DOCTORS V PATIENTS

30 JUNE 1981

MR SLAPAK HAS RECEIVED A CHALLENGE FROM THE PORTSMOUTH TRANSPLANT OLYMPIC TEAM TO COMPETE AGAINST THE BTS MEMBERS AT: SWIMMING, SQUASH, CROSS COUNTRY, TENNIS, TABLE TENNIS, AND GOLF, AT 2.30 pm ON THE DAY BEFORE THE BTS MEETING.

Members interested please contact Mr Slapak at Portsmouth:
Tel; 0705 22331 ext 251

BRITISH TRANSPLANTATION SOCIETY

PORTSMOUTH MEETING
1ST JULY

Platelet Activation in Renal Transplant Recipients

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Platelets have been detected by electron microscopy and by localisation of labelled platelets, within rejecting allografts, and platelets are prominent in xenograft destruction. We have studied platelet activation and localisation by measuring intraplatelet serotonin concentration in circulating platelets, the plasma concentration of platelet factor 4 (PF4) the serum concentration of platelet-activating material (PAM), and the renal localisation of platelet membrane antigen and PF4, using immunofluorescent techniques. Sixteen transplant recipients were studied thrice weekly for 12-16 weeks after grafting in a serial study, and a further 88 patients were studied on at least one occasion 3 months to 7 years after grafting. Eleven transplant biopsies from rejecting allografts were studied, all within the first three months after grafting. Intraplatelet serotonin fell immediately after grafting to very low levels, which remained low for 12 weeks; thereafter, levels rose to low or low normal. In contrast, plasma concentrations of PF4 were almost all normal for 12 weeks, but became raised thereafter. There was no correlation between the amount of PAM in the circulation and depeletion of intraplatelet serotonin, whereas all biopsies showed strong positive for platelet membrane antigen and PF4. We conclude that there is strong in vivo platelet activation in all allograft recipients, that this activation takes place principally within the allograft and not in the circulation and that the pattern of activation during the first three months following grafting differs from that in chronic stable grafts.

ABSTRACT

Detection of Donor-specific Antibodies binding to Endothelium in Renal Allografts using an Indirect Immunoperoxidase Technique.

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It is known that endothelial cells express ABH, HLA-A -B -DR antigens and are targets for graft rejection. Furthermore antibodies specific for renal endothelium have been demonstrated in patients with irreversible renal vascular lesions.[1] These antibodies appear to be directed against endothelial specific antigens shared with monocytes and are distinct from HLA-A, -B and DR.[2] In order to study the role of recipient donor specific antibodies in the vascular rejection of grafts, we have adapted the immunoperoxidase technique described by Paul et al.[3] Various antisera have been tested for staining of the vascular endothelium in pretransplant needle core biopsies. Polyspecific alloantisera to HLA-A, -B, -C and to HLA-DR have been shown to stain the endothelium. Specific staining for HLA A2 and HLA DR4 has been demonstrated and appropriate absorption of these antisera using donor spleen cells removed the specific staining pattern. In these reactions the endothelium of the peritubular capillaries was more strongly reactive than the larger vessels. Serial serum samples from graft recipients have been investigated for their staining patterns on respective donor kidney tissue. Data will be presented on the development and specificity of antibodies to donor kidney in recipient sera and in acid eluates from failed grafts. These findings will be correlated with routine immunoperoxidase examination of biopsies subsequent to transplantation.

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Presentation

Pancreatic transplantation in the rat:
A simplified method using aortic interposition and cuff techniques

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Microvascular techniques involving the transplantation of organs such as the rat pancreas can be tedious, time consuming and require considerable training. A method of aortic interposition using cuff techniques at either end is described with the transplanted segment carrying the blood supply to the pancreas . The segment of aorta can include the renal veins to enable simultaneous renal transplantation to be performed, if required. The portal vein is subsequently anastomosed to the ipsilateral renal vein after prior nephrectomy by a similar method. The slightly larger vessel is always drawn over the smaller one. Circumferential 7.0 silk sutures are used to secure the vessels around extraluminal polyethene cuffs.

A total of 37 pancreatic isografts have been performed, each vascular anastomosis taking approximately 5 minutes to complete, with consequent warm ischaemic times of less than 15 minutes. Revascularization was achieved in all without problems. The recipients had been made previously diabetic with Streptozotocin. Animals were sacrificed over a period of six months. They remained normoglycaemic. Histological examination showed some degree of intimal vascular proliferation at the anastomotic site in all cases. Pancreatic appearances were comparable with those achieved to conventionally anastomosed organs.

Rat Pancreas allotransplanation; a short-term comparison of rejection patterns following different methods of dealing with exocrine drainage.

N.J. LINDSEY, M.S. NOLAN, C.P. SAVAS, P.F. BOYLE, D.N. SLATER and M. FOX, Transplantation Laboratories, Royal Hallamshire Hospital, Sheffield.

This presentation describes the effect of duct ligation, latex obliteration and free drainage upon the histological appearance and function of short-term pancreatic allografts. Results were compared with isografts and assessed by histology, serum glucose, insulin and amylase levels.

15 allografts were performed using WAG female donors and AGUS male recipients. These were sacrificed on days 2, 6 and 11. 9 AGUS isografts were also performed as controls.

On day 2 there was no evidence of rejection in the allografts. By day 6, ligated and obliterated isografts showed greater degrees of exocrine damage and cellular infiltration than the free draining isografts; islets appeared normal in all 3 groups. The ligated and obliterated allografts showed more exocrine damage than their isograft counterparts. Although the cellular infiltrate was similar in intensity, at this stage, in both iso- and allografts, the allografts contained a greater percentage of immunoblasts. In contrast, free draining iso- and allografts showed similar degress of exocrine damage, but the allografts contained more cellular infiltration particularly by immunoblasts, however this was less than in the other allograft groups. Ligated and obliterated allografts started to show islet abnormalities by day 6, histological destruction and loss of function being complete by day 11 in all groups.

A comparison of single dose Cyclosporin and Cyclophosphamide for anti rejection therapy

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Immunosuppression is customarily given on a daily basis as a continuous course. Cyclosporin is the most recent immunosuppressive agent used in this way and has been shown to be effective in the rat[1].

We have previously shown in Lewis - D.A. heart grafts that a single dose of Cyclophosphamide is most effective if given when the histology shows early graft rejection[2].

The present study compares single dose Cyclosporin A with single dose Cyclophosphamide.

Therapy	No. of rats	Graft survival in days median	(range)
Nil	13	11	(8 - 14)
Cyclosporin 125 mg/Kg			
Day 1	6	22.5	(14 - 41)
Day 3	6	31	(21 - 100+)
Day 5	6	20.5	(10 - 100+)
Cyclophosphamide 50 mg/Kg			
Day 1	5	26	(15 - 41)
Day 3	6	100	(14 - 100+)
Day 5	7	21	(15 - 27)
Cyclophosphamide 25 mg/Kg			
Day 3	6	68	(17 - 100+)

A single dose of Cyclosporin does prolong graft survival especially if given on day 3 when histology shows early rejection. However Cyclophosphamide given at the same time is equally effective. Furthermore single doses of Cyclosporin are more toxic, six animals dying, three with retro-peritoneal haemorrhage.

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The value of 'blind' high-dose steroid prophylaxis in the prevention of early acute rejection of renal transplants.

B D PENTLOW, R Goffin, P Harrison, J Campbell Mackenzie, A S Parker and H J O White

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This study compares the results of two approaches to the problem of early acute rejection of renal transplants using 'conventional' immunosuppressive agents.

Patients receiving renal transplants (n=62) were allocated to one of two immunosuppressive regimes. The groups were matched regarding age, sex, tissue typing and prior blood transfusions.

Group I. 31 patients received standard maintenance doses of prednisolone and azathioprine. Acute rejection was treated with 3 g. intravenous methyl-prednisolone.

Group II. 31 patients given similar initial doses of prednisolone and azathioprine received 200 mg/d of prednisolone in addition from day 3, reducing to 40 mg/d after 2 weeks. Severe acute rejection was treated similarly with methyl-prednisolone.

The results were assessed at 12 weeks. One patient in Group I died, but none in Group II. In Group I 12 grafts were lost due to rejection (39%). In Group II only 3 grafts were lost (10%). This difference is statistically significant ($p < 0.01$ χ^2 test). The incidence and severity of steroidal facies was somewhat higher in Group II. Wound infection was commoner in Group I (10 against 3) as was secondary haemorrhage (4 against 0); these complications mainly followed removal of rejected grafts.

'Blind prophylactic' treatment reduced the incidence of early graft rejection. Since the study was terminated, a further 15 patients were treated as in Group II and all have functioning grafts. Only one of 40 patients (2½%) managed as in Group II that had had prior blood transfusions rejected the graft in this period of study. This regimen appears to be an effective and safe method of reducing early acute rejection: the long term results are not known. It is particularly suitable when there is not an immediate diuresis.

EARLY EXPERIENCE WITH CYCLOSPORIN A IN RENAL TRANSPLANT PATIENTS, USING CALNE'S REGIME

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Eleven patients age 21 - 54 have received Cyclosporin A (CYA) alone as initial prophylactic anti rejection therapy following cadaveric renal transplantation (follow up 1 - 5 months)

The dose regime was:

17.5 mg/kg/day x 14 days reducing by 2 mg/kg/day at monthly intervals thereafter. All patients had an early diuresis after transplantation.

Results:

of the 11 patients:

9 have satisfactory graft function

6 remain on CYA alone with good graft function (serum creatinine $< 200\ \mu M/L$); one of these patients experienced mild rejection, reversed with 3G. Solumedrone

2 patients suffered severe rejection and treatment was changed to Azathioprine and steroids, and 1 of these lost her graft

2 patients underwent severe nephrotoxicity and other side effects of CYA, and good graft function returned after conversion to Azathioprine and steroids

1 patient died at 10 days with jaundice and coronary artery insufficiency

Early results of CYA blood levels in these patients suggests a correlation between side effects and plasma concentration of CYA. Further data on blood levels as yet unavailable, will be presented.

A controlled trial of cyclosporin A

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Patients undergoing cadaveric renal transplantation have been randomised either into treatment with cyclosporin A (CyA) 17½ mgm per kg reducing to 12½ mg per kg by the third month or to Azathioprine 2.5 mgms per kg and Prednisolone 30 mgs per day reducing to 20 mgms per day by three months. Patients were excluded from the trial if they were to receive a DR compatible kidney or if the transplanted kidney was not excreting at least 100 ml/hour during the first 8 hours after transplantation. Thus, randomisation of the patient into each arm of the trial was carried out at this time. CyA was to be given for 3 months after transplantation, at which time patients were to be converted to Azathioprine and Prednisolone. The protocol also allows patients to be converted from CyA to Azathioprine and Prednisolone if they had more than two rejection episodes or if side effects were unacceptable.

To date 16 patients have been entered into the cyclosporin A arm of the trial and thirteen patients into the Azathioprine and Prednisolone arm of the trial. Follow-up ranges from 1 week to 15 months. Of the 16 patients in the cyclosporin A arm of the trial, three patients rejected their kidneys during the first 3 months, while a fourth patient rejected the kidney after cessation of CyA at three months. 2 patients were converted to Azathioprine and Prednisolone after a third injection episode, while CyA was discontinued in 2 patients because of unacceptable side effects. In the Azathioprine and Prednisolone arm of the trial, two patients have rejected the kidneys and a third has died, death being associated with rejection therapy.

Side effects included psychosis, hirsutism, gum hypertrophy, neurasthesiae, but infection was a problem in only one patient with a primary CMV infection. Biopsies were performed in the cyclosporin A patients on day 7, day 21 and day 90. No biopsies were normal, all showing a greater or lesser degree of cellular infiltrate with mild vascular changes in two instances. Renal function improved in most patients on conversion to Azathioprine and Prednisolone.

CyA alone has proved to be a potent immunosuppressive agent, possibly as effective as Azathioprine and Prednisolone. However it seems possible that it may need to be used with steroids in the early months after transplantation to obtain the optimal effect. Studies of blood levels currently in progress may clarify this point.

STRUCTURE AND FUNCTION OF SMALL BOWEL ALLOGRAFTS TREATED WITH CYCLOSPORIN A

Mongrel dogs received orthotopic total small bowel allografts using a technique similar to that described by Lillehei, but with venous drainage to the vena cava. Half the dogs received no immunosuppression, and half received Cyclosporin A 25 mg/kg/day intramuscularly for four weeks, then orally.

The ten untreated dogs survived a mean of 12.5 days (range 7-25) They lost up to 30% of their initial weight and all had severe diarrhea, frequently with melena as a terminal event. Rejection with hemorrhagic necrosis was the usual cause of graft failure.

The mean survival of eleven dogs receiving Cyclosporin A was 79 days (range 9-221) with early deaths being due to pneumonia and volvulus. In all those animals dying in the first 3 months, the intestinal mucosa was indistinguishable from normal, but there was considerable smooth muscle hypertrophy Lymph nodes and spleen were small with gross central lymphoid depletion. The longest survivors so far lived 203 and 221 days, and one Cyclosporin A treated dog remains alive and well at 165 days.

Long surviving animals remained healthy, with good appetites and passing formed stools. Their weights were steady and plasma proteins normal. Xylose absorption curves are no different from those seen in two autografted dogs, although slightly depressed as compared to normal.

Barium meal and follow through studies show some rigidity of the transplanted bowel, suggesting thickening of the bowel wall. However, luminal diameter and mucosa are normal. Transit time is around 60 min. (normal 150 min.)

Those animals dying at 203 and 221 days both had acute terminal illnesses with anorexia, weight loss and severe diarrhea. At autopsy the bowel mucosa showed some ulceration and villous atrophy, with a lymphoid infiltrate suggesting that these changes were due to acute rejection. Blood levels of Cyclosporin A were low (<200 ng/cc) during the last two months of their lives, thereby allowing rejection to occur as a late event.

Cyclosporin A has been shown to be effective in allowing total small bowel allografts to survive long term, with essentially normal structure and good function.

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Cyclosporin A has been shown to be the single most effective agent in preventing rejection of kidney, liver, pancreas, heart and bone marrow allografts in laboratory animals and in man. It is usually administered by mouth into a normal intestine.

Oral Cyclosporin A, dissolved in olive oil, is shown to precipitate rapidly after contact with gastric juice or bile, but appears in intestinal lymph, probably absorbed in fat droplets.

Cyclosporin A levels in intestinal duct and thoracic duct lymph have been measured in normal dogs and pigs. Peak concentrations of Cyclosporin A in lymph are up to 1250 ng/cc within one hour of injecting the drug into the intestinal lumen (25 mg/kg in olive oil), whereas portal vein and systemic blood levels rise more slowly with peak levels of 500 ng/cc after 2 hours.

Intestinal duct lymph, when viewed under the microscope, contains dark particles after the drug is given, and it is presumed that these are the solid precipitate of Cyclosporin A.

Ten mongrel dogs receiving orthotopic total small bowel allografts survived a mean of 12.5 days (range 7-25 days) with no immunosuppression.

Eleven dogs received orthotopic total small bowel allografts and Cyclosporin A 25 mg/kg/day intramuscular for four weeks (until lymphatics reconnected), then orally. Blood levels of Cyclosporin A were all above 1000 ng/cc whilst the drug was administered intramuscularly. The mean survival in this group was greater than 78 days (range 9-221 days). Oral Cyclosporin A absorption curves in long surviving animals were similar to those in intact animals, with peak levels of 500-1000 ng/cc 2 hours after the oral dose was administered.

Two dogs receiving orthotopic total small bowel allografts were given Cyclosporin A 25 mg/kg/day orally from the time of surgery. Survival was 14 and 25 days, both dogs dying with bleeding peptic ulcers and histologically normal allografts. In these dogs, the highest blood level of Cyclosporin A during the first 6 days was 200 ng/cc, but after this time, levels comparable to those found in intact animals were found.

Hence, it would appear that inadequate absorption of oral Cyclosporin A occurs during the first week after small bowel allografting, possibly due to disruption of intestinal lymphatics. However, after the first week, the allografted intestine absorbs the drug in similar amounts and at a similar rate as absorbed by the intact intestine.

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ROLE OF ADRENERGIC SYSTEM IN HYPERTENSION AFTER RENAL TRANSPLANTATION

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The mechanism of hypertension despite normal graft function remains obscure. In 11 hypertensive (HT) and 10 normotensive (NT) transplantees and 13 controls we measured plasma noradrenaline (NA), plasma renin activity (PRA) and plasma aldosterone concentration (PA) at rest and during 40° head up tilt. The HR and BP response to infusions of 0.05 ug/kg/min of NA and 0.02 ug/kg/min of isoprenaline was also measured as was blood volume (BV) and total exchangeable sodium (ES) in the transplanted groups.

Mean BP (± SD) was 110 ± 14/71 ± 6 in controls, 130 ± 17/77 ± 8 in NT and 155 ± 15/103 ± 17 mm Hg in HT at rest, showing no change with tilt in any group. There was no difference in basal NA levels in the 3 groups (1.28 ± 0.81 nmol/l controls; 1.98 ± 0.92 NT; 1.81 ± 1.08 HT). The mean change in plasma NA rise with tilt was significant in the control group (0.96 ± 0.76; $P < 0.005$) and NT group (0.62 ± 0.69; $P < 0.02$) but not the HT group (0.27 ± 0.69). There was no correlation between PRA or PA with BP in NT or HT group. Following NA infusion the BP rise and reflex bradycardia was 3 times greater in the HT group compared to the controls and 1.5 times greater compared to the NT group. The same HR and BP response was seen in all groups following isoprenaline infusion. ES was 37.6 ± 6.4 mmol/kg in NT and 44.8 ± 8.4 in HT transplantees ($P < 0.05$) and BV was 4.25 ± 1.11 l in NT and 5.35 ± 1.25 in HT group ($P < 0.05$).

The increased sensitivity to NA in HT transplantees in whom ES and BV were also increased suggests that post transplant hypertension may be due to increased alpha receptor sensitivity associated with volume expansion.

RENAL ALLOGRAFT RUPTURE CAUSED BY FRUSEMIDE

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Transient renovasodilatation following the administration of ethacrynic acid and frusemide has been demonstrated in dogs. These diuretics are believed to act on the loop of Henle, as evidenced by their interference with the concentrating mechanisms of the kidney. Loop diuretics have been reported as producing an increase in outer cortical blood flow and a decrease in outer medullary and juxtamedullary cortical blood flow.

We report three cases of rupture of the renal allograft following the administration of frusemide.

Case 1 (P.N.) On the eighth post-operative day he experienced abdominal pain or sudden onset two hours after the administration of 250 mg of frusemide orally. Exploration of the graft revealed a 3 cm capsular rent. An open biopsy showed cellular and vascular rejection. Post exploration graft function remained poor and nephrectomy was carried out on the 28th day.

Case 2 (V.D.) On the twelth post-operative day she experienced abdominal pain of sudden onset two hours after the administration of 250 mg of frusemide orally. Exploration of the graft revealed a small capsular tear. An open biopsy showed vascular rejection. Graft function improved but subsequently she lost her graft on day 252 due to chronic vascular rejection.

Case 3 (A.G.) On the fifth post-operative day his graft was explored for suspected ureteric obstruction. This was confirmed at exploration and the ureter was re-implanted. 100 mg of intravenous frusemide was administered pre-operatively. Within a few minutes the graft became tense and pulsatile and a 2 cm capsular rent appeared. An open biopsy showed cellular rejection. Graft function recovered and is satisfactory at day 136.

CONCLUSION - Frusemide is a loop diuretic which produces an increase in outer cortical blood flow. In Case 3 renovasodilatation and tearing of the capsular was actually observed to occur. We conclude that the increased outer cortical blood flow in the oedematous, acutely rejecting kidney is responsible for these tears.

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13 PLASMA EXCHANGE IN ACUTE RENAL ALLOGRAFT REJECTION - A CONTROLLED TRIAL

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Recent successes in the use of intensive plasma exchange (IPE) for the treatment of antibody mediated disease (1) have resulted in attempts to extend this technique to the treatment of allograft rejection and some encouraging preliminary results have been reported. (2) We present the results of a controlled trial of IPE in the treatment of acute renal allograft rejection in 37 patients. Entry into the trial was limited to patients with clinical features of acute rejection which had failed to respond to steroid pulse therapy and with histological evidence of myointimal proliferation in the vessels of the graft.

The patients were randomly divided into 2 groups. Group A received standard immunosuppression together with IPE daily for 6 consecutive days at a mean exchange volume of 40.6 (S.D. ± 7.0) ml plasma per kg body weight per day. Replacement was by P.P.F. or albumen solution. Serum concentrations of immunoglobulins fell to a mean of 10% of normal over the period of exchange. The control group B received standard therapy only. There were no significant differences between the two groups in age, sex, HLA matching, ischaemic times, operative techniques or post-operative management.

TABLE 1: GRAFT SURVIVAL

	FAILED GRAFTS			FUNCTIONING GRAFTS
	≤ 30 DAYS	30-90 DAYS	>90 DAYS	
GROUP A - 23 patients	11	4	3	5 (mean 520 days)
GROUP B - (controls) 14 patients	7	2	0	5 (mean 478 days)

Table 1 gives figures for graft survival from day of entry into the trial and shows no significant difference between the two groups. Similarly analysis of changes in creatinine levels and urine output over a period of 7 days following entry into the trial revealed no differences. Patients with cytotoxic activity in their sera remained so although the titres of antibody fell. Our figures show no beneficial effects from the use of plasma exchange in the treatment of acute renal allograft rejection in the context of a controlled trial, this will be discussed.

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THE EFFECT OF BLOOD TRANSFUSION AND HLA-DR MATCHING ON KIDNEY TRANSPLANT SURVIVAL IN THE WESSEX REGION 14

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The effect of blood transfusion and the HLA DR matching on kidney graft survival has received considerable attention in recent years. The beneficial effects claimed by some workers for pre-transplant blood transfusion are disputed by others. The effect of pre-graft blood transfusion on the first 150 cadaver donor transplants performed in the region has been analysed after exclusion of 13 non-immunological/technical failures. 82 of the later transplants in the series, matched originally on the basis of the HLA A & B locus only, are the subject of the DR analysis. Blood transfusion was given in the form of whole blood or packed cells. No attempt was made to give leucocyte free blood and frozen blood was not used. DR typing was performed on separated donor spleen B lymphocytes, whilst the recipient DR type was determined either before or at the time of transplant. The DR technique was that recommended for the 7th Histocompatibility Workshop. Separation of the B cells was by T rossetting with neuraminidase treated sheep red cells. Antisera were available to measure DR1 - DRw8. Our data shows no beneficial effect of pre-transplant blood transfusion in our region:-

Graft Survival:-	3 months	6 months	12 months
Transfused (103 cases)	64%	59%	53%
Non-transfused (34 cases)	70%	62%	47%

p = not significant

A separate analysis which includes per-operative blood transfusion does not alter these figures. Those patients receiving a DR-well matched kidney had significantly better graft survival than those who received donor incompatibilities although the DR well matched transplant tended to have less HLA incompatibilities (average 1.2) than those with DR incompatibilities. (Average 1.6). Graft survivals were as follows:-

No. of DR incompatibilities	3 months	6 months	12 months
0	94% (18)	94% (17)	84% (13)
1	59% (39)	55% (34)	37% (24)
2	55% (25)	41% (22)	37% (18) (patients at risk)

p = 0.0005 at all points

The effect of DR incompatibilities on the survival on second and subsequent grafts (24 patients is shown below).

No. of incompatibilities	3 months	6 months	12 months
0	8 (8)	8 (8)	6 (6)
1	2 (8)	2 (8)	1 (6)
2	3 (8)	1 (7)	1 (6)

The number of grafts surviving is shown and grafts at risk are included. Although the number of cases in each group is small our findings are clearly in agreement with data from the 8th Workshop in that patients receiving second subsequent transplant had superior graft survival when they received an HLA-DR well matched kidney.

DNCB PATCH TESTING IN PATIENTS ON THE HAEMODIALYSIS/TRANSPLANT PROGRAMME - PORTSMOUTH 1979-81

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To date 75 patients on the dialysis/transplant programme have been DNCB patch tested, of these 40% were patch test positive and 60% patch test negative.

31 of these patients (18 positive and 13 negative) have had a subsequent transplant.

Actuarial analysis of graft survivals in the two groups, patch positive and patch negative reveals no difference in graft survival between the two groups at 6 or 12 months.

Previous reports have suggested that good graft survival correlates with low DNCB score [1,2], and also indicate a higher proportion of patch test negative patients on the population tested. Our initial results correlated well with other studies with regard to the proportion of patients patch test positive and negative, but new patients who have only been on dialysis for a short period of time show a significantly different result from those in our initial group.

There are differences between the patch test positive and patch test negative patient groups with regard to the number of transplants received pre patch test, number of months of haemodialysis pre patch test, number of transfusions pre patch test, and ages of patients at the time of patch test.

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Studies of immunoresponsiveness in Transplant Patients and Changes with Blood Transfusion.

M. Midwinter, B.K. Shenton, P.S. Veitch, G. Proud, D.M.A. Francis, R.M.R. Taylor.
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Many centres have shown the beneficial effect of pre-transplant blood transfusions on subsequent graft survival. How the transfusion confers this effect is still uncertain.

This study examines the changes induced in a group of chronic renal failure patients after the standard regime in Newcastle of 3 units of whole blood.

Plasma suppressive activity (P.S.A.) has been shown in a 3 year prospective study to correlate with the success of a kidney graft[(1)]. This P.S.A. has been shown to be largely associated with the plasma protein α_2-Macroglobulin[(2)]. P.S.A. was measured by a cellular electrophoretic technique.

α_2-M is known to be a protease inhibitor and the proportion of α_2-M - protease complex to uncomplexed α_2-M is known to change depending on the method of collection of the blood. It has been shown that the complex of α_2-M and protease is more suppressive than free α_2-M in mixed lymphocyte cultures[(3)].

In this study P.S.A. of plasmas collected in Soybean trypain inhibitor[(4)] (to prevent protease binding), Li Heparin and serum were shown to differ significantly.

The plasmas were also fractionated by gel filtration chromatography and suppressive activity of the fractions measured. By immunospecific affinity chromatography on concentrated pools of suppressive regions, it has been shown that suppressive regions are associated with α_2-Macroglobulin, IgG (suppressive for allogeneic cells) and a low molecular weight protein sharing antigenic determinants with Fc fragment of IgG. Storage of the Macroglobulin pool and refractionation with another gel column showed the liberation of a low molecular weight ($<10^3$) protein with suppressive activity.

1. P.S. Veitch et al (1980) Br.J.Surg. 67 ; 703-707.
2. G. Proud et al (1979) Br.J.Surg. 66 ; 678-682.
3. W.J. Hubbard et al (1981) J.Immunol. 126 ; 292-299.
4. P.C. Harpel (1973) J.Exp.Med. 138 ; 508-521.

THE PORTSMOUTH NON-SNATCH TECHNIQUE

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Despite increasing acceptance of heart beating cadaveric donors for kidney transplantation, laparotomy in a number of units does not begin until after cardiac arrest. Furthermore, an estimated 5-10% of kidneys (up to 100 kidneys per year) are irretrievably damaged during removal in the United Kingdom. Finally, multiple organ procurement may delay removal of kidneys for some time after cardiac arrest. For these reasons, we have used an intra aortic double balloon catheter** for kidney procurement normally introduced immediately after cardiac arrest (1). Kidneys have been flush cooled with Hyperosmolar Citrate*. At re-anastomosis, using intermittent cooling via an orthopaedic sock, cooling has been maintained, until the moment of revascularisation.

138 kidneys were perfused with Hyperosmolar Citrate via an intra-aortic double balloon catheter (1). The mean warm ischaemic time was 4.3 minutes and a mean core temperature of 14°C was obtained within 7 minutes of cooling. No kidney was damaged during procurement, the operating time being approximately one hour. Mean cold ischaemic time was 10.8 ± 3.4 hours with a mean anastomotic time of 37.4 ± 3.8 minutes. Immediately prior to revascularisation mean core temperature was 8.2°C. 58.8% of the kidneys sustained life immediately. The mean number of dialyses required by the others was 1.8. A urine output of one litre was reached at a mean of 2.6 days after transplantation. 98% of these 87 cadaveric grafts, thus procured, were life supporting at one year.

A video film of the technique of procurement will be shown.

1) M. Slapak et al. Transplantation Proceedings 11, 478, 1979.

* Manufactured by Queen Alexandra Hospital, Cosham, Portsmouth, Hants.

** Manufactured by Warne Surgical Limited, Andover, Hants.

CHANGING WORK PATTERNS IN TRANSPLANTATION 1972-1980

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To assess possible changes in workload patterns in transplantation we have examined the timing of donor nephrectomies and transplants involving this unit from 1972-1980. The date and time of 317 donor nephrectomies and 236 transplants were available for study. The results showed a small increase in the number of donor kidneys from about 24/year in 1972 to 35/year in 1980. Other important developments in the pattern of work since 1972 have occurred however. Although there has been no major change in the timing of donor nephrectomy, the number of transplants carried out during accepted working hours has increased from less than 30% in 1972 to 98% in 1980. This is a reflection of an increase in average cold ischaemic time from 8.4 hours to 20.5 hours over the same period. In addition, most transplants are carried out during weekdays with Saturday and Sunday being the least busy days (5% less than weekdays). These figures support our impression that renal transplants are now semi-elective procedures and there has been an increase in the number of man-hours devoted to them during the ordinary working day. If this trend is apparent in other centres, it has important implications for future staffing of transplant units and tissue typing laboratories.

TUBERCULOSIS IN ASIANS FOLLOWING RENAL TRANSPLANTATION

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Though pulmonary infections are a substantial cause of morbidity and mortality in renal transplant recipients, tuberculosis has been reported infrequently. Routine Isoniazid chemoprophylaxis was not thought justified because of hepatotoxicity (Thomas et al., 1979). In a series of indigenous Asian patients undergoing cadaveric renal transplantation tuberculosis has been a significant problem.

Between 1972 and 1980 twenty four Asian patients (age range 19 - 45) have received thirty cadaveric renal transplants. Thirteen patients have functioning transplants (average follow up 29.9 months) and four returned to haemodialysis. Seven deaths occurred, five from infective complications including three cases of tuberculosis.

Of six patients previously treated for tuberculosis, two received prophylaxis at time of transplantation as did two patients with no history. None of these patients developed T.B. during follow up (mean follow up 19.5 months). Of the remaining sixteen patients (mean time at risk 17.6 months) five developed tuberculosis, 2 - 14 months post operatively. In all positive sputum identification was obtained within two weeks of the suspicious chest x-ray. Three patients died, 2, 4, and 12 weeks after commencing antituberculous chemotherapy. In each case tuberculosis was a major factor in their death. All Asian patients undergoing transplantation should receive prophylaxis against tuberculosis. Tuberculosis is rare in transplanted whites and negros in the same population.

Thomas et al. (1979) Arch. Surg., 114, 597-599.

NOTES