Expenditure: Administration	£699.33
Meeting expenses	£1,301.59
Printing expenses & Biological Council Calender	£157.40
Refund of subscriptions, etc.	£72.00
Total expenditure	£2,230.32
Excess of expenditure over income:	£159.87
Balance sheet at 30th September, 1976.	£1,123.11

Dr. Elves estimate for the year ending 30.9.77 indicated the likely total income required would be £1,475 for the year. As the membership of the Society is approximately 300, Dr. Elves proposed that this expenditure would be covered by increasing the Annual Subscription of members to £5 from £3. During the discussion that followed, Professor Morris suggested an annual membership of £4, and other members suggested economies could be achieved by cutting down the number of meetings a year from three to two. The idea of a registration fee was not approved by the membership. The Committee was instructed to consider the possibility of reducing the number of meetings per year to one in London and one in the provinces and to discuss the matter again at the next business meeting.

Dr. Elves proposal that the Annual Subscription should be increased to £5 was voted on, and the motion carried by a majority.

Finally the Treasurer indicated that the Bankers Order payment system was not satisfactory, and in future all subscriptions would be requested, and should be paid in the form of a cheque.

6. **Future Meetings.**
Mr. Barnes announced that the next meeting of the Society would be on the 20th April, 1977, at the Wellcome Building, and would consist of scientific sessions and a business meeting. There would be a summer meeting of the Society on 13th July, 1977, at Nottingham University.

7. **Working party on training in Transplant Surgery.**
Professor Peter Morris was in the process of convening his working party and reported that his initial approaches to the Royal College of Surgeons and the Specialists Advisory Committee had evoked interest, and a wish to hear the recommendations of his Committee.

8. **Shortage of Kidneys for transplantation.**
Mr. Barnes indicated that a plateau in the number of kidneys available for transplantation had been reached. Professor Calne drew attention to the lack of liver donors being made available and suggested that there is room for improved co-operation between members of the Transplantation fraternity in increasing the supply of organs.

9. **Concessionary travel arrangements for members of the Society.**
Very few members had taken advantage of Express Boyds package tour to the U.S.A. for the New York meeting of the Transplantation Society, and the arrangements had had to be cancelled. Professor Brent said that Al Italia may make concessionary arrangements for people interested in travelling to the Rome meeting of the Society in 1978.

10. The General Secretary reported that the Committee had decided to present a light pointer to the Wellcome Foundation, as a small token of thanks for their generosity in the past, and hopefully in the future.

11. **Any other business.**
(a) The Chairman said he had received a letter from the Biological Council drawing attention to Mr. Burden's private members bill concerning the licensing of experimental animals, and signed a memorandum from the Council on behalf of the British Transplantation Society, opposing the Bill.
(b) Several members expressed concern at the poor facilities offered to the Society at the Wembley Conference Centre. Mr. Rake, Officer of the Wembley Conference Centre, appeared later on in the meeting to apologise to the membership, and explained that the management had only taken possession of the building 24 hours before the B.T.S. meeting started, but as a gesture 50 per cent of the hire fee would be refunded.

(Signed) J. R. Batchelor, Chairman.
R. A. Sells, General Secretary.

MEETING OF THE BRITISH TRANSPLANTATION SOCIETY

20th April, 1977

THE WELLCOME BUILDING, EUSTON ROAD, LONDON

Chairman:	**Mr. Miles Fox**
10.00 a.m.	**Paper 1**—The Pattern and Incidence of Rejection of Orthotopic Human Liver Transplants. **R. Y. Calne, R. S. Williams, B. M. Herbertson.**
10.15 a.m.	**Paper 2**—Peptic Ulceration, Gastric Secretion and Renal Transplantation. **G. Williams, G. D. Chisholm, A. D. Mee, J. E. Castro, J. H. Baron.**
10.30 a.m.	**Paper 3**—The effect of Increasing Islet Numbers on Survival of Pancreatic Islet Allografts in Immunosuppressed Diabetic Rats. **D. R. A. Finch, P. J. Morris.**
10.45 a.m.	**Paper 4**—The effect of Ischaemia on Morphology and Insulin Secretory Capacity of Islets of Langerhans in the Rat. **E. H. McLaren, D. Bardsley, R. D. G. Milner, D. N. Slater, Y. F. Mangnall, A. Smythe, M. Fox.**
11.00 a.m.	**Paper 5**—Pancreatic Islet Transplantation: Effects on Metabolic Changes and Secondary Complications of Experimental Diabetes in the Rat. **Y. Mangnall, A. Smythe, D. Slater, R. D. G. Milner, I. Strachan, M. Fox.**
11.15 a.m.	Coffee
Chairman:	**Dr. D. Briggs**
11.45 a.m.	**Paper 6**—Blood Transfusion, Graft Survival and Rejection Episodes. **R. W. Blamey, M. S. Knapp, Maxine Salisbury.**
12.00	**Paper 7**—The Effect of Blood Transfusions on Kidney Graft Rejection in Dogs. **J. Fabre, M. Bishop, T. Sen, Judith McKenzie, Keryn Williams, P. J. Morris.**
12.15 p.m.	**Paper 8**—Blood Transfusions induce Prolonged Kidney Allograft Survival in Rhesus Monkeys. **A. A. van Es, R. L. Marquet, J. J. van Rood, M. W. Kalff, H. Balner.**
12.30 p.m.	**Paper 9**—Recognition of B-cell and non-HLA Antibodies in Pretransplant Renal Patients. **A. Ting, Keryn Williams, P. J. Morris.**
12.45 p.m.	**Paper 10**—The Role of the One Way M.L.C. in Predicting Rejection Episodes and their outcome in the first six months following Live Related Donor Renal Transplantation. **C. L. Kennedy, J. E. Castro.**
1.00 p.m.	Lunch
2.00 p.m.	Business Meeting

Chairman:	**Professor L. Brent**
2.30 p.m.	**Paper 11**—Immunological Monitoring of Transplant Patients—The Role of the Cell-Mediated Immunity Assay. **Keryn Williams, P. J. Morris**
2.45 p.m.	**Paper 12**—Unusual Antibody Activity in Renal Transplant Rejection. **Heather M. Dick, J. A. Roberts, P. Hercus.**
3.00 p.m.	**Paper 13**—Rabbit anti-mouse Thymocyte Antibody as an Adjuvant in the Preparation of further Antithymocyte Sera. **Teresa Lai, M. O. Symes.**
3.15 p.m.	**Paper 14**—Is Niridazole Immunosuppresive in Man? **B. Jones, Michelle Bird, P. Massey, D. Millar, J. Miller, Suzanne Reeve J. R. Salaman.**
3.30 p.m.	**Paper 15**—Pharmacological Control of the Immune Response by Blockade of the Early Hormonal Changes following Antigen Injection. **W. Pierpaoli, G. J. M. Maestroni.**
3.45 p.m.	**Paper 16**—A Comparison of Two Types of Steroid Premedication in Renal Transplantation. **M. H. Simms, A. D. Barnes.**
4.00 p.m.	TEA
Chairman:	**Mr. M Slapak**
4.30 p.m.	**Paper 17**—What Causes Agonal Vascular Spasm in Kidney Donors? **C. Dhabuwala, Michelle Bird, D. Miller, J. R. Salaman.**
4.45 p.m.	**Paper 18**—Function of the Perfused Rat Kidney in Evaluation of Renal Preservation Solutions. **M. C. Bishop, Sarah Bullock, B. D. Ross.**
5.00 p.m.	**Paper 19**—Warm Ischaemically Injured Canine Kidney Preservation with Hypertonic Citrate Solution: The Importance of Mannitol. **B. D. Pentlow, W. J. Wall, P. G. Kostakis, P. G. Baker, D. P. Smith, Jennifer Underwood, R. Y. Calne.**

FUTURE MEETINGS

Wednesday, July 13th, 1977—City Hospital Nottingham. (Organiser Mr. Roger Blamey). A.M. Scientific Sessions. P.M. Symposium on "Lymphocyte Movement".

Wednesday, October 19th, 1977—Wellcome Foundation Building, Euston Road, London. Symposium on "HLA and Diseases". (Organisers, J. R. Batchelor and P. Morris).

Members of the British Society for Immunology are particularly welcome to attend this meeting.

SUBSCRIPTIONS 1977. Special announcement by the Treasurer.

Members will recall that at the Annual General Meeting in October it was agreed that the subscriptions should be raised to £5 per annum,payable by cheque in December. A large number of members have already paid their new subscriptions as a result of the Treasurer's circular letter at the end of last year. However, there are still a significant number of subscriptions outstanding. It would be appreciated if these could be sent to the Hon. Treasurer as soon as possible in order to avoid the expense of sending out a reminder. Cheques should be made payable to the British Transplantation Society. Please remember also to cancel all existing standing orders in favour of this Society.

1. THE PATTERN AND INCIDENCE OF REJECTION OF ORTHOTOPIC HUMAN LIVER TRANSPLANTS

R. Y. Calne, R. S. Williams and B. M. Herbertson

Cambridge University and King's College Hospital

The experience of liver transplantation in Denver of more than one hundred and ten orthotopic liver grafts and in the Cambridge/King's College Hospital series of sixty-one provides a sufficient number of patients surviving the early post-operative period in whom the incidence of rejection can be determined. In each of these series, uncontrollable rejection occurred in less than ten per cent. This is markedly different from the experience in renal and cardiac allografts from unmatched cadaver donors where inexorable rejection has occurred in about fifty per cent of cases within the first year.

This report is concerned with observations of the Cambridge/King's College Hospital transplants. In many patients, between the first and second week, there were transient disturbances of the liver function attributable to rejection which subsided, in some cases, following increased steroid treatment but, in others, without any change in management. The pattern of severe rejectio is manifested by a relentless increase in the serum Bilirubin and Alkaline Phosphatase levels and slowly progressive liver failure. The morphology shows liver cell death with mononuclear cell infiltration similar to hat seen in rejection of other organ grafts. Complete destruction of intra-hepatic bile ducts was a feature cosidered to be a manifestation of rejection in a number of our cases. The data of man will be presented and an attempt will be made to correlate these findings with observations of organ graftings in the pig.

PAPER 2

2. PEPTIC ULCERATION, GASTRIC SECRETION AND RENAL TRANSPLANTATION

G. Williams, G. D. Chisholm, A. D. Mee, J. E. Castro and J. H. Baron

Urology and Transplantation Unit, and Department of Surgery, Royal Postgraduate Medical School, London

A group of 54 patients on haemodialysis for chronic renal failure subsequently underwent renal transplantation. Basal and maximum acid output, and the incidence, morbidity and mortality of peptic ulcer disease were studied. Basal and maximum acid outputs, and the incidence of peptic ulcer in the period before transplantation were not significantly different from control patients without renal failure.

After transplantation, symptoms of peptic ulcer were common (24%) and four of six patients who developed gastrointestinal bleeding, died.

In men, peak (but not basal) gastric acid output was significantly increased after the transplant and this was associated with a 30% incidence of symptoms of peptic ulcer. In women, only 10% had symptoms and there was no significant change in basal or peak acid values. Peptic ulceration occurring after transplantation was not related to total steroid dose, hyperparathyroidism or blood urea levels.

A history of dyspepsia, abnormal barium meal or gastric hypersecretion did not identify the patient on haemodialysis who was at risk after transplantation from peptic ulceration or its complications. Thus, the routine screening of these patients for peptic ulcer disease has no practical value in their management, nor is the incidence of fatal complications sufficient to justify routine prophylactic anti-ulcer acid lowering surgery before renal transplantation.

3. THE EFFECT OF INCREASING ISLET NUMBERS ON SURVIVAL OF PANCREATIC ISLET ALLOGRAFTS IN IMMUNOSUPPRESSED DIABETIC RATS

D. R. A. Finch and P. J. Morris

Nuffield Department of Surgery, University of Oxford

Cyclophosphamide (10 mg/Kg/day for 14 days) ncreased the functional survival of (DA X Lewis) F1 pancreatic islet allografts in Lewis recipients from a mean of 4.2 days to 6.8 days when the minimum number of islets necessary to consistently achieve normoglycaemia in syngeneic animals (600 – 800) was used. Increasing the number of islets three-fold to 1,500 – 3,000 per recipient resulted in a significant further prolongation of graft survival with one of the six animals in this group remaining normoglycaemic for the period of observation of 100 days ($p = 0.01$). This was attributed to greater functional reserves of graft tissue.

In contrast, the function of (DA X Lewis) F1 islets in DA recipients where rejection was modified by 500 µl of DA anti-Lewis antiserum, was not further prolonged by increasing the islet number ($p = >0.05$). These results are consistent with a peripheral mechanism of enhancement in this experimental model.

It is suggested that greater numbers of islets may be needed for successful human islet transplantation than has hitherto been suggested by syngeneic animal experiments if conventional immunosuppressed drugs are to be used.

4. THE EFFECT OF ISCHAEMIA ON MORPHOLOGY AND INSULIN SECRETORY CAPACITY OF ISLETS OF LANGERHANS IN THE RAT

E. H. McLaren, D. Bardsley, R. D. G. Milner, D. N. Slater, Y. F. Mangnall, A. Smythe and M. Fox
Department of Clinical Research, Royal Hospital, Sheffield

As part of the study of transplantation of islets of Langerhans, the effect of ischaemia on the pancreas, and the maximum period of ischaemia compatible with functional survival requires to be determined.

The blood supply to the tail of the pancreas of adult rats was occluded by clamping for 30, 60 and 90 minutes, at body temperature or 4°C. Histological examination of the ischaemic portion was subsequently performed at intervals of up to three months. In a further series of experiments islets were isolated by collagenase digestion from control fresh pancreas or tissue subjected to 30 or 60 minutes warm ischaemia. Insulin release was studied in a perfusion system.

Warm ischaemia for 60 and 90 minutes caused extensive exocrine necrosis maximal at seven days. The changes could be almost totally prevented by cooling to 4°C during the period of ischaemia. None of the experimental procedures caused light microscopical changes in the islets. Collagenase digestion of ischaemic pancreas produced smaller numbers of islets compared with controls. The characteristic insulin secretory response to 20 mM glucose was seen in seven out of 10 controls but this response was only seen in one of seven experiments with ischaemic islets.

Conclusion:

(1) In the rat, the exocrine pancreas is affected by 60 minutes' warm ischaemia while the islets appear to be more resistant.
(2) Cooling during the period of ischaemia will prevent these changes.
(3) In spite of their normal appearance in the intact pancreas, ischaemic islets isolated by collagenase digestion are functionally impaired.
(4) These results may explain the difficulty experienced in isolating islets from cadaver human pancreas.

5. PANCREATIC ISLET TRANSPLANTATION: EFFECTS ON THE METABOLIC CHANGES AND SECONDARY COMPLICATIONS OF EXPERIMENTAL DIABETES IN THE RAT

Y. Mangnall, A. Smythe, D. Slater, R. D. G. Milner, I. Strachan and M. Fox
Department of Clinical Research, Royal Hospital, Sheffield

The hyperglycaemic state in streptozotocin-induced diabetic rats can now be reversed following isogeneic transplantation of Islets of Langerhans. The aim of the present experiments was to study certain metabolic changes following prolonged diabetes in the rat together with complications which occur in the eyes and the kidneys and effect thereon of successful islet transplantation.

One month after induction of diabetes, rats were transplanted intra-peritoneally with collagenase digested isogeneic, neonatal rat pancreases. The low serum insulin, hyperglycaemia, glycosuria, and loss of body weight seen in the diabetic rats were restored to normal in 80% of the transplanted animals. However, 60% of these rats had an abnormal glucose tolerance test, but this condition was stable and did not alter over the 10 month period of study. Hepatic glucokinase, pyruvate kinase and glycogen levels which were reduced in the diabetic state had returned to normal three months after successful transplantation. Diabetic rats showed a progressive development of lens opacities and glomerular mesangial deposits from one month after induction of diabetes. However, after successful transplantation the development of cataracts was either arrested or reversed and there was also arrest in further mesangial deposition.

Islet cell transplantation can therefore reverse the metabolic changes in the rat with arrest of development of kidney and lens lesions characteristic of the uncontrolled diabetic state.

6. BLOOD TRANSFUSION, GRAFT SURVIVAL AND REJECTION EPISODES

R. W. Blamey, M. S. Knapp and Maxine Salisbury
Nottingham City Hospital

A series of 27 successive cadaveric first transplants carried out at one centre over the last three years has been examined for graft survival and function, and for the numbers of rejection episodes; these have been contrasted with whether the patients received, or did not receive, pre-operative blood transfusion. All except one of the transfused group received four pints of blood or more. Grafting was carried out paying no attention to HLA matching.

Analysis by life curves gives the following figures for observed graft survival rates.

		Graft Survival (%)		
	No.	*3 months*	*1 year*	*2 years*
Whole series	27	72	48	46
Patients with Pre-operative transfusion	9	100	75	66
Patients without Pre-operative transfusion	18	42	37	28

These are very close to the National figures (N.O.M.S. Annual Report 1975-76).

Six kidneys were lost from early rejection (within three months) and one from late rejection (at fourteen months) and none of these had received pre-operative transfusion. Thus, no kidney from the transfused group has been lost from rejection: a significant difference ($p<0.05$).

To date, 10 grafts have survived for more than one year: six from the transfused group and four from the untransfused. No difference is seen between these groups in Serum Creatinine level nor Prednisolone dose, at one year after transplantation, nor in the numbers of rejection episodes occurring early (between the transplant and three months) or late (between three and twelve months).

7. THE EFFECT OF BLOOD TRANSFUSIONS ON KIDNEY GRAFT REJECTION IN DOGS

J. Fabre, M. Bishop, T. Sen, Judith McKenzie, Keryn Williams and P. J. Morris

Nuffield Department of Surgery, University of Oxford

Recent data suggests that pregraft blood transfusions improve kidney graft survival. Here this hypothesis is tested in unrelated mongrel dogs. Two groups of six dogs were transfused, each dog receiving fresh blood from three donors. The first group were transfused twice weekly for four-five weeks with 60 ml of blood, 20 ml from each of three dogs, the same three donors being used for each recipient. Kidney grafting was performed two-four days after the last injection. The second group received 50 ml of blood on three occasions two weeks apart. A different donor was used for each injection and kidney grafting was performed four weeks after the third injection. Each dog was bled weekly and the serum tested for lymphocytoxins and haemagglutinins, against the three blood donors as well as a random panel of eight dogs. A control group of six dogs did not receive pregraft blood transfusions, and all three groups received post operative azathioprine and prednisolone. Blood donors were not used as kidney donors.

The group receiving twice weekly blood injections produced strong and broadly reactive lymphocytotoxins. By the end of the transfusion schedule three of the six dogs had a positive cross-match against all eight dogs tested as potential donors, two dogs were positive against seven out of eight potential donors, and one dog was positive against three out of eight. No transplants across a positive cross-match functioned. Of the three negative cross-matches one died at nine weeks with excellent renal function and the other two died with functioning kidneys in the first week.

The group receiving fortnightly transfusions developed much weaker and less broadly reactive lymphocytotoxins, though all six dogs produced lymphocytotoxins against at least one of the blood donors. By the time of transplantation one dog produced positive cross matches against all seven potential donors, and his kidney never functioned. One dog was positive to six out of seven potential donors, one to three out of seven, one to two out of seven and two to only one out of seven. Survival times of these five negative cross matches were 26, 31, 46, 50 and 60 days, only the last dog dying from rejection.

8. BLOOD TRANSFUSIONS INDUCE PROLONGED KIDNEY ALLOGRAFT SURVIVAL IN RHESUS MONKEYS

A. A. van ES, R. L. Marquet, J. J. van Rood, M. W. Kalff and H. Balner

Eurotransplant Foundation and University of Leiden

In the course of the last few years an increasing number of kidney transplantation centres have been confronted with declining survival rates, unlikely to be attributable to changed policies with regard to HLA-matching, indications for grafting, immunosuppressive treatment, etc. The only major changes seemed to be related to the pretransplant history of the patients.

It was noted that recipients with the least favourable transplant survivals had usually received few blood transfusions or none at all. The hypothesis that conditioning of patients by multiple pre-transplant blood transfusions might be the cause of prolonged graft survival, was tested in a prospective study carried out in rhesus monkeys, using a protocol which paralleled the clinical situation.

Kidney transplantation was performed in unrelated rhesus monkeys, uremic death of the transplanted animals was taken as the end point of graft survival. A standard regimen consisting of Azathioprine (4 mg/kg) and Prednisolone (2 mg/kg) was given. Five transfusions, each consisting of 20 ml fresh whole citrated blood were given before transplantation. Kidney transplantation was performed 11 to 23 days after the last transfusion. Kidney donors as well as blood donors were nearly always matched for two or three SD-antigens with their respective recipients. Different blood donors were used for the pre-treatment of each recipient.

Experimental groups:

a Eight recipients were transfused and received immunosuppressive treatment.
b Six recipients received immunosuppression only.
c A group of ten rhesus monkeys received neither blood transfusion nor immunosuppression.

Results:

The mean survival times (MSTs) for *a* compared with *b* were 48.8 ± 25.3 and 11.0 ± 1.4 days, respectively. The control group *c* showed a MST of 11.4 ± 3.5 days. The effect of the blood transfusions on kidney graft survival appeared to be most marked when the interval between the last transfusion and transplantation was short. Surprisingly, two transfused monkeys with a positive crossmatch did not reject their kidneys hyperacutely; in fact, they showed a similar prolongation of graft survival and similar histology as the animals with a negative cross-match.

Recently seven rhesus monkeys received a kidney transplant after *only one* blood transfusion. The MST was 32.7 ± 22.6 days, which was not significantly different from the MST after five transfusions.

The phenomenon was therefore unlikely to be due to any of the specific immunological mechanisms which are thought to account for the induction of specific anti-donor type antibodies in immunological enhancement.

9. RECOGNITION OF B-CELL AND NON-HLA ANTIBODIES IN PRETRANSPLANT RENAL PATIENTS

A. Ting, Keryn Williams and P. J. Morris

Nuffield Department of Surgery, University of Oxford.

The sensitisation status of patients awaiting a renal transplant appears to play a major role in determining transplant outcome. It has generally been accepted that a positive crossmatch (using the standard NIH cytotoxicity test) is a contraindication to transplantation. Recipients with high levels of lymphocyte antibodies, therefore, represent a difficult group of patients to transplant.

At least three types of lymphocyte cytotoxic antibodies in pretransplant patients have been defined; those antibodies that react with (i) HLA-A, B, C antigens, (ii) B-cell antigens, and (iii) non-HLA antigens.

At present we have transplanted 11 recipients with a positive B-cell crossmatch. Eight of the transplants are functioning between six and 215 days post-operation. Three kidneys were lost, one for technical reasons, and the other two for rejection.

Of the 30 patients waiting for a transplant eight have antibodies that react with between 50 and 100% of a random lymphocyte panel but react only with 0 to 20% of a chronic lymphocytic leukemia cell panel. These antibodies are autoantibodies. They are detectable by immunofluorescence on lymphocytes and appear to be both IgG and IgM. Absorption with autologous and allogeneic lymphocytes and platelets removes some but not all antibody activity.

These antibodies appear to be directed against non-HLA antigens and their role in transplantation is to be determined.

Recognition of both B-cell and non-HLA antibodies may mean that more patients with cytotoxic antibodies can receive a successful transplant.

10. THE ROLE OF THE ONE WAY M.L.C. IN PREDICTING REJECTION EPISODES AND THEIR OUTCOME IN THE FIRST SIX MONTHS FOLLOWING LIVE RELATED DONOR RENAL TRANSPLANTATION

C. L. Kennedy and J. E. Castro

Urology and Transplantation Unit, Royal Postgraduate Medical School, London

A positive correlation between graft survival and a low stimulation index with the two way mixed lymphocyte culture (MLC) in both living related and a cadaver donor renal transplantation has been well established. The recent report of HLA identical kidneys being forcefully rejected by sibling recipients suggests that there are other antigenic systems present which can influence the results of renal transplantation. We therefore studied the one way MLC to see if it predicted the incidence and severity of rejection episodes in the first six months after living related donor renal transplantation.

Twenty-one patients, three women and 18 men, whose ages ranged from 10 to 52 years (mean 33 years) were studied. The MLC was calculated both as a stimulation index (SI) and a relative response (RR). Six patients were HLA identical with their donors and their MLCs were consistently lower (SI 0.71 : 5.94, RR 27 : 49) than those with two or one antigens in common. They were also subject to significantly fewer rejection episodes (1 : 2.3). There was no difference between those groups with one or two antigens in common. Those with SI> or RR>60% developed twice the number of rejection episodes as those with SI< or RR<60% and these episodes tended to be more severe. Two patients rejected their grafts, one HLA identical, the other a haplotype in common. Both required transplant nephrectomy. In the remainder the grafts were all functioning well at six months (Creatinine 75 – 216 mmol/litre).

We therefore conclude that there is a relationship between HLA typing and the MLC and that good matching on HLA system decreased the incidence of rejection episodes though identical HLA matches can still reject. Different degrees of MLC are probably of value in predicting rejection episodes in living related donor renal transplantation.

11. IMMUNOLOGICAL MONITORING OF TRANSPLANT PATIENTS—THE ROLE OF THE CELL-MEDIATED IMMUNITY (CMI) ASSAY

Keryn A. Williams and P. J. Morris

Nuffield Department of Surgery, University of Oxford.

Assays of CMI have been performed on 16 patients who received kidneys from cadaver donors together with three who received kidneys from living related donors, to determine whether they were presensitized to their donor at the time of transplantation. Initially, both donor spleen cells and donor PHA blasts were used as target cells, and both four and 16 hour assays were set up; the combination of donor spleen cell targets and the 16 hour assay appeared to give the greatest sensitivity with acceptable background levels. Of five patients with a positive CMI cross-match, two subsequently lost their grafts compared with the loss of two grafts in the 11 patients with negative cross-matches. Post-operatively, evidence of positive CMI developed in seven patients, usually but not invariably during the course of clinically apparent rejection episodes.

12. UNUSUAL ANTIBODY ACTIVITY IN RENAL TRANSPLANT REJECTION

Heather M. Dick, J. Roberts and P. Hercus

Tissue Typing and Clinical Immunology Department, Royal Infirmary, Glasgow.

In the search for explanations for the unexpected rejection of some kidney grafts, some unusual antibodies have been detected. These are lymphocytotoxic antibodies, active at 22°C and occurring in patients with negative cross-match tests against donor cells at the time of transplantation. In one patient, the antibody was reactive against donor lymphocytes of an earlier (rejected) transplant, but only after the second (also unsuccessful) transplant. The antibody in this patient does not appear to have HLA specificity nor is it reactive with B lymphocytes. A similar phenomenon occurred in a second patient, whose serum sample taken one day after his second graft showed reactivity against donor lymphocytes of both 1st and 2nd grafts. The presence of these antibodies did not correlate well with the activity of the serum against a selected lymphocyte panel normally used for pretransplant screening, nor did it appear to be the result of donor-recipient HLA-A or B incompatibilities, which were minimal or did not occur in these patients.

13. RABBIT ANTI-MOUSE THYMOCYTE ANTIBODY AS AN ADJUVANT IN THE PREPARATION OF FURTHER ANTI-THYMOCYTE SERA

Teresa Lai and M. O. Symes

Department of Surgery, University of Bristol

Mouse thymocytes were incubated with rabbit anti-mouse thymocyte sera. The antiserum coated thymocytes were then used to immunise rabbits for the production of further anti-thymocyte sera.

When the antiserum used for coating was itself immunosuppressive, the resulting antiserum showed a greater ability to promote the growth of A-strain mammary carcinoma transplants in CBA-PC mice than did a comparable antiserum raised against normal rabbit serum coated thymocytes.

GROWTH OF A-STRAIN TUMOURS IN ANTI-THYMOCYTE SERUM TREATED CBA(PC) MICE

Antiserum	*No. of mice with progressively growing tumours* / *Total number of mice in the group*		
	Day 28	Day 49	Day 70
AT(P_1)†S*	1/8	1/8	0/8
AT(NRS)S	2/13	0/12	0/12
AT(P_2)S	11/48	11/46	10/43
AT(NRS)S	13/44	16/41	7/33
AT(P_3)S	25/59	23/56	17/49
AT(NRS)S	15/57	16/53	7/45
	(p=3.0%)		(p=5.0%)
AT(P_4)S	4/9	5/9	4/8
AT(NRS)S	2/13	0/12	0/12
		(p=0.06%)	(p=1.45%)

* AT(I)S etc. anti-thymocyte (coated with rabbit anti-mouse thymocyte serum P_1) serum etc.

† Rabbit anti-mouse thymocyte sera P_1 and P_4 were not immunosuppressive. Antisera P_2 and P_3 were immunosuppressive.

By varying the concentration of immunosuppressive antiserum III used for cell coating it was found that at too high or low a concentration, further antiserum showing increased potency was not obtained.

It is suggested that the anti-thymocyte antibody may act as an adjuvant to the immunogenicity of thymocyte surface antigen.

14. IS NIRIDAZOLE IMMUNOSUPPRESSIVE IN MAN?

B. Jones, Michelle Bird, P. Massey, D. Millar, J. Miller, Suzanne Reeves and J. R. Salaman

K.R.U.F. Institute of Renal Disease, The Royal Infirmary, Cardiff

Niridazole (Ambilhar) an antischistosomal drug, has recently been shown to be immunosuppressive in mice. We have already demonstrated to the Society that Niridazole can extend the survival of cardiac allografts in rats from seven to 20 days and when given in conjunction with Azathioprine and Prednisolone, almost indefinite survival of grafts can be obtained. We have also examined the effect of Niridazole on the one-way human mixed lymphocyte cultures (MLC) and shown that serum and urine from rats treated with Niridazole contain metabolites which can cause a profound depression of the MLC. Niridazole itself had no effect. Our recent experiments with human subjects taking Niridazole have shown that they too form metabolites that will depress the MLC. When Niridazole was taken for three days at 25mg/Kg the serum contained factors that caused a 52% depression of the MLC. A 95% depression was observed with sera from other patients who were taking Azathioprine and

Prednisolone in addition. The serum of a patient on Azathioprine and Prednisolone alone caused only a 30% depression at this time interval. Suppressive factors were also sought in the urine of a transplanted patient taking Niridazole in addition to Azathioprine and Prednisolone. A dialysate of the urine was tested in the MLC and also injected into groups of seven rats bearing heart allografts. As can be seen in the table, MLC depression was observed and a significant prolongation of heart allograft survival achieved. Urine obtained three weeks later when Niridazole had been stopped (the other drugs were continued at the same dosage) was much less suppressive.

Drugs taken by urine donor	Depression of MLR	MST rat allografts	SD	P	
Nil	0	7.6 days	1.0	< 0.02	
Niridazole, Azathioprine and Prednisolone	74%	11.2 days	2.9		NS
Azathioprine Prednisolone	49%	8.3 days	0.9	< 0.05	

It would seem therefore that Niridazole is converted into immunosuppressive metabolites in man. Characterisation of these metabolites is currently under way in the hope that they may be used eventually in clinical renal transplantation.

15. PHARMACOLOGICAL CONTROL OF THE IMMUNE RESPONSE BY BLOCKADE OF THE EARLY HORMONAL CHANGES FOLLOWING ANTIGEN INJECTION

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Much experimental work attests to the modulation of the immune response by several hormones. These hormones are involved in the differentiation of the thymo-lymphatic system to adult status. The present communication shows that interaction of allogeneic cells in vivo elicits rapid changes of gonadotropins levels in blood. The administration of antigen and a combination of drugs known to act on both central neuroendocrine regulation and adrenergic receptors on cell membrane results in the induction of specific unresponsiveness, essentially complete in the case of humoral immune response. The combination of the three drugs was also tested in transplantation immune reactions. An impressive prolongation of the rejection time for allogenic skin grafts was obtained in outbred albino mice grafted with skin from inbred C57BL/6 mice. The grafts were retained as long as 30 days with no sign of rejection. A very pronounced suppression of the runting syndrome was also obtained in newborn albino mice innoculated with spleen cells from C57BL/6 mice which had been previously made "unresponsive" to albino mice alloantigens by drug-alloantigens treatment. The unresponsive condition induced is specific for the antigens injected and long-lasting. The effect of the combination of the three drugs on the immune response can be prevented by administration of a combination of gonadotropins and adrenocortico tropic hormone (ACTH).

16. A COMPARISON OF TWO TYPES OF STEROID PRE-MEDICATION IN RENAL TRANSPLANTATION

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Sixty-four consecutive renal allograft recipients were premedicated alternately with either hydrocortisone 200mg. I.V. or methyl prednisolone 1gm I.V. together with azathioprine in a dose of 5mg/kgm. All patients then received a uniform immunosuppressive regime of prednisone and azathioprine.

Episodes of acute transplant rejection were treated with increased doses of steroids. Follow up is for between two and 13 months.

In the methyl prednisolone group acute rejection episodes were treated in 19 patients and in five patients rejection was irreversible. Three kidneys were removed because of infarction and there were nine deaths due to various causes, none directly connected with transplant rejection. Nineteen of the transplanted kidneys continue to function.

In first transplants, acute rejection episodes were treated within the first seven days in 13 patients receiving hydrocortisone and in three patients receiving methyl prednisolone. Methyl prednisolone pre-medication may postpone early acute rejection, though having little effect on ultimate graft survival, and the study is continuing.

17. WHAT CAUSES AGONAL VASCULAR SPASM IN KIDNEY DONORS?

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It is well recognised that kidneys from a cadaveric donor can exhibit severe vasospasm, initiating a chain of events which ultimately leads to a complete renal shutdown. The cause of this spasm is not clear, but can usually be prevented by preliminary administration of phenoxybenzamine to the donor. We have investigated the ability of renal ischaemia, hypotension and hypercarbia to induce renal vascular spasm in anaesthetised rats.

Renal blood flow and arterial pressure were monitored in these experiments using renal venous cannulation and a pressure recording transducer respectively. Renal ischaemia was induced by clamping the renal pedicle for one hour and the renal blood flow was measured after releasing the clamp. Renal ischaemia alone was found to be a very weak inducer of renal vascular spasm. On the other hand, one hour of hypotension (B.P. = 50mm.Hg) caused a significant increase in renal vascular resistence after the blood pressure had been restored to normal levels. Preliminary adrenalectomy or the administration of phenoxybenzamine were able to prevent this spasm from occurring. Hypercarbia caused by far the most significant reduction in renal blood flow but the protection afforded by phenoxybenzamine was significantly less.

It would appear therefore, that in the rat hypercarbia and hypotension are far more deleterious to renal blood flow than renal ischaemia alone. The efficiency of adrenalectomy and phenoxybenzamine in preventing renal vascular spasm in the hypotension experiments suggest that adrenalin or noradrenalin were responsible for these effects.

18. FUNCTION OF THE PERFUSED RAT KIDNEY IN EVALUATION OF RENAL PRESERVATION SOLUTIONS

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A variety of solutions have been used to flush kidneys before storage for transplantation. A method of comparing their efficacy is required which allow the effects of storage on several components of function to be studied in the whole kidney.

Here, function of the isolated perfused rat kidney was measured after flushing and storage with Sacks, Collins and Perfudex solutions and with hypertonic citrate solution (Ross and Marshall, 1976). The ratios of concentrations of ^{14}C Inulin in perfusate and urine (U/P Inulin), glomerular filtration rate (UV/P Inulin), and sodium handling (fractional and total sodium reabsorption) were compared.

Function progressively deteriorated with increasing periods of cold storage in all solutions, but was significantly better maintained in kidneys perfused and stored in hypertonic citrate than with Sacks, Collins or Perfudex solutions. Kidneys freeze-clamped after storage and perfusion for 30 minutes with bovine albumin had a lower content of ATP and total adenine nucleotide than controls. Measures to prevent losses of adenine nucleotide during storage and perfusion improved function in citrate perfused kidneys.

These findings suggest that the perfused rat kidney is a useful and convenient model for the rapid selection of perservation solutions. The superiority of hypertonic citrate over earlier solutions has been confirmed.

Ross, H., Marshall, V. C. and Escott, M. L. (1976). 72-Hr Canine Kidney preservation without continuous perfusion. Transplantation **21**, 498-502.

19. WARM ISCHAEMICALLY INJURED CANINE KIDNEY PRESERVATION WITH HYPERTONIC CITRATE SOLUTION: THE IMPORTANCE OF MANNITOL

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Ross et al (1976) demonstrated immediate life sustaining function of canine kidneys flushed with hypertonic citrate solution and stored in this on ice for 72 hours. Warm ischaemia was negligible.

This solution has been evaluated; also the importance of mannitol in preservation of canine kidneys subjected to significant warm ischaemia and then autografted after 24 hours cold preservation.

Group I. No intravenous mannitol given. None of six dogs whose autograft was subjected to 30 minutes warm ischaemia survived. One of five dogs with warm ischaemia to 15 minutes survived. All kidneys had histological evidence of tubular regeneration.

Group II. 0.5 gram/kilogram of mannitol administered intravenously prior to renal ischaemia and again prior to graft revascularisation. All three dogs with autografts exposed to 15 minutes warm ischaemia survived. When the warm ischaemic period was increased to 30 minutes, five out of six dogs survived.

It is concluded that hypertonic citrate solution gives excellent preservation of warm ischaemically injured canine kidneys provided that intravenous mannitol is given. If mannitol is not given results are inferior, although kidneys so preserved might well support life after the initial period of acute tubular necrosis.

Reference:

Ross, H., Marshall, V. C. and Escott, M. L. (1976). Transplantation 21, 498-502.