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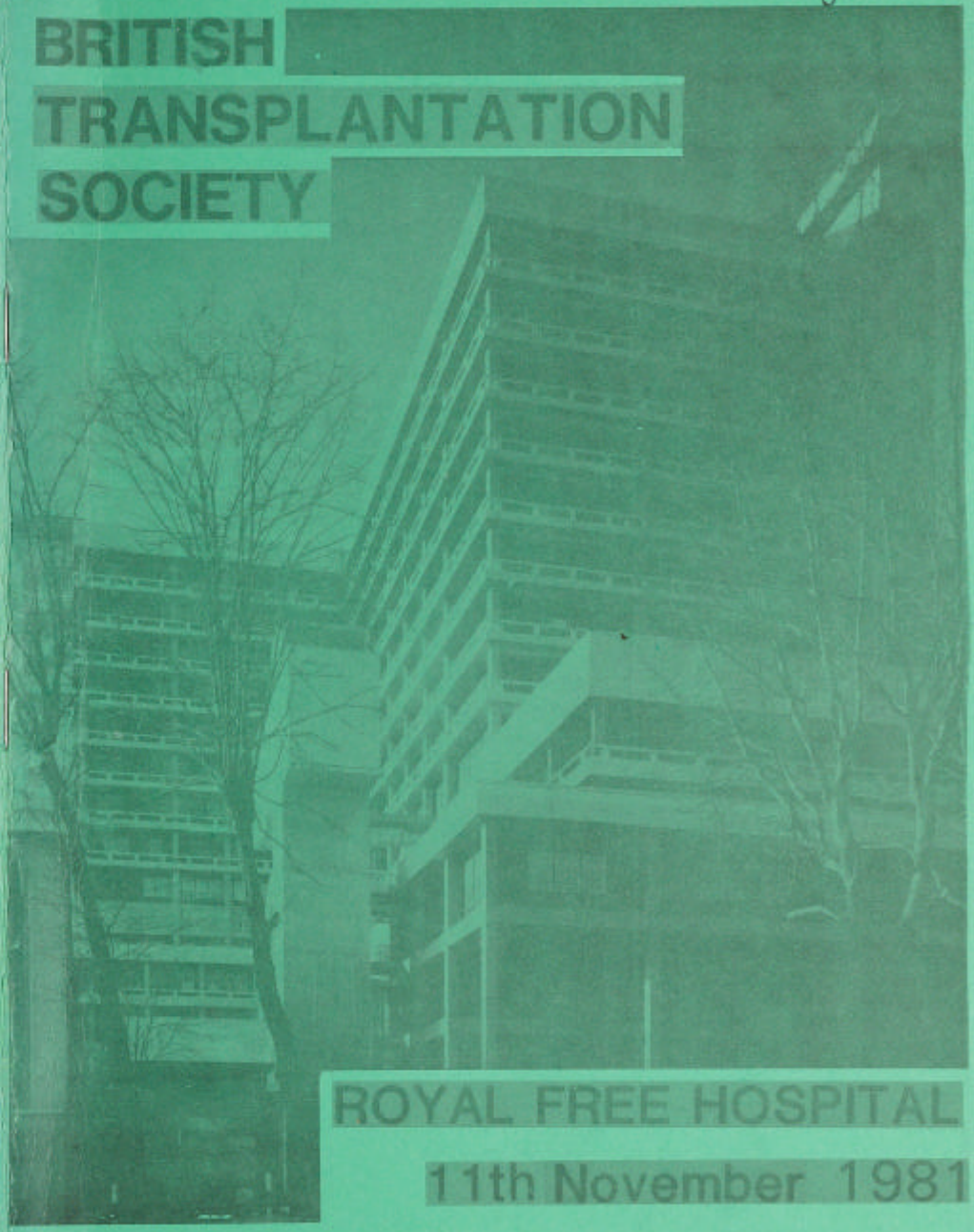
BRITISH TRANSPLANTATION SOCIETY



ROYAL FREE HOSPITAL

11th November 1981

ABSTRACTS....BOOKING FORM....SOCIETY BUSINESS

The effect of decomplementation with cobra venom factor in passive immunological enhancement of mouse skin allografts.

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Passive immunological enhancement of normal tissue allografts is achieved with anti-donor antibody at or about the time of transplantation. In mouse skin graft models the phenomenon is F_c dependent and IgG_1 antibody is the best enhancing subclass. Murine IgG_1 immunoglobulin has both complement-fixing and opsonizing properties. To distinguish the importance of these properties in the context of enhancement we examined passive enhancement of B10-D2 ($H\text{-}2^d$) to ($A \times C57)F_1$ ($H\text{-}2^{a/d}$) skin allografts in recipients decomplemented by treatment with cobra venom factor (CVF). Graft survival was increased from 11 to 15 days in mice treated with 0.2 ml anti-donor serum at the time of transplant and this enhancement was not affected by CVF treatment, median graft survival being 15½ days in CVF-treated recipients.

Previous experiments have shown that radiolabelled anti-donor reactive lymphocytes (ARC) are taken up to the reticuloendothelial system (RES) in mice grafted with allogeneic skin and given donor-specific enhancing antibody, but not in untreated allograft recipients. Because it has been suggested that removal of circulating ARC in mice treated with enhancing serum may be an important mechanism in allograft protection an experiment was performed to ascertain whether antigen-reactive cell opsonization (ARCo) occurs in recipient mice treated with both CVF and enhancing antibody. Radiolabelled donor-specific ARC were taken up by the RES in recipient mice treated with enhancing serum (Localization Index 2.92 $\pm$ 0.27, $p < 0.001$), but not in untreated controls (LI 1.23 $\pm$ 0.05, NS). Treatment with CVF did not interfere with ARC opsonization in mice bearing enhanced grafts (LI 2.46 $\pm$ 0.37, $p < 0.05$). In summary, the mechanism of immunological enhancement is independent of complement and therefore is probably dependent on the opsonizing properties of enhancing antibody. Furthermore, the ARCO mechanism, which may be important in enhancement, remains operative in the absence of detectable serum C3.

Induction of suppressor cells by a single transfusion in rats.

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In the BN/Ro to Wag/Ro rat donor-host combination, a single injection of 1 ml of donor blood 7 days before transplantation leads to permanent acceptance of BN/Ro hearts. In this model of specific unresponsiveness, it has been demonstrated earlier that suppressor cells are present in the steady state phase, at 5-6 weeks after transplantation. Adoptive transfer of spleen cells led to permanent survival of BN/Ro hearts in 45 % of the cases, whereas transfer of thymocytes always resulted in permanent graft survival.

In the current study it was investigated whether suppressor cells would be present after a single transfusion, before transplantation. Wag/Ro recipients were transfused with 1 ml of BN/Ro blood and adoptive transfer of spleen cells or thymocytes was performed after 7 days. Transfer of $1\text{-}3 \times 10^8$ thymocytes to normal or irradiated (450 Rads), syngeneic recipients did not lead to prolonged graft survival of subsequently transplanted BN/Ro hearts. However, 10^8 spleen cells given to non-irradiated recipients led to a marked prolongation of BN/Ro hearts in most cases. The results suggest that a single transfusion can evoke the induction of suppressor cells in this specific donor-host combination.

Presentation

EFFECT OF BLOOD TRANSFUSION ON TUMOUR GROWTH

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Although the mechanism by which pretransplant blood transfusion benefits subsequent renal allograft survival has not been fully explained there is evidence to suggest that blood transfusion results in non-specific immunosuppression of the recipient[1-3]. In view of this apparently non-specific immunosuppression a pilot study was undertaken to examine the effect of prior blood transfusion on tumour growth in an animal model.

Three groups, each of five WAB rats received on two occasions, three days apart, either, (1) 2.0 ml of compatible allogeneic blood from PVG/C rats, (2) 2.0 ml of syngeneic WAB blood, or (3) 2.0 ml 0.9% saline. Fourteen days later 0.1 ml of homogenate from a single Methyl Cholanthinene induced sarcoma (MC7) was injected subcutaneously into each rat. Tumours were measured daily and then excised and weighed 14 days after passage. Lymphocyte reactivity to PPD and PHA and plasma suppressive activity (PSA) were measured using the TREN test[4] before each transfusion or infusion, immediately before tumour passage and immediately before tumour excision.

Lymphocyte reactivity fell significantly and PSA increased significantly after allogeneic transfusions but not after syngeneic transfusion or saline infusion. When lymphocyte reactivity was low and PSA was high (allogeneic transfusion group) tumour inoculation was followed by significantly increased tumour growth as measured by daily calculation of tumour volume and final tumour weight.

The study supports the hypothesis of non-specific immunosuppression induced by allogeneic blood transfusion and demonstrates in an animal model that tumour growth is significantly increased following allogeneic blood transfusion.

1. Proud G, Shenton BK, Smith BM. Blood transfusion and renal transplantation. Brit.J.Surg 1979; 66: 678-682.

2. Watson MA, Briggs JD, Diamonopoulos AA, et al. Endogenous cell mediated immunity, blood transfusion and outcome of renal transplantation. Lancet 1979; 2: 1323-1326.

3. Veitch PS, Shenton BK, Proud G, Taylor RMR. Plasma suppressive activity and kidney graft survival. Brit.J.Surg. 1980; 67: 703-707.

4. Shenton BK, Proud G, Smith BM et al. Blood transfusion and renal transplantation. Lancet 1978; 1: 824.

The work described in this study has not been previously published, read at a scientific meeting or submitted for consideration to another Society.

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Cyclosporin A interferes with the blood transfusion effect in rats if administered during transfusion.

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After conditioning with donor blood a heart transplant survives indefinitely in the BN/RO to Wag/Ro combination whereas accelerated rejection (5-6 days) occurs in the Wag/Ro to BN/Ro combination. Normally, a heart graft is rejected in 8-9 days in both strains. As we have reported previously, postoperative administration of Cyclosporin A (CyA) can overcome the sensitizing effect of donor blood in the Wag/Ro to BN/Ro combination, whereas it does not affect the beneficial transfusion effect in the opposite combination.

It was investigated whether CyA would interfere with the expression of both opposite transfusion effects, when it was administered during transfusion. CyA in olive oil was administered intramuscularly in dosages of 5-15 mg/kg/day on days -8, -7 and -6; the transfusion was given on day -7. Heterotopic heart transplantation was performed on day 0.

In the BN/Ro to Wag/Ro combination pretreatment with CyA only, caused prolonged graft survival (50 % indefinite). In blood-conditioned animals pretreated with CyA, a moderate prolongation of graft survival (17 days) was obtained.

In the Wag/Ro to BN/Ro model, pretreatment with CyA alone did not affect normal graft rejection. In blood-conditioned recipients treated with CyA a variable interference with the sensitizing transfusion effect was observed. Depending on the dose of CyA used a further acceleration of rejection (<5 days) or a moderate prolongation of survival (8-12 days) was obtained.

It can be concluded that pretreatment with CyA does interfere with the beneficial blood transfusion effect, but hardly with the sensitizing effect.

Passive enhancement of rat renal allografts with non-cytotoxic mouse monoclonal xenoantibodies

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Monoclonal antibodies offer clear advantages in terms of specificity, reproducibility and ease of production over conventional sera, and this applies particularly to the clinical application of passive enhancement. Non-cytotoxic monoclonal xenoantibodies would be of particular value, since the absence of cytotoxicity would circumvent the problem of hyperacute rejection, and mouse monoclonal antibodies to human MHC antigens are already in existence.

In this study, we test the effectiveness for passive enhancement of rat renal allografts of two non-cytotoxic mouse monoclonal xenoantibodies, one directed at class I (SD) antigens and the other at class II (Ia) antigens. Both antibodies show some allospecificity, and were tested in several different MHC incompatible strain combinations, chosen such that the monoclonal antibodies reacted with the donor but not the recipient strain. The antibody F21-105-1, directed at RT1-A (class I or SD) antigens, interacts with all strains tested except the PVG/c strain, and was tested in the LEW to PVG/c and WAG to PVG/c combinations. The antibody F17-23-2, directed at RT1-B (class II or Ia) antigens, interacts with all strains tested except the PVG/c, AUG and WAG strains and was tested in the LEW to PVG/c and LEW to WAG combinations. In all strain combinations conventional allosera were tested for comparison with the monoclonal antibodies. Our results demonstrate that both of the non-cytotoxic monoclonal xenoantibodies are as effective as conventional allosera for passive enhancement in weak strain combinations but that in strong donor-recipient combinations they might not be quite as effective as conventional allosera. Nevertheless, they are likely to be useful reagents for testing the efficacy of passive enhancement in the clinical situation.

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Immune responses to AS/AUG F_1 heart allografts were studied 2, 4, 6, 8 and 30 days after transplantation in untreated AS rats or AS rats given a short post-operative course of AS anti-Aug antiserum. The following assays were used to monitor the response to transplantation: i) response of whole blood to phytohaemagglutinin (PHA); ii) spleen cell response to lipopolysaccharide (LPS); iii) inhibition of leucocyte migration by donor antigen (LMT); iv) complement dependent cytotoxicity (CDC); v) antibody dependent cell mediated cytotoxicity (ADCC). The whole blood response to PHA doubled by day 6 after transplantation in both the untreated and serum treated groups of rats but had returned to normal values by day 30. In contrast the spleen cell response to LPS was only significantly raised (by 2-5 fold) by day 30 in these two groups. Both groups of rats showed sensitisation to donor antigen in the LMT assay with maximal inhibition occurring at day 6. Although in the serum treated group the LMT index returned to normal values by day 30, there was still appreciable inhibition of migration at day 30 in the group of rats that had rejected their allografts. The difference in the levels of complement fixing anti-donor antibody was marked. In the untreated group a peak of antibody activity occurred on day 8 although this had declined by day 30. However, in the serum treated group only low levels of antibody were detected in the first week but this had increased to a high level by day 30. Injection of the same dose of AS anti-Aug serum into normal rats showed that the level of anti-donor antibody declined over two weeks and was negligible by day 20. ADCC in the first week of transplantation showed a similar pattern to the complement fixing antibody activity. However the presence of complement fixing antibody in the serum treated group at day 30 was not accompanied by any ADCC activity. These results indicate that in the allografted AS rat treated with anti-donor antibody cellular immune responses are still present, and that the survival of the allograft depends on the change in the type of humoral response. This could be due to the continual presence of circulating complement fixing antibody and/or the absence of complete effector mechanisms such as ADCC.

ACUTE REJECTION OF MHC-IDENTICAL KIDNEYS IN THE RAT

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Immunization of MAXX ($RT1^n$) rats with spleen and lymph node cells from BN ($RT1^n$) results in the formation of alloantibodies which are directed against the endothelium of the peritubular and venous endothelium of BN, BUF and WKA kidneys. The antiserum reacted also with the monocytes but not the lymphocytes (T and B) or erythrocytes of the appropriate strains, and thus seem to recognize the rat analogue of the human endothelial monocyte (E-M) system. With kidneys from 7 MHC-congenic lines it was demonstrated that the endothelial antigens are coded for outside the MHC region. In a segregating population of 32 animals, the endothelial antigens segregated independently from the MHC, Ag-F, tubular basement membrane antigens and the albinism trait. Furthermore the antigen seems to be expressed as a dominant allele.

In transplantation experiments of BN kidneys into MAXX recipients it was demonstrated that an E-M incompatibility of the graft does not provoke rejection. Pretransplant immunity against donor E-M antigens resulted, however, in accelerated acute rejection; this rejection was donorspecific since third party (LEW) kidneys were rejected like first-set grafts. This model shows that graft rejection in presensitized recipients of a MHC-identical kidney can occur through non-MHC alloantigens.

PANCREATIC TRANSPLANTATION IN THE RAT: LONG TERM STUDY FOLLOWING DIFFERENT METHODS OF MANAGEMENT OF EXOCRINE DRAINAGE

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One of the major problems with transplantation of the pancreas is how to manage the exocrine secretion. We have compared four of the techniques previously used, in an animal model. Pancreatic isotransplantation was performed by microsurgical techniques in streptozotocin induced diabetic rats. Each group contained at least six animals, the duct system was either ligated, left open to drain freely into the peritoneal cavity or obliterated with either latex or Ethibloc. Blood glucose levels, intravenous glucose tolerance tests and oral glucose tolerance tests together with insulin assays were performed at regular intervals and histological studies were performed at 1 and 9 months post transplant.

Although the majority of animals (25 out of 28) remained normoglycaemic throughout the period of study, oral glucose tolerance tests performed at 6 months indicated the beginning of impairment of endocrine function in some of the ligat freely draining and Ethibloc groups, while i.v. glucose tolerance tests showed, impairment in all groups, when compared to age, matched non-transplanted controls. Histologically, all long term grafts, even the duct open ones showed similar degrees of damage, including fibrosis coupled with a mixed cellular infiltrate and widespread disruption of both exocrine and endocrine tissue.

At one month, all grafts appeared similar with a mixed cellular infiltrate acinar degeneration and many islets showing the possible development of new beta cells. The only exception to this pattern was in the duct open grafts which had areas showing less acinar-degeneration.

The effect of blood transfusions, Cyclosporin A and conventional immunosuppression on canine renal allograft survival.

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Pretransplant bloodtransfusions have a beneficial effect on renal allograft survival in dogs treated postoperatively with azathioprine and prednisolone. In a previous study we showed that this effect was absent when Cyclosporin A (CyA) was used as the only immunosuppressant. Conflicting reports have been published regarding the usefulness and safety of the combined administration of CyA and azathioprine and prednisolone. The present study was undertaken to investigate: 1) the immunosuppressive potency of a combined immunosuppressive regimen, 2) the inherent side effects of this combination therapy and 3) the expression of a bloodtransfusion effect, in a dog renal allograft model.

Pairs of beagle dogs received 3 pretransplant bloodtransfusions at -4, -3 and -2 weeks before operation. Each dog of a pair, most of which were identical littermates, received a kidney from the same mongrel donor. Postoperative immunosuppression consisted of Cyclosporin A, 10 mg/kg/day for 28 days and/or the combination of prednisolone, 1 mg/kg/day and azathioprine, 2 mg/kg/day for 65 days, tapered off for another 50 days. From the results given in the table (a compilation of previous and current results), the following conclusions can be drawn.

1) CyA is a potent immunosuppressive drug.
2) In nontransfused recipients CyA alone gives similar results as CyA + imuran and prednisolone.
3) If CyA is given as the only drug to transfused recipients, no beneficial transfusion effect is demonstrable.
4) A beneficial effect of transfusions is present only if azathioprine and prednisolone are given postoperatively, alone or in combination with CyA.

Table

Transfusions	CyA	Im/predn.	Survival(days)	Median survival	% prolonged survival (>60 days)
-	-	-	7,8,8,9,12,12,13,14	11	0
-	-	+	11,15,16,19,20,29,30,48,>60	20	11
+	-	+	21,26,49,51,>60 (6x)	>60	60
-	+	-	11,33,34,42,42,44,47,48	42	0
+	+	-	42,13,37,40,44	37	
-	+	+	26,30,33,37,41,43,47,>60	39	13
[illegible]	+	+	35,35,40,46,>47*,>60 [illegible]	>47	[illegible]

* [illegible] of eye [illegible]

Authors: Bradley, B.A., Laundy, G.J., Johnson, P., Jones, T.J. and Stinchcombe, V.

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Investigations into "Rejector Phenotypes".

There are two reasons why patients who have rejected renal allografts may have unique phenotypes:-

1) With rare phenotypes (eg. HLA-DRw9 and Lewis a^-b^-), histocompatibility for HLA and Non-HLA is difficult to achieve. Thus in rejectors, rarer phenotypes might occur with higher frequencies.

2) Immune response genes may dictate the structure of receptors on alloreactive T cells and, in turn, regulate the allograft response. In experimental models the uniqueness of these alloantigen receptors is in linkage with two genetic systems, namely, the MHC and the allotype of the constant portion of the heavy chain of immunoglobulin G. Thus a disturbed frequency of certain couplings of HLA and Gm markers might be expected.

In a series of 103 rejectors, no disturbance in the frequency of ABO (including A_1 and A_2), Rhesus, Lewis, Kell, Duffy, P, Lutheran, Kidd and MNSs phenotypes was found. HLA-A, B and DR were within the expected range but the frequency of apparent homozygotes for HLA-A, C and DR was elevated.

By contrast, HLA and Gm combined phenotypes showed a marked disturbance especially between G1m(2) and certain HLA-A, B and DR allelomorphs.

Several explanations of these data have yet to be excluded before it can be claimed as evidence for immune response gene control. The original renal disease may have been associated with this disturbance. Alternatively improved survival of the renal allografts may have, in certain HLA-Gm phenotypes, depleted them from the rejector population.

DONOR HEART PROCUREMENT AND FUNCTION

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Improved methods for preserving donor heart function means that it is now possible to accept donor organs from most hospitals within a 500 mile radius of the transplant centre. Cardiac donors should be less than 35 years of age and have a stable circulation at the time of heart excision. Size compatibility between donor and recipient is also important.

Ninety four enquiries concerning heart donation were received between December 1978 and July 1981. Of these, 22 hearts were used and 21 were considered unsuitable because of age (8), medical (10), or legal (3) considerations. Inadequate facilities to enable heart transplantation to be undertaken at the time of enquiry was the commonest reason for having to decline an offer.

Ages of the donors ranged from 16 to 35 (mean 21) years. Donor hearts were transported by road (6) and a combination of road and air (16). Total ischaemic time was 108 to 205 (mean 160) minutes. Early function of the transplanted heart, as judged by the incidence of spontaneous defibrillation and a mean postoperative cardiac output of 6.9 litres/minute, was excellent in all cases. Fourteen of the 22 patients are alive six weeks to two years after transplantation. Six have been investigated one year post-transplant and shown angiographically to have normal ventricular function and normal coronary arteriograms.

In a small densely populated country such as the United Kingdom there should be enough suitable donor hearts to allow continued evaluation of cardiac transplantation for the treatment of terminal heart disease. Our early experience confirms that the provision of a normal cardiac output immediately after transplantation is of crucial importance, as it is on this that the recovery of other organ systems previously compromised by chronic congestive cardiac failure depends.

ABNORMAL CIRCADIAN PATTERNS OF URINARY SODIUM EXCRETION AND RENAL ALLOGRAFT REJECTION

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Twenty-four hour urine sodium excretion rates are not often helpful when diagnosing renal allograft rejection. Consideration of excretion rates, with particular attention to the time of excretion, and to changes in the distribution during the 24 hours, might give more diagnostically useful information.

Subjects collected a "night" urine from the time of retiring to the time of getting up, and a "day" urine from the time of getting up until noon. Thirty-four healthy control subjects, 25 patients in kidney failure (including moderate, severe and dialysis-dependent subjects) and 14 patients who had received renal transplants have been studied on this protocol for 170, 110 and 125 days respectively. During the periods studied in those patients with a functioning transplant, a total of 7 rejection episodes were observed (diagnosed and treated by a clinical team unaware of the urinary findings). The day of onset of deterioration in function in these episodes was determined retrospectively by analysis of plots of the weight-corrected reciprocal of plasma creatinine (Lancet, 1977)

In all groups a close correlation ($p < 0.001$) was found between excretion rates for daytime and night time periods. The regression line for control subjects was quite different to that calculated in the other groups reflecting the abnormal circadian pattern of urine flow in renal failure and in transplant recipients. In only two subjects after transplant was there a normal pattern with "day" sodium > "night" sodium excretion.

On only eight occasions did the ratio of log "day" to log "night" urine change abruptly (the log transformation is necessary to obtain a normal Gaussian distribution of results). On seven occasions the change occurred at the time when calculated in retrospect, renal function started to deteriorate due to rejection. This change in excretion pattern would have been the earliest indication of rejection using all currently utilised routine methods. The change is transient but is obvious when considered in the context of the regression line for patients with that pattern of urine flow. In this series there were no false negatives when independent clinical retrospective analysis of records is used as the criteria for the diagnosis of rejection. The only false positive could be attributed to diuretic administration.

This method, especially if combined with prospective computer analysis of urinary sodium or chloride by the Kalman filter, already studied in 28 other patients after transplantation (BTS 1980), can be used to monitor patients and to indicate a need for other diagnostic procedures.

SPONTANEOUS PLAQUE FORMING CELLS IN RENAL TRANSPLANT PATIENTS

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A protein A-sheep red blood cell/anti-human IgG plaque assay, originally developed by Gronowicz et al (1976) to detect single antibody secreting cells, was used to measure the number of spontaneous plaque forming cells (PFC) in the peripheral blood mononuclear cell fraction taken from 8 renal transplant patients, 9 haemodialysis patients and 7 normal subjects. The number of PFCs in the blood of patients on haemodialysis was not significantly different from that of normal individuals; this being 490 ± 378 PFCs/10^6 mononuclear cells (mean ± standard deviation; range 60 - 1467 PFCs/10^6 cells). However, in the blood of renal transplant patients taken during the first four weeks after transplantation, PFC numbers varied markedly. Six patients had a relatively smooth post-operative course, one individual having no evidence of rejection and 5 patients having minor episodes which were readily controlled by intravenous steroids. Three of these patients were followed almost daily and 3 monitored intermittently but none showed a persistent increase in the levels of PFCs. However, of the remaining two patients, on which plaque assays were performed on a daily basis, one patient developed very high PFC values (up to 10,000 PFCs/10^6 cells) some days before a major rejection episode which finally resulted in the removal of the transplanted kidney and the eighth patient, who also gave high PFC values (8,000 PFCs/10^6 cells), required treatment for persistent rejection. The increase in PFC numbers was not accompanied by any significant change in the levels of circulating immunoglobulins. The PFC response did not seem to be directly affected by the immunosuppressive treatment given post-operatively. These preliminary results reflect the changes in B lymphocyte activity that occur in response to transplantation and may be important in distinguishing humoral versus cellular types of rejection.

Reference

Gronowicz E., Coutinho A & Melchers F. 1976. Eur J Immunol; 6: 388.

The Influence of EA Inhibition on Renal Allograft Survival

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In certain human renal transplant recipients anti-B lymphocyte antibodies can be detected before transplantation. The effect of their presence on graft outcome is unclear perhaps because of antibody heterogeneity and the use of varying detection methods.

Transfused cadaver donor renal allograft recipients were assessed for the presence of pre-transplant anti-B lymphocyte antibodies in different ways. Sera from 43 such patients from Aberdeen and Edinburgh were examined by lymphocytotoxicity at 3 temperatures and EA inhibition (EAI) assays. The latter assay detects Fc receptor blocking antibodies by a rosette inhibition method. The target cells used in both assays were donor, normal panel and leukaemic (CLL) B lymphocytes.

Lymphocytotoxic antibodies were detected infrequently both pre- and post-transplant and no statistically significant correlation could be made with 1 year graft survival.

Results of the EAI assay pre-transplant indicated (a) $^{10}/_{12}$ grafts with, but only $^{6}/_{20}$ grafts without anti-donor antibodies survived 1 year ($p < 0.05$) (b) $^{10}/_{12}$ grafts with, but only $^{5}/_{24}$ grafts without anti-normal panel EAI survived 1 year ($p < 0.05$) (c) $^{17}/_{22}$ grafts with, but only $^{6}/_{21}$ grafts without anti-CLL antibodies survived 1 year ($p < 0.01$).

The results from this study therefore indicate that EA inhibiting antibodies detected pre-transplant enhance the survival of human renal allografts.

RENAL TRANSPLANTATION WITHOUT CUSHINGISM

A CONTROLLED TRIAL OF LOW DOSAGE PREDNISOLONE

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In recent years several transplant centres have adopted a low dosage steroid policy for patients undergoing kidney transplantation. We have compared such a regime with a more conventional high dose policy in a randomised controlled clinical trial. All patients having a first cadaver kidney graft between January 1980 and May 1981 were randomised to receive either high dose steroids (150 mg/day changing every 3 days to 100 mg/day, 80 mg/day, 60 mg/day, 50 mg/day, 45 mg/day; then reducing by 5 mg a week to 30 mg/day, and by 5 mg a month to 15 mg/day) or a low dose regime (25 mg/day for 6 weeks reducing thereafter by 5 mg a month to 15 mg/day). Both groups received Azathioprine 2 mg/Kg in addition. Rejection was treated with Methylprednisolone 1g i.v. daily for up to 5 doses and some patients failing to respond were also given a week's course of ALG (30 mg/Kg).

Forty three patients were admitted to the trial, 21 received high dose steroids and 22 the low dose regime. The patients were well randomised for the following factors: age, sex, time on dialysis, blood transfusions, HLA-AB match, presence of antibodies and ischaemic times. The results were as follows (without exclusion):

	Graft Survival	Patient Survival	Kidneys Rejected	Cushingoid Facies	Weight Gain First 3 Months
High dose (n=21)	14(6[illegible])	18(86[illegible])	5	10 patients	5.5 ± 5.2 Kg
Low dose (n=22)	16(7[illegible])	18(82[illegible])	5	3 patients	0.2 ± 3.[illegible] Kg
				p< 0.02	p< 0.00[illegible]

Low dosage steroids gave excellent graft survival with a low morbidity. Rejection was seen no earlier in this group nor were rejection episodes more frequent (1.2 v 1.1 rejections/patient). Patients on low dose steroids rarely became cushingoid and weight gain was not a problem.

ANTILYMPHOCYTE GLOBULIN IN THE TREATMENT OF STEROID NON-RESPONSIVE ACUTE RENAL ALLOGRAFT REJECTION

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At the last meeting of the Transplantation Society in Boston two controlled trials were reported showing that the addition of ALG to conventional steroid treatment significantly increased the proportion of kidneys that recovered function.[1,2.] Also, Light et al showed that the administration of ALG to patients with rejection, who were not responding to steroids, could produce a return of function in some.[3.] Accordingly since June 1980 we have given ALG to all our patients with acute renal transplant rejection when it became clear that high doses of steroids had failed to reverse the rejection.

Twelve patients have been treated so far - eleven male and one female, average age 35.9 years. Eleven had received cadaver kidneys and one a living donor graft. Ten of these patients had become anuric or oliguric at the time of starting ALG and had already recommenced dialysis. Renal biopsies (9 kidneys) showed vascular rejection in all with some cellular rejection as well. Previous antirejection treatment had comprised prophylactic azathioprine and steroids, and 3½ - 11 (average 5) grams methylprednisolone. ALG (Hoechst - Pressimune) was given i.v. 30 mg/Kg daily for seven days and seven of the eleven patients responded. In two, the rejection was halted but function gradually deteriorated some weeks later and the kidneys were removed. Five patients recovered good function and the kidneys are still working four - twelve months later. Latest serum creatinine levels range from 92 μmol/L - 380 μmol/L (mean 184 ± 100).

Since we have not observed a similar return of function on a comparable group of rejecting patients treated before 1980 without ALG we would suggest that ALG may be of value in this situation.

1. Filo, R.S., Smith, [illegible], Leapman, S.B. Transplant. Proc. 1981. 13. 1. 482.
2. Nowygrod, [illegible], Appel, G., Hardy, M.A. Transplant. Proc. 1981. 1. 469.
3. Light, J.A., Alijani, M.R., Biggers, J.A. et al. Transplant. Proc. 1981. 13. 1. 475.