serum creatinine and creatinine clearance, urinary protein, urea and electrolytes and full blood
count are done. If sugar is detected on routine urine testing, the blood sugar is estimated. At longer intervals the serum calcium and alkaline phosphatase are estimated. HBs Ag testing is carried out at frequent intervals over the first six months. All patients were HBs Ag negative at the time of the transplant and remain negative.

METHOD OF ANALYSIS

The data on patient and graft survival were analysed by the life-table method (Cutler and Ederer, 1958) and the cumulative survival rate and its standard error expressed as percentages. The analysis was completed for survival of grafts and patients at 31st December 1976.

RESULTS

Table I shows the source of all the grafts. The four kidneys taken from live donors functioned immediately and three of them continue to func-

| Source              | Number of grafts | Number of patients |
|---------------------|------------------|--------------------|
| Identical twin      | 1                | 1                  |
| Parent to child     | 3                | 3                  |
| First cadaver graft | 87               | 87                 |
| Second cadaver graft| 7                |                    |
| Third cadaver graft | 2                | 2                  |
| Total               | 100              | 91                 |

Table I

Kidney Transplants in Belfast, 1968-1976

The remaining patient died, with excellent graft function, 22 months after the transplant from a catastrophic haematemesis at home. He had been treated for rejection three weeks previously, the rejection having been thought to have been precipitated by failure to take his immunosuppressive drugs during a New Year holiday in Scotland.

Seventy-six patients survive, one of whom has returned to haemodialysis to await a second graft. Two patients died three months after return to regular haemodialysis. The cumulative patient survival is shown in Table II and 80.7 per cent survive two years or longer, no deaths
| Months | 0-3 | 3-6 | 6-12 | 1-2 | 2-3 | 3-4 | 4-5 | 5-6 | 6-7 | 7-8 |
|--------|-----|-----|------|-----|-----|-----|-----|-----|-----|-----|
| Patients at risk | 91  | 81  | 72   | 64  | 51  | 33  | 21  | 10  | 9   | 3   |
| Deaths | 8   | 3   | 1    | 1   | 2   | 0   | 0   | 0   | 0   | 0   |
| Lost to follow-up* | 0   | 0   | 0    | 0   | 0   | 0   | 0   | 0   | 0   | 0   |
| Withdrawn alive‡ | 2   | 6   | 7    | 12  | 16  | 12  | 11  | 1   | 6   | 3   |
| Cumulative survival | 91.1 | 87.6 | 86.2 | 84.7 | 80.7 | 80.7 | 80.7 | 80.7 | 80.7 | 80.7 |
| (± S.E.) (%) | 3.0 | 3.5 | 3.6  | 3.9 | 4.6 | 4.6 | 4.6 | 4.6 | 4.6 | 4.6 |

| Months | 0-3 | 3-6 | 6-12 | 1-2 | 2-3 | 3-4 | 4-5 | 5-6 | 6-7 | 7-8 |
|--------|-----|-----|------|-----|-----|-----|-----|-----|-----|-----|
| Grafts at risk | 100 | 81  | 72   | 63  | 50  | 32  | 22  | 10  | 9   | 3   |
| Failures | 13  | 3   | 1    | 0   | 0   | 0   | 0   | 0   | 0   | 0   |
| Lost to follow-up* | 4   | 0   | 1    | 1   | 2   | 0   | 0   | 0   | 0   | 0   |
| Withdrawn alive‡ | 2   | 6   | 7    | 12  | 16  | 12  | 11  | 1   | 6   | 3   |
| Cumulative survival | 86.6 | 83.3 | 82.1 | 82.1 | 82.1 | 82.1 | 82.1 | 82.1 | 82.1 | 82.1 |
| (± S.E.) (%) | 3.5 | 3.8 | 3.9  | 3.9 | 3.9 | 3.9 | 3.9 | 3.9 | 3.9 | 3.9 |

| Months | 0-3 | 3-6 | 6-12 | 1-2 | 2-3 | 3-4 | 4-5 | 5-6 | 6-7 | 7-8 |
|--------|-----|-----|------|-----|-----|-----|-----|-----|-----|-----|
| First grafts at risk | 91  | 74  | 66   | 57  | 45  | 30  | 21  | 10  | 9   | 3   |
| Failures | 11  | 3   | 1    | 0   | 0   | 0   | 0   | 0   | 0   | 0   |
| Lost to follow-up* | 4   | 0   | 1    | 1   | 2   | 0   | 0   | 0   | 0   | 0   |
| Withdrawn alive‡ | 2   | 5   | 7    | 11  | 13  | 9   | 11  | 1   | 6   | 3   |
| Cumulative survival | 87.5 | 83.8 | 82.5 | 82.5 | 82.5 | 82.5 | 82.5 | 82.5 | 82.5 | 82.5 |
| (± S.E.) (%) | 3.5 | 3.9 | 4.1  | 4.1 | 4.1 | 4.1 | 4.1 | 4.1 | 4.1 | 4.1 |

* Died with functioning graft
‡ Not yet completed time interval

occurring between three and seven years. Eight of the 15 patients who died had excellent graft function up to the time of death (Table III)

TABLE III

Causes of death related to kidney transplant

| With functioning graft: | Number of patients |
|-------------------------|--------------------|
| Myocardial infarction    | 3                  |
| Cerebrovascular accident | 1                  |
| Cerebral syndrome        | 1                  |
| Late infection           | 2*                 |
| Haematemesis             |                    |

| Without functioning graft: | |
|----------------------------|----------|
| Death on dialysis, graft rejected | 1       |
| Cerebral syndrome          | 2       |
| Stenosis ureter, chest infection | 1†      |
| Cerebrovascular accident   | 1       |

Total 13

* one at three months, one at nine months
† one at one year
and postmortem examination of the transplant showed no evidence of rejection or other abnormality. The causes of death in these eight patients were myocardial infarction (3), cerebrovascular accident (1), cerebral syndrome (1), late chest infection (2), haematemesis (1). Four died with non-functioning grafts and another patient died soon after removal of an early rejected graft. This patient and two of the others died from a peculiar cerebral syndrome, cause unknown; an association with ingestion of flurazepam, or a combination of flurazepam and diazepam, was suspected but could not be proved (Taclob and Needle, 1976). One died from a cerebrovascular accident at 10 days post-transplant and the other patient from unrecognised ureteric obstruction and chest infection at one year. Infection caused no deaths within the first 60 days after transplantation although chest infection led to two of the later deaths, which followed leucopenia due to antirejection therapy including high dosage (6 mg/kg body weight) of azathioprine and also actinomycin C. There have been no further deaths from infection since it was decided to treat rejection episodes with increase in prednisolone without increase in azathioprine, and actinomycin C was omitted.

**Table IV**

*Fate of all cadaver kidney grafts 1968-1976*

| Number of grafts | Number of grafts functioning |
|------------------|-----------------------------|
| First            | 87                          | 64                          |
| Second           | 7                           | 5                           |
| Third            | 2                           | 2                           |
| Total            | 96                          | 71 (73.9%)                  |

The fate of all the cadaver grafts in shown in Table IV and overall 73.9 per cent of the grafts survive. Two of the 71 surviving grafts have poor function after 3½ years (serum creatinine 515 and 770 umol/l), one from recurrence of chronic pyelonephritis in the graft (Hill, Loughridge, Bharucha and McGeown, 1977), one probably from chronic rejection although the precise cause is not known. The other 69 grafts have adequate to excellent function. The survival of the small number of second and third grafts is gratifying, both third grafts surviving. One patient who received three grafts thrombosed the first two grafts on the third day, but the third graft continues to operate after more than two years. A second patient received three grafts; the first was removed at the primary operation because the middle two-thirds did not become vascularised, the second was rejected at three weeks, and the third continues to function at over nine months.
The cumulative survival of all grafts is shown in Table II and is 82.1 per cent (S.E. \( \pm 3.9 \)) from one to seven years.

The cumulative survival of all 91 first transplants (including the four live donor grafts whose survival does not differ from the cadaver donor grafts) is shown in Table II. The life table method of calculation makes an allowance for the eight patients who died with excellent graft function (Table III). The cumulative survival of first transplants is 82.5 per cent (S.E. \( \pm 4.1 \)) from one to seven years.

**Table V**  
*Cause of loss of graft*

| Cause of loss of graft | Number of grafts |
|------------------------|------------------|
| Rejection              | 5                |
| Arterial problems      | 5*               |
| Venous thrombosis      | 2                |
| Primary non-function   | 2                |
| Haemorrhage            | 1                |
| Stenosis of ureter     | 1                |
| Early death of patient | 1                |
| Death with functioning graft | 8         |
| Total                  | 25               |

* Rejection could be excluded in 1 only, although pathological appearances not typical of rejection in others.

The cause of the loss of graft is shown in Table V. It can be seen that rejection clearly was responsible for five of the graft failures and may have contributed to four of the five arterial thromboses although the pathological appearances were not typically those of rejection. Rejection was not implicated in the loss of the remaining 16 grafts.

There were 19 first transplants without a mismatch on the B locus and the cumulative graft survival of the group was 94.6 per cent (S.E. \( \pm 5.3 \)) from three months to seven years. There were 48 first transplants with one mismatch on the B locus and the cumulative graft survival of this group was 77.1 per cent (S.E. \( \pm 4.3 \)) at three months, 70.7 per cent (S.E. \( \pm 5.4 \)) at one to seven years. Seventeen first transplants had two mismatches on the B locus and the cumulative graft survival was 75 per cent (S.E. \( \pm 10.8 \)) at three months to seven years. These differences were not statistically significant (p > 0.05).

There were 48 patients of group 0 receiving a first transplant and their cumulative graft survival was 93.6 per cent (S.E. \( \pm 3.6 \)) at three months, 88.6 per cent (S.E. \( \pm 4.8 \)) at one to seven years. Twenty-eight patients of
group A received a first transplant from a donor of group A and their cumulative graft survival was 77.4 per cent (S.E. ±8.1) at three months, 69.3 per cent (S.E. ±9.1) at one to seven years. These differences were not statistically significant (p>0.05).

**TABLE VI**

*Transfusions before first transplant*

| Number of units of blood* | Number of patients | Number with functioning grafts |
|---------------------------|--------------------|-------------------------------|
| 0                         | 6                  | 3                             |
| 1 - 9                     | 32                 | 29                            |
| 1 - 4                     | 16                 | 14                            |
| 10+                       | 31                 | 28                            |
| **Total**                 | **69**             | **60**                        |

* Packed cells or whole blood

The number of units of blood given before the first transplant was known accurately for 69 patients and this is shown together with the fate of the grafts in Table VI. The small number of patients who did not receive blood precludes statistical analysis although it appears that first grafts did less well in these patients than in those who received blood, but the quantity given does not seem to have affected the outcome.

In patients treated by dialysis for less than nine months the cumulative function of first transplant was 71.2 per cent (S.E. ±5.2) at three months and 69.0 per cent (S.E. ±5.5) at one year. In patients dialysed for longer than nine months it was 93.3 per cent (S.E. ±3.7) at three months and 85.9 per cent (S.E. ±5.3) at one year. These differences were significant at three months (p<.01) but not at one year (p>0.05).

The 10 patients treated by peritoneal dialysis did not differ significantly from those treated by haemodialysis as the grafts of eight functioned well for long periods. Seven of the eight grafts still function while one was lost on the death of the patient from myocardial infarction at 26 months. The remaining two grafts were rapidly rejected—it may be of significance that these two recipients were not transfused.

**REHABILITATION**

Seventy-four of the 76 remaining patients have been well rehabilitated. One patient who has returned to haemodialysis to await a second graft is not fully rehabilitated, and one who was disabled by peripheral neuropathy before haemodialysis remains disabled although living at home and
capable of caring for personal needs. Two further patients who were working full-time have ceased to work because of severe angina. One received his graft at the age of 53, developed venous thrombosis of the graft after a few weeks, the thrombus was successfully removed (Clarke, Kennedy, Hewitt, McEvoy, McGeown and Nelson, 1970), underwent transurethral prostatectomy at the age of 59 and still has a serum creatinine of 85 umol/l at the age of 61. The second was 46 at the time of the graft and three years later had a myocardial infarct followed by persistent angina but his serum creatinine remains unchanged at 280 umol/l after four-and-a-half years. The remaining 72 patients are all capable of full-time work although not all have been able to find a job because of the high level of unemployment here.

DISCUSSION

It is generally accepted that the patient with a successful kidney transplant becomes more fit and has a better quality of life than the patient treated by regular dialysis. The mortality following transplantation is thought to be considerably higher than that associated with regular dialysis. Sixty-six of our 91 patients who received a kidney graft survive, and moreover, eight died with functioning grafts. In four of these the cause of death (myocardial infarction in three, cardiovascular accident in one) could not be attributed to the transplant operation, although attributable to the hypertension and chronic renal failure prior to it. Two deaths occurred more than three months after removal of the rejected transplanted kidney. Including all these deaths, the over-all survival of patients was 83 per cent. The cumulative survival of our patients after transplantation was 86.2 per cent at one year, 84.7 per cent at two years, and 80.7 per cent at five years. The most comparable figures are those reported for Europe by EDTA for patient survival after the first cadaver graft (Gurland, Brunner, Chantler, Jacobs, Schärer, Selwood, Spies and Wing, 1976) of 72.8 per cent at one year, 65.8 per cent at two years and 60.7 per cent at three years. They can also be compared with the survival figures on home dialysis, which is generally considered to give the best survival rates, reported by EDTA (Gurland et al., 1976), of 93.1 per cent at one year, 86.7 per cent at two years and 80.8 per cent at three years, and with those reported by Henari et al (1977) of 91.2 per cent at one year, 82.6 per cent at two years and 71.5 per cent at five years.

Seventy-four per cent of all the grafts survive. The cumulative survival of the first graft was 82.1 per cent at one to seven years. The cumulative survival of first cadaver grafts reported by EDTA was 50.1 per cent at one year, 43.9 per cent at two years and 39.4 per cent at three years (Gurland et al., 1976). There were only four living donor grafts in our series and as their fate was similar to the cadaver grafts, and as their number was small, it seems reasonable to combine the results.
Infection is the commonest cause of death following transplantation (Henari et al., 1977) and accounted for 37.5 per cent of all deaths during the first 60 days after transplantation in the EDTA series (Gurland et al., 1976). The low incidence of serious sepsis in our patients after transplantation and the fact that no patient died from sepsis during their hospital admission for the transplant can mainly be attributed to the reverse barrier nursing in our specially ventilated unit and the care taken to follow the strict discipline involved. However, the sparing use of steroid and the fact that anti-lymphocyte serum was not used may also have been important. Falling renal function is investigated as a matter of emergency as it is our policy to prescribe anti-rejection therapy only after careful exclusion of other causes of falling graft function, and when a kidney fails to remove it rather than persist too long with high dosage of steroid. Episodes of fever due to cytomegalic virus infection were the commonest reason for readmission during the first three months. During the high fever associated with cytomegalic virus infection the serum urea and creatinine became elevated in some patients, but this was not a manifestation of rejection and we feel it should not be treated by increased dosage of steroid.

Immediate function of the graft was exceptional in the 96 cadaver kidney grafts, presumably because of the relatively long warm and total graft ischaemia times. Only one patient received a kidney with zero warm ischaemia (from a continental donor). The majority of the patients required one or more haemodialysis (or peritoneal dialyses in patients previously treated in this way) in the post-operative period. However, the early period of acute renal failure, even when the initial warm ischaemia was prolonged, did not adversely affect the future function of the graft. The three patients who received the kidneys with the longest warm ischaemia (two of 70, and one of 80 minutes) have excellent function seven to eight years after the graft was carried out. Eight of the kidneys which function well had a total ischaemia time of over 720 minutes, and the kidney with the longest total ischaemia of 855 minutes continues to function well over three years later. White, Evans and Calne (1968) have also noted that acute renal failure does not prejudice the future of the graft.

In grafts which functioned during the first 24 hours a fall in urine volume, associated with swelling of the graft and fever, often occurred on the third to fourth day. This was probably due to acute tubular necrosis rather than to rejection, but if it was due to rejection it usually recovered gradually and spontaneously without anti-rejection therapy.

At first we thought that the degree of fitness of the recipient at the time of transplant was very important but surprisingly the ten patients transplanted from peritoneal dialysis, who were in general the least fit, did not differ from the patients transplanted from haemodialysis as 80 per cent had functioning grafts at one year.
The frequent use of bilateral nephrectomy may have affected the results in several ways. There is no doubt that the patients required more blood transfusions after the nephrectomy and there have been many recent suggestions that blood transfusion improves graft survival in patients (Festenstein, Sachs, Paris, Pegrum and Moorehead, 1976; Opelz and Terasaki, 1976; van Hooff, Kalff and van Poelgeaste, 1976) and in animals (van Es, Marquet, van Rood, Kalff and Balner, 1977). We have noted that the incidence of urinary tract infection is lower amongst our nephrectomised patients (Douglas, Clarke, Kennedy, McEvoy and McGeown, 1974) than in other series (Hamshere, Chisholm and Shackman, 1974; Steen, Pedersen and Vejlsgaard, 1975). The bilateral nephrectomy did not lead to the death of any patient although several developed troublesome wound infections and two were left with wound hernias.

The excellent survival of the grafts is not easily explained. Thirty-five patients received a first transplant with none or one HLA mismatch, and 48 with two or more mismatches, so that in more than half the patients the match grade was not particularly good. The 19 first transplants without a mismatch on the B locus had a cumulative survival of 94 per cent (S.E. ± 5.3) compared with a survival of 75 per cent (S.E. ± 10.5) in those with two mismatches on this locus, but the difference was not statistically significant.

Most of the patients received kidneys of the identical rather than the compatible ABO group, and the NOMS data for 1976 suggest that group A recipients receiving kidneys from group A donors do better than those receiving kidneys from group O donors. However, the 28 group A patients, despite receiving group A kidneys as their first transplant, did less well than the 58 group O patients (group A 69.2 per cent, group O 88.6 per cent at one year). The numbers are small and the differences may well have occurred by chance, but they are in the same direction as other reports that group O recipients have superior graft survival (Joysey, Roger, Evans and Herbertson, 1973; Opelz and Terasaki, 1977). Opelz and Terasaki suggested that this might be due to the fact that in general group O patients wait longer on dialysis before receiving their transplant. This is true of our patients and we have found that patients dialysed for longer than nine months had better cumulative survival of their first grafts than those dialysed for less than nine months (93.3 per cent and 71.2 per cent at three months, P > 0.01; 85.9 per cent and 69 per cent at one year, P > 0.05). This is in keeping with Opelz and Terasaki's suggestions. The patients who waited longer on dialysis usually received more blood.

We have satisfactory data on the transfusions received by 69 patients before the first transplant. Only six did not receive blood but three of those lost their graft within a few weeks while 57 of the 63 patients receiving blood have functioning grafts. However, the quantity of blood did not appear to be important, provided blood was given (Table VI).
Unfortunately, statistical analysis of these small numbers is not meaningful.

Rejection clearly accounted for five of the 17 grafts which were lost. There were five lost from arterial thrombosis, but one of these was certainly mechanical. Arterial thrombosis is often associated with rejection (although these four were not typical examples of rejection by any other criteria) but even if they are considered due to rejection, at most nine out of the 17 lost grafts were from this cause.

It is clearly important to establish the cause of a rise in plasma urea or a decline in graft function as these are by no means always due to rejection. Vascular and ureteric lesions must be considered and we have found ureteric obstruction an important and frequent cause of late fall in graft function (Doherty, Douglas and McGeown). It should be remembered that the plasma urea and creatinine rise during acute febrile episodes and this is not an indication for increasing steroid. There were only two kidneys with primary non-function although NOHMS data suggest that about 17 per cent of transplanted kidneys never function.

Meticulous follow-up seems essential so that complications can be detected and treated promptly.

The survival of our patients treated by cadaveric kidney transplantation is nearly as good as that claimed for home dialysis and the survival of grants is well above the European average. The costs of regular dialysis therapy continue to escalate and we believe that the only hope of providing treatment for a substantial proportion of those who could benefit lies in transplantation (McGeown, 1977). The scarcity of kidney donors continues and we must convince our colleagues that kidney transplantation is a worthwhile method of treatment capable of returning many to full health and fitness.

Summary

One hundred kidney transplants have been carried out on 91 patients, there being seven second transplants and two third transplants. Four transplants were from living related donors, 96 from cadavers. Seventy-six patients survive, all but one with functioning kidneys. The cumulative survival of patients was 82 per cent at two years and 80.7 per cent at five years. Eight patients died with functioning grafts, and two of the other deaths occurred more than three months after removal of a rejected kidney and return to haemodialysis. There were no deaths from sepsis in the first 60 days after transplantation. The cumulative survival of all grafts was 82.1 per cent at two and five years. The cumulative survival of first grafts was 82.5 per cent at two and five years.
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