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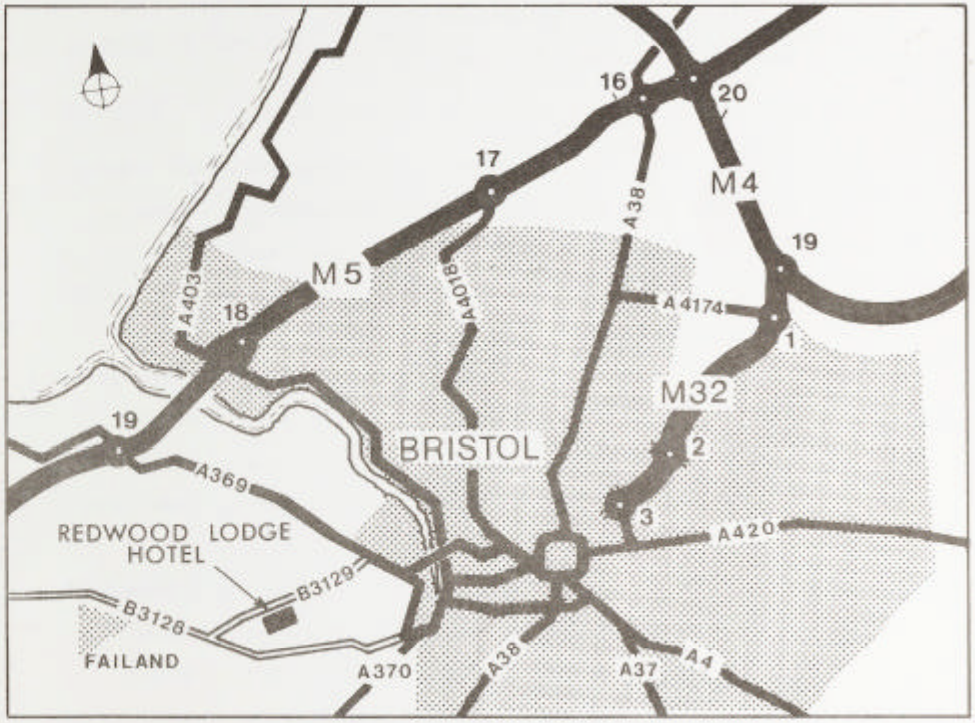

BRISTOL

30th & 31st March 1982

THE ROLE OF COMPLEMENT IN ACUTE ANTIBODY-MEDIATED REJECTION OF SKIN XENOGRAFTS IN THE MOUSE.

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Rat skin grafts, carried by immunosuppressed mice, can be acutely destroyed by intravenous administration of mouse antirat antibody. The velocity of the reaction and the histologic sequence of events depend on the amount of antibody administered: low doses give an Arthus-like rejection while at high doses a Shwartzman-like pattern occurs. Depletion of C3 by Cobra Venom factor treatment did not prevent acute rejection after intravenous injection of high doses of antiserum but changed the reaction from a Shwartzman-like to an Arthus-like pattern. Conversely suppletion of rabbit complement caused a violent Shwartzman-like graft destruction after injection of low doses of antibody, that in complement-normal mice gave an Arthus-like reaction. The results show that complement can greatly amplify the antibody-mediated immune vasculitis and can substantially modify its histologic pattern. It is, however, not an absolute requirement for the occurrence of the destructive process.

The work described in this summary has not been previously published.

The work contained in this summary has been read at a scientific meeting, (for the Dutch Association of Immunology, Dec. 17, 18 1981, Amsterdam).

DINITROCHLOROBENZENE (DNCB) SKIN TESTING:- NO CORRELATION WITH OUTCOME AFTER RENAL TRANSPLANTATION.

K.R. HARRIS, A. O'DURNY, B. WALMSLEY, S.M. TABER, N. ALLEN, M. SLAPAK.

As a result of the increased interest in recent years in the role of host factors[1] (responder - non responder status) of transplant recipients a number of studies have attempted to evaluate host responsiveness using DNCB skin testing [2.3].

This paper presents the findings of our study of DNCB responsiveness in patients on the dialysis/transplant programme, and also reports the findings in 49 patients who received 1 or more transplants post DNCB testing.

DNCB responsiveness in the total patient population showed a correlation with length of time on dialysis pre testing, 62% of patients having a negative response.

For the transplanted patients, examination of DNCB scores of patients who had functioning grafts at 6 months as compared with patients whose grafts had failed within this period revealed that patients with failed graft had a similar mean DNCB score (3.79) as a group than had patients with a functioning graft (3.68).

Actuarial analysis of graft survivals for the two groups DNCB negative and DNCB positive revealed no difference in graft survival at 6, 12 and 18 months post transplantation.

We therefore conclude that on the figures available at present we cannot demonstrate a correlation between DNCB skin reactivity and outcome of renal transplantation.

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A COMPARISON OF THE TEEM TEST TO LYMPHOCYTE TRANSFORMATION AND THE APPLICATION OF THESE TO EVALUATING LYMPHOCYTE DOSE RESPONSE TO IMMUNOSUPPRESSANTS.

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Although it has been shown to be clinically relevant, the immunological significance of the TEEM test has been disputed and its relationship to transformation assays has not been clearly defined. The aims of the study were:

i) to determine in the two test systems, the response of normal lymphocytes to a standard antigen after preincubation with matched doses of hydrocortisone. ii) to define lymphocyte sensitivity from normal and uraemic subjects, to immunosuppressive drugs in the TEEM test.

Lymphocytes from normal healthy volunteers were stimulated in both test systems with a recall antigen, purified protein derivative or myobacterium tuberculosis PPD (33ug/ml).

i) A highly significant correlation ($p < 0.001$) between lymphocyte inhibition and log cortisol concentration was found.

Cortisol(conc/µg/100ml)	100	25	6.25	1.6
TEEM % Inhibition	93 ± 3	77 ± 12	12 ± 9	5 ± 5
Transformation % Inhibition	75 ± 22	70 ± 36	41 ± 32	31 ± 32

i) In the TEEM test, lymphocytes from healthy adult volunteers were compared to lymphocytes from potential renal transplant recipients in terms of the dose of immunosuppressive drugs required to produce 50% inhibition of response (ID^{50}).

Immunosuppressant ID^{50} (µg/100ml)	Normals(n=5)		Uraemics(n=5)
Hydrocortisone	17.6 ± 4.4	p 0.005	6.0 ± 3.2
Prednisolone	2.7 ± 0.9	p 0.02	1.3 ± 0.6
Cyclosporin A	1.4 ± 0.4	p=NS	1.0 ± 0.3

We conclude that in both test systems, hydrocortisone in the same dose range induces significant suppression of lymphocyte response to PPD. The TEEM test measures a lymphocyte dose response to immunosuppressants which compares favourably with published data in other assay systems and demonstrates a signficant difference between normal and uraemic subjects. It is hoped this application of the TEEM test which takes 4 hours compared to 7 days for lymphocyte transformation, might provide a more satisfactory means of screening potential transplant recipients preoperatively for lymphocyte sensitivity to immunosuppressants.

Are HLA-DRw6 positive recipients high responders in renal transplantation?

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1 = Eurotransplant Foundation, 2 = Dept. of Immunohaematology, 3 = Dept. of Nephrology, University Hospital, Leiden, Holland

Of 183 HLA-A, -B and -DR typed Dutch cadaver kidney recipients who rejected their first renal allograft, 65 were found to be HLA-DRw6 positive, whereas on the basis of the frequency of HLA-DRw6 in the Dutch population only 42 were expected ($p<0,01$).
All patients received blood transfusions before transplantation and no difference is found in the average number of HLA-A, -B and -DR mismatches of both groups. When the interval between transplantation and transplantectomie is compared there is a striking difference between the two groups. 56 Of the 65 HLA- DRw6 positive patients lost their graft within 3 months, versus only 62 of the 118 HLA-DRw6 negative patients ($p<0,00001$). From 78 Patients (31 HLA-DRw6 positive and 47 HLA-DRw6 negative) pretransplantation and posttransplantectomy sera were tested in a cytotoxicity assay for antibodies reactive with T-cells, B-cells and monocytes. Before transplantation no difference in sensitisation was found between the two groups. Both groups showed a similar frequency of antibodies reactive with T-cells, B-cells and monocytes. After transplantectomy however there is a striking difference between the two groups. 78% Of the HLA-DRw6 positive patients had antibodies (versus 45% before transplantation), while in the group of HLA-DRw6 negative patients the degree of sensitisation did not change (49%). The significant difference between the two groups was due to a higher frequency of antibodies to B-cells and monocytes in the HLA-DRw6 positive group. The reactivity of the sera taken within 2 months after transplantectomy, the period inwhich the patients immune system is still influenced by the corticosteroid treatment, was compared with the reactivity of the sera taken during a later period. Sera of the HLA-DRw6 negative patients show very low antibody reactivity when taken within 2 months after transplantectomy, whereas after two months the percentage of sensitized patients increased. In contrast the HLA-DRw6 positive patients show a strong humoral immune response whether or not corticosteroids were given. This phenomenon might be the explanation for the finding of Dumble et al. who found that corticosteroid resistant patients had a significant worse graft prognosis.

In conclusion we think that HLA-DRw6 positive recipients are high responders in renal transplantation because of:
1. A high incidence of HLA-DRw6 in patients who rejected their graft;
2. A faster rejection pattern;
3. In the HLA-DRw6 positive patients corticosteroid therapy seems to be less effective in reducing antibody production.

Not previously published
Not read at any scientific meeting

MECHANISMS OF CARDIAC ALLOGRAFT PROLONGATION BY CYCLOSPORIN A.

IF Hutchinson, NL TIlney (introduced by RMR Taylor). Department of Surgery, Peter Bent Brigham Hospital, Boston, M.A.

Mechanisms of immunosuppression of the fungal peptide, Cyclosporin A (CyA) have been studied using acardiac allograft rat model. The drug (15mg/kg) was administered into 150 recipients for 7 days only from the day of grafting. Despite major histocompatibility differences (WiFu → LEW and LBN → LEW), all allografts functioned > 100 days without rejection episodes in consistently healthy animals. To detect effect of cells with suppressor characteristics, thermocytes or splenic lymphocytes ($1x10^8$) from groups of LEW recipients bearing LBN hearts for 7, 14, 21 and 50 days, were adoptively transferred into syngeneic untreated rats transplanted with LBN hearts 24 hours later. Test grafts survived 12-16 days, significantly ($p < 0.001$) longer than in unmodified animals (MST$\pm$SD= 7$\pm$0.5 days). Immunological activity of CyA treated grafted rats was then tested. LMC mounted by lymphocytes from various host lymphoid compartments including cells infiltrating the grafts, was reduced significantly (3-8%) in untreated controls, LMC = 24 - 39% ($p < 0.0001$). Anti-donor antibody activity (CDC, ADCC and reverse indirect hemolytic plaque assay) were also significantly decreased. Indefinite graft survival despite discontinuing CyA suggests emergence of suppressor cells; these cells in turn, may cause profound abrogation of cellular and humoral host effector mechanisms.

The work described in this summary has been published in "Transplantation" September 1981 and read at the Americal Federation of Clinical Research Washington, D.C.

A STUDY OF THE IMMUNOSUPPRESSIVE EFFECT OF PLASMA EXCHANGE AND CYCLOSPORIN A IN COMBINATION IN A RAT CARDIAC ALLOGRAFT MODEL.

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The immunosuppressive effects of Cyclosporin A (CYA) and Plasma Exchange in combination using varying doses of CYA were evaluated in a PVG to Wistar rat cardiac allograft model. In a control group of non-immunosuppressed animals the mean time for rejection was 10.7 $\pm$ 0.9 days. Oral doses of 5mg/kg/day of Cyclosporin A given for 14 days post-operatively produced virtually complete suppressic of rejection with a mean survival of 50 days. A dose of 2 mg/kg/day had almost no immunosuppressive effect with a mean survival of 15 $\pm$ 11.4 days.

A new technique for plasma exchange in rats was developed. Plasma Exchange at a volume of 45 mls/kg/day from the 6th to 10th post operative day produced no immunosuppressive effect with a mean cardiac survival of 9.25 $\pm$ 0.3 days. Plasma Exchange combined with a sub-optimal dose of Cyclosporin A, 2mg/kg/day, produced no significant improvement in cardiac survival of 15.1 $\pm$ days. These findings confirm the results previously established in our unit using a rabbit cardiac allograft model that Plasma Exchange alone is not effective in prolonging allograft survival and suggests there is no synergutic effect between Cyclosporin A and Plasma Exchange.

Changes in human natural killer (NK) cell activity in the first month after renal transplantation

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The cells which mediate natural cytotoxicity (NK cells) against certain cell lines are at least partially identical with those which mediate antibody dependent cellular cytotoxicity (ADCC). The role of ADCC in human renal allograft rejection is not known. Using the cytotoxic activity of peripheral blood lymphocytes against the myeloblastoid cell line K562 in a 4 hour ^{51}Chromium release assay we have examined NK cell activity before and at 48-72 hour intervals after transplantation in eight patients receiving immunosuppression with prednisolone and azathioprine. The change in NK activity over each 48-72 hour period was compared with the change in serum creatinine observed over the same period. Of 32 observations when NK activity rose, this was accompanied by a rise in the serum creatinine in 19, and in 29 instances when NK activity fell the serum creatinine fell in 23 ($\chi^2 = 8.2$, $p < 0.01$). When changes in NK activity in one 48-72 hour period were compared with the change in serum creatinine in the following period it was found that of 35 occasions when NK activity rose, this was followed by a rise in serum creatinine in 18, and of 33 observations when NK activity fell, this was followed by a fall in serum creatinine in 27 instances ($\chi^2 = 8.2$, $p < 0.01$).

Since the NK activity of 24 haemodialysis patients was not significantly different from that of 29 healthy control subjects (means 54.5% $\pm$ 14.2% and 59.9% $\pm$ 10% respectively at 100:1 effector target ratio) it seems unlikely that the change in serum creatinine influences NK reactivity. These observations suggest that NK cells, and thus the cells available for mediating ADCC, are generated during the in vivo allo-immune response in man and that their activity may be modified by immunosuppression.

This work has not been read at a scientific meeting.

The work described in the summary is currently in press.

Fc receptor blocking antibodies can develop after Blood Transfusions

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Pre-transplant blood transfusions are known to improve renal transplant survival. The presence of pre-transplant antibodies which block Fc receptor sites on B lymphocytes have also been shown to correlate with improved graft outcome. The stimulus to the development of these antibodies is not known but a possible source might be pre-transplant blood transfusions.

In this study sera from six previously untransfused prospective transplant recipients were assessed, during an elective blood transfusion regime, for the development of (1) Fc-receptor blocking antibodies by the EA rosette inhibition (EAI) assay and (2) lymphocytotoxic antibodies. The target cells used were specific transplant donor and leukaemic (CLL) B lymphocytes. Patients were given at least three units of whole blood over a three month period and more if therapeutically necessary.

The results show (a) anti donor B lymphocyte activity:- In the five cases where donor lymphocytes were available no EAI was present pretransfusion but developed post-transfusion in one case. One other patient had pre and post transfusion anti B lymphocytotoxic antibodies. (b) anti-CLL panel activity:- In $^{2}/_{6}$ cases there was no pre or post-transfusion EAI. In $^{1}/_{6}$ (a multiparous woman) EAI was present pre and post transfusion. In $^{3}/_{6}$ cases EAI was negative pre transfusion and positive post-transfusion. In three patients lymphocytotoxicity was present after transfusion but no correlation could be made with the development of EAI.

These preliminary results suggest that blood transfusions may be a source of Fc receptor blocking antibodies.

The work described in this summary has not been previously published.
The work contained in this summary has not been read at a scientific meeting.

HIGH OR LOW DOSE STEROIDS FOR IMMUNOSUPPRESSION

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The optimum dose of steroids for maintenance immunosuppression in clinical kidney transplantation has not been established. We have examined the merits of high and low dose steroid therapy in in-bred rats given heterotopic cardiac allografts.

In untreated SA recipients, Wistar hearts were rejected in a median time of 8 days (Group 1). Groups of rats were treated with different immunosuppressive protocols and the results are shown in the table.

GROUP	MAINTENANCE THERAPY*	BOLUS THERAPY**	n	MST	GRAFT SURVIVAL
1	NIL	NIL	8	8	6,7,7,8,8,8,9,11.
2	A 4mg/Kg P 4mg/Kg	NIL	9	9	7,8,8,9,9,9,9,10,10.
3	A 4mg/Kg P 0.5mg/Kg	NIL	8	10	6,7,8,10,10,10,11,70.
4	A 4mg/Kg P 4mg/Kg	YES	7	28	15,18,26,28,44,56,>150.
5	A 4mg/Kg P 0.5mg/Kg	YES	7	>150	7,21,>150,>150,>150,>150,>150.
6	A 4mg/Kg P 0.5 →4mg/Kg	NO	7	123	15,27,52,123,>150,>150,>150.

* A - Azathioprine i/p, P - Prednisolone i/p.
** Bolus therapy - Methylprednisolone 16 mg/Kg on days 5 & 6.

Neither high dose (4mg/Kg) nor low lose (0.5mg/Kg) of Prednisolone prolonged graft survival when given daily with Azathioprine (Groups 2 & 3). Significant prolongation was achieved however ($p < .005$) when Methylprednisolone 16mg/Kg was administered in addition on days 5 & 6 following transplantation (Groups 4 & 5). Changing from a low dose maintenance therapy to a high dose on day 6 had the same effect as giving Methylprednisolone (Group 6). It would seem from these results that high doses of maintenance steroids are no more effective than low doses, and their administration during the first post transplant week fails to delay rejection. However when high doses are given for the first time at the onset of rejection, graft survival can be greatly prolonged.

The work described in this summary has not been previously published nor read at a previous scientific meeting.

Classification of Centres According to their Post-transplant Performance

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Thirty-one centres in the UK and Ireland were compared for post-operative results. Death with a functioning transplant, non-immunological failure and graft rejection were examined. The method was applied to discrete post-operative time interval. For example, rejection had a bimodal distribution with two intervals; 0 to 25 days and 26 to 130 days. Each centre was compared with every other centre using the Logrank test. Groups which were not significantly different from each other were clustered into HIGH survival, LOW survival and INTERMEDIATE. This method provides a sliding scale which depends on the existence of a significant differential between HIGH and LOW. If all centres performed equally well, no significant differences would exist between them and variations in rank order would be attributable to sampling error.

That such an utopian state of affairs is still far off, is illustrated by the fact that wide differences exist between centres and the probability that they occur by chance is, in many cases, less than 1 in 1,000. Some rank HIGH by all parameters whereas others rank HIGH for deaths and LOW for rejection and vice versa. A clear difference exists when performance between 0 and 25 days is compared to 26 to 130 days, presumably reflecting environmental risks.

This method provides a rational basis for the future investigation of the "centre effect".

The work described in this summary has not been previously published.
The work contained in this summary has not been read at a scientific meeting.

Cellular immune reactions with endothelium.

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Endothelial cells are the first contact between the transplanted vascularized organ and the immune system of the host. It is likely that the antigens present on the endothelial cells will play an important role ir the initiation in the process of graft rejection.

Endothelial cells have been reported to carry both class I, class II and E-M (Endothelial - Monocyte system) antigens. In the clinical situation anti-endothelium antibodies have been observed to be correlated with graft rejection. Moreover endothelial cells have been reported to have antigen presenting cell properties, MHC restricted, making them essentially important in the process of graft rejection in well matched kidneys.

We have studied whether canine endothelial cells can stimulate lymphocytes and whether endothelial cells can be recognized as target by cytolytic T lymphocytes. Both arterial and veneus endothelial cells have been cultured from veins and arteries obtained by surgery on otherwise healthy dogs. Both veneus and arterial endothelial cells appeared to be very sensitive targets in a ^{51}Cr release test; CTL generated in a mixed lymphocyte culture specifically lysed stimulator type target endothelial cells. Lymphocyte stimulation by endothelial cells appeared to induce lymphocyte proliferation and generation of CTL. The cytotoxic potency of CTL generated with allogeneic veneus endothelial cells was higher for veneus endothelial than for arterial endothelial cells and for PHA stimulated lymphoblasts. In accordance CTL generated with allogeneic arterial cells showed preference for arterial targets. Moreover cold target inhibition experiments showed that endothelial cells carry other target antigens than PHA stimulated lymphoblasts. These data would favor the use of ^{51}Cr labelled endothelial cells instead of PHA stimulated lymphoblasts for monitoring of graft rejection. Since damage of endothelium by CTL might cause intravascular thrombosis and so irreversibly damage the grafted organ, information on the presence of CTL directed versus endothelium may be important.

The work described in this summary has not been previously published.

The work contained in this summary has not been read at a scientific meeting.

B Lymphocyte Antibodies Associated with Successful Pregnancy

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It has been suggested that inadequate maternal recognition of the fetus leads to abortion because antibody blocking factors are not produced. We have recently reported that renal allograft survival was significantly improved when non-cytotoxic Fc receptor blocking antibodies were present in recipient sera prior to transplantation. Sera from normal pregnant women and from women at the time of spontaneous abortion were assessed for the presence of Fc receptor blocking antibodies by the EA rosette inhibition (EAI) assay against paternal B lymphocytes. The results indicated that EAI was present in $^{6}/9$ women during the first trimester of a normal first pregnancy and in $^{0}/9$ women at the time of spontaneous abortion. The mean level of EA inhibitory activity for the normal pregnant women was 34.4 ± 15.3% and for the women who aborted 5.4 ± 7%; the statistical difference between the two groups were highly significant ($p < 0.001$). EA inhibitory activity was shown to be present in the IgG fraction of the sera and was not removed by platelet absorption.

The work described in this summary has not been previously published.
The work contained in this summary has not been read at a scientific meeting.

A CORRELATION OF RENAL FUNCTION PRIOR TO CARDIAC ARREST AND AFTER TRANSPLANTATION IN 105 NON HEARTS BEATING CADAVERIC DONORS.

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The function of kidneys removed from non heart beating cadaveric donors for renal transplantation was studied immediately prior to nephrectomy and serially post-transplanted for a period of 1 to 52 months. A non-snatch technique using an intra-aortic balloon and hyperosmolar citrate[1] was employed. In 18 recent donors creatinine clearance studies were performed approximately one hour prior to cardiac arrest. Of 130 kidneys transplanted locally with mean warm ischaemic time of 4.3 ± 2.6 minutes and a mean cold ischaemic time of 10.7 ± 4.5 hours, 53% had immediate life supporting function. In 47% of patients a mean of 3.4 ± 2.1 haemodialysis were required. Their overall one year graft survival date is 48.9%.

From 18 donors in whom agonal creatinine clearances were performed 34 kidneys were transplanted, 2 being discarded due to anatomical abnormalities. Twenty nine of these kidneys (85%) assumed immediate life-supporting function following transplantation. The mean donor creatinine clearance in this group was 46.8 ± 28.0 mls/min. (range 6-95 mls/min). Five recipients required a mean number of 4.8 ± 3.4 haemodialysis. The mean creatinine clearance in these kidneys was 58.1 ± 24.5 mls/min. (range 23-85 mls/min), (not statistically different from the previous group). It is of particular interest that an 8½ year old donor with a creatinine clearance of 4 mls/min. in the last hour prior to cardiac arrest had immediate life-supporting function, the recipient being discharged from hospital with a serum creatinine of 200 mmols/l at 14 days.

We conclude that although impaired renal function prior to cardiac arrest is of importance, poor renal function in the hour prior to death, particularly in young patients, has no relevance and does not correlate with post transplantation function.

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The use of routine urine cytology as a detector of virus reactivation in renal allograft recipients.

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In an initial study 57 transplanted patients' urines were routinely screened for virus inclusions, of these 7 were positive. Serial virus antibody titres showed these to be due to Human Polyoma Virus (HPV) infection. Four of these 7 patients had ureteric stenosis.

We will report on a prospective study on a further 48 patients. Of these 25 showed a rise in antibody titre to HPV (BK and JC) and in 19 this was preceeded by the appearance of virus inclusions. In 29 there was a rise in antibody titre to Cytomegalovirus (CMV) preceeded by inclusions in only 7 cases. Fourteen patients with viral infection had associated leukopaenia and pyrexia, 9 leukopaenia only, 4 pyrexia only and 14 were asymptomatic. One patient in this study had a transitory episode of ureteric obstruction proven by retrograde pyelography.

6 patients were CMV seronegative pre-transplant and later developed primary infections. All had leukopaenia and pyrexia. Five had clinical chest infection, one with acute pancreatitis. Virus inclusions were detected in urine in 4. All had functioning allografts during their infections.

This prospective study confirms the value of cytological screening of transplant urines in providing early warning of virus infection.

DOES CYCLOSPORIN A INDUCE DONOR SPECIFIC NON-RESPONSIVENESS?

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It has been demonstrated in several different animal species that cessation of Cyclosporin A treatment does not inevitably lead to the loss of the allograft which was being protected from rejection by the Cyclosporin A immunosuppression. The establishment of this graft acceptance depends on the duration of therapy and the type of graft implanted. We have studied this graft acceptance state to ascertain its stability and specificity.

PVG ($RT1^c$) rats were induced to accept heterotopic DA ($RT1^a$) allografts by two weeks' i.m. treatment with 15 mg/kg Cyclosporin A per day. Measurement of Cyclosporin A blood levels failed to detect any significant depot of the drug in these animals. The stability and specificity of graft acceptance was tested by challenging these (PVG) recipients at 1, 2, 4, 8, or 16 weeks post-transplant with either DA (donor specific) or WAG ($RT1^u$, third party) skin grafts. The results showed that the heart graft acceptance went through three phases. The first was stable but non-specific. The second was both unstable and non-specific, and the final phase was both stable and specific. A study of this final stage showed a specific deficit in the immunological competence of peripheral blood lymphocytes, lymph node lymphocytes from the same rats were fully competent. Serum failed to transfer this graft acceptance state to naive recipients.

Part of this work has been presented previously at the XII International Course on Transplantation and Clinical Immunology and published in the Proceedings. Part has never been presented or published.

IDENTIFICATION OF LYMPHOCYTE SUBPOPULATIONS IN RENAL ALLOGRAFT RECIPIENTS USING MONOCLONAL ANTIBODIES AND A CELL-SORTER.

N.P. Carter, P.C. Cullen, J.P. Thompson, R.F.M. Wood & P.J. Morris.

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The monoclonal antibodies OKT3, OKT4 and OKT8 were used to define lymphocyte subpopulations in the peripheral blood of 22 laboratory workers and 13 renal allograft recipients. OKT3 is reactive with all T lymphocytes, OKT4 with helper-inducer T cells and OKT8 with suppressor-cytotoxic T cells. The proportion of lymphocytes reacting with each of these antibodies was analysed using an Ortho Cytofluorograf cell sorter. The procedure used to identify and count labelled lymphocytes using this instrument will be described.

The mean values ($\pm$ S.D.) for OKT3, OKT4 and OKT8 in the 22 laboratory workers were 77%($\pm$7%), 49%($\pm$10%) and 28%($\pm$6%) of lymphocytes respectively. The mean ratio ($\pm$ S.D.) of helper-inducer T cells to suppressor-cytotoxic T cells (T4/T8 ratio) was 1.9($\pm$0.8). The T4/T8 ratio was measured repeatedly over a five week period in 4 of these laboratory workers. Little fluctuation in the ratio was observed, the greatest variation being between 1.7 and 2.2 in one individual.

The T4/T8 ratio was determined at least five times weekly in 13 patients during the first three weeks after transplantation, and at less frequent intervals thereafter. No patient maintained a constant ratio. Results from this preliminary clinical study will be presented and the use of the T4/T8 ratio in the diagnosis of rejection will be discussed.
