BRITISH TRANSPLANTATION SOCIETY

10TH ANNUAL CONGRESS

28 – 30 March 2007

The Manchester International Convention Centre
Manchester

Welcome to Manchester

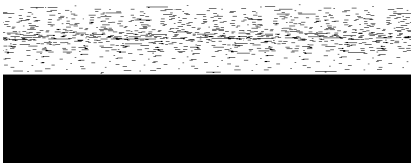
Welcome to Manchester! As Chairperson of the BTS 10th Annual Congress Local Organising Committee I am pleased to offer you a delicious menu of speakers, topics and social events, all designed to make BTS 2007 productive and enjoyable.

The Manchester International Convention Centre boasts all the facilities needed for a successful event in a comfortable environment. The nearby "Convention Quarter" of Manchester brings accommodation of all levels and social venues within a few minutes of the Congress hall.

If you get time to take a break from the busy Congress agenda you will find bustling and modern Manchester within easy reach.

On behalf of the LOC I would like to thank our sponsors and exhibitors for their support of the 10th Congress.

Have a great time at BTS 2007!



PHIL DYER
Local Organiser

Other Local Organisers: Anne Beasley, Beatrice Coupes, Patrick Flynn, Susan Martin, Kay Poulton, Lorna McWilliam, Julian Pratt, Faieza Qasim, Hany Riad, Stephen Sheldon, Judith Worthington

ACKNOWLEGEMENTS

The British Transplantation Society would like to give special thanks to their Corporate Partners for their support throughout the year and during the Congress:

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Genzyme

The abstracts for this meeting were kindly reviewed by:

Kesh Baboolal, Steve Bell, Laura Buist, Beatrice Coupes, Chris Dudley, Sue Duncalf, Phil Dyer, Jayne Fisher, Martin Howell, John Kirby, Leslie Logan Scott, Karen Morgan, Paulo Muiesan, James Neuberger, Marlene Rose, Deirdre Walsh, Chris Watson

SPONSORSHIP

A S T E L L A S	Delegate Bags Lanyards Pre-Meeting Liver Symposium A4 Pads
W Y E T H	SCOR.UK Meeting
TEVA	Internet Café Programme Book Abstract Book
GENZYME	£5000 travel bursary scheme
MANCHESTER INSTITUTE FOR NEPHROLOGY AND TRANSPLANTATION (MINT)	£5000 travel for Speaker

BRITISH TRANSPLANTATION SOCIETY

Company and Charity Annual General Meeting

Thursday 29 March 2007 (12.30 - 13.15)

MICC, Manchester

1. Welcome
2. Minutes of the last AGM held on 30 March 2006 (held as BTS Registered Charity No. 1098584 Company No. 4691176)
3. President's Report
4. Vice President's Report
5. General Secretary's Report
6. Treasurer's Report
    a. Financial Report
    b. Presentation of accounts (to be accepted by members)
    c. Appointment of auditors –

        To reappoint Mitchell Charlesworth as auditors to the Society from 1 November 2007 to 31 October 2008
7. 11th Annual Congress, Glasgow
8. Any other business
9. Close of the meeting

By order of the Board of Directors

Date: 7 March 2007

Registered Charity Number 1098584
Registered Company Number 4691176

BRITISH TRANSPLANTATION SOCIETY
Minutes of the Annual General Meeting - *Reg. Charity 1098584 & Reg. Company 4691176*

Thursday 30 April 2006 at 13.00, The Pentland Suite, EICC, Edinburgh

1 Apologies had been received from Henry Brown.

2 The minutes from the last AGM of the new charity held on 7 April 2005 were approved and accepted as a true record of the meeting.

3 President's Report

3.1 Secretariat Update
It was reported that Triangle Three will no longer be the secretariat for the BTS.

Tender for a new secretariat went out via advertisement in the Guardian. This was taken hand in hand with the Renal Association (RA). Close contact with John Feehally (president of the RA) and Triangle Three are kept to make sure procedures run smoothly.

3.2 Rule Changes (see appendix A)
It was reported that rule changes had been sent out to all members of the society in advance, to make sure they are aware of the changes. These were presented again today for feedback and any changes that had been made were reported.

Rule 1: New Structure of Council

The new structure of the council was looked at. It had been restructured to make sure that all constituent parts had a representation. All present had agreed with the principle of it and was accepted.

Rule 2: Membership

It was noted that in principle the text was fine, however the members had found that the wording of the first two lines, which had stated: "**To be a BTS member of good standing, the individual must be registered with the professional body which is appropriate for their particular interest…"** had not been correct, and could be misinterpreted to mean that anyone not registered in a professional body could not be a member of the society.

It was noted that the wording was not meant literally and to correct this, had now seen amended to: "**To be a BTS member of good standing, the individual must be registered with a professional body but only if this is appropriate for their particular interest…"** The amended version was presented again.

Again it was agreed in principle the text was acceptable but few members were still concerned about the details of the wording. It was noted that it would be taken back to council in the next executive and council meeting for further discussion and changes to the wording which would take into account the views of members.

3.3 Review of Certain Constituent Parts (see appendix A)
Correspondence was sent to all members from the president about the review of each constituents in the post.

The structure had been looked at and a few comments were noted. The Basic Science and Liver pre-meeting symposia had been successful, and it was suggested that the structure will continue in future meetings.

Other concerns were addressed by changing the rules for the structure of the council. A couple of the members raised an issue regarding the wording of one of the constituent parts, in particular "Transplant Surgery". It was felt that the title should identify the word Renal and should therefore be called "Renal Transplant Surgery". The President noted that each title had been previously decided on to identify constituents.

3.4 Bids for 2009

It was reported that the two likely places to hold the 12th annual congress of the BTS, would be London or Liverpool. Proposals had been accepted from both and site visits for each had been carried out by two people from the Council along with a Triangle Three Secretariat.

The Executive and Council decided that Liverpool will be the venue for the 2009 BTS congress. It was noted that the London bidders had been formally informed of this decision. The President thanked them for their outstanding proposal.

It was reported that the process for bidding and deciding on venues would be the subject of a review by the new treasurer (Anthony Warrens).

3.5 ATC & ESOT Bursaries

It was reported that these had been popular and the scheme was held to be a success by those who participated.

Bursaries for the WTC were currently advertised on the BTS website.

The scoring scheme for the bursaries had recently been reviewed by Chris Dudley, details on the web. Members were encouraged to apply soon to avoid missing the deadline.

4 Vice President's Report

4.1 British Transplantation – Intensive Care Society Joint meeting

The one-day meeting of the British Transplantation – Intensive Care Society joint meeting will take place in the Royal College of Surgeons, London, on the 17th July 2006. It was reported that the venue's maximum capacity is about 200. The proceedings from the meeting would be published and distributed to members of both societies. It was also reported that there would be six topics for debate:

- *Trends in neurosurgical practice and organ donation – towards non-heart-beating donors?*
- *Diagnosis of death and logistics of non-heart-beating donor organ retrieval*
- *What do we expect of each other?*
- *Why do relatives refuse? Who should ask?*
- *The Human Tissue Act – what does this imply?*
- *Does Society have the right to expect citizens to be organ donors?*

4.2 Clinical Trials Group

It was reported that a steering group had been formed, chaired by Chris Watson, to establish a new Clinical Trials subcommittee with the aim of fostering investigator-driven trials in transplantation in the UK. The rules governing the committee would be the same rules as for other BTS subcommittees.

4.3 ESOT Meeting 2011

It was reported that council were considering making a bid for UK site to hold the ESOT meeting in 2011. The bid needs to come from a national society who would host the meeting. Information regarding the bid, such as investigation of possible venues, was still required.

5 General Secretary's Report (see appendix B)

5.1 Secretariat Tender

It was reported that Triangle Three is still under contract with the BTS until the end of 2006. Tender documents for a new secretariat had been drawn up and advertised in the society Guardian on the 22nd March 2006, along side a separate advert for the Renal Association Secretariat tender. It was also reported that a six week deadline had been given for tenders to reach the society, and four executives of the society in addition to Wilson Wong (past General Secretary) and Steve Powis (past Treasurer) will be involved in the tendering process and interviews. It was noted that eight companies had shown interest to date, and the date set for interviews would be at the end of May 2006.

5.2 Election results

The elections had again been run by the Electoral Reform Services (ERS). There had been 36.9% ballots returned by the Society. The vote had been done by Single Transferable Voting.

The results were as follows:

Councillors (2 positions)	*First pref*	*Excl Muiesan*	*Excl Pettigrew*	*Excl Prasad*	*Excl Manas*
Simon Bramhall	36	41	52	61	70
Nizam Mamode	49	54	61	67	81
Derek Manas	40	48	50	60	
Paulo Muiesan	30				
Gavin Pettigrew	31	35			
Raj Prasad	37	42	45		
Colin Short	58	59	67	80	98

Ethics (2 positions)	*First pref*
John Henry Brown	89
Antonia Cronin	99
Vassilios Papalois	60

Treasurer (1 position)	*First pref*	*Excl Rowe*	*Excl Pratt*	*Excl Nicholson*
Michael Nicholson	59	63	73	
Neil Parrot	77	84	94	114

Julian Pratt	40	42		
Peter Rowe	37			
Anthony Warrens	69	82	97	117

General Secretary (1 position)
Only one name was put forward for general secretary, and that was Chris Watson. This was not opposed by anyone, which meant he had now been elected as the new general Secretary.

5.3 Membership
The total current membership stood at 787 full members and 31 associate members. There had been 63 new applications made up to 23 January– a list of names could be found in the abstract book. 63 more new applications were made since then – a list of names were presented at the AGM.

5.4 Abstracts
There had been 227 abstracts submitted for the 9th Annual Congress of the BTS. Of the 161 abstracts that were accepted, 61 were orals and 100 were poster presentations. 66 abstracts were not successful.

5.5 Bursary Schemes
There had been seven applications made for the two Clinical Training Fellowships sponsored by Astellas and Novartis. Short-listed candidates for interview would be notified after the Annual Meeting. There would also be two Travel Awards, the BTS / Morris and BTS / Wyeth awards; five applications had been made.

5.6 New Members
A list of new members was given in the abstract book, and the names of more recent members were given.

6 Treasurer's Report (see appendix C)

6.1 Financial report
It was noted that the fees for Corporate Partners for 2006 would be increased. It was reported that one Bronze Partner had resigned from the BTS.

6.2 Presentation of accounts
Summary accounts had been distributed at the AGM. Full accounts were available from the Secretariat. It was noted that the budget for 2005 – 2006 had shown that a profit of £5,000 had been made and the biggest expense on the account would be the 2006 congress, further details on expenses will be determined after the Congress.

Financial risks to the society were discussed, including keeping insufficient reserve funds, cancellation of congress, the later the cancellation the higher the cost. It was noted that the new Treasurer, Anthony Warrens, would need to undertake a more detailed risk review.

The general reserve funds have been set at £80,000, and currently stand at £40,000 so would need to increase.

It was noted that membership subscription for 2007 will increase for consultants only from £75.00 to £80.00. Normal and Reduced membership subscriptions will remain the same as in 2006.

These accounts were accepted and approved by the members.

6.3 Appointment of auditors

The Executive and Council had decided to reappoint Mitchell Charlesworth as the auditors for the Society for the period 1 November 2006 – 31 October 2007. There were no objections received by the members.

7 2007 Congress: Manchester

Phil Dyer reported that the meeting would be held from 28-30 March at the Manchester International Conference Centre (MICC) in Manchester. Phil Dyer and Beatrice Coupes were co-chairing the local organising committee. It was reported that the scientific programme was well under way and the social events had been looked at. Flyers in the form of postcards had been produced, which were included in the delegate bags, and in invitation letters sent to relevant departments.

The pre-meeting symposia are being negotiated at the moment.

It was noted that there were further concerns about the change of Secretariat and the effects it may have on the running of the congress.

8 Any other Business

Members commented on the abstract deadline date for the Manchester 2007 congress. It was felt that the date was too far ahead of congress and asked if it could be reviewed for the next congress in 2008 - this would be looked into further.

The two recently retired Councillors, Kesh Baboolal and Neil Parrot, were all thanked for their time given to the Society. Peter Rowe will now step in as chair of the Ethics committee.

John Forsythe made special thanks to Wilson Wong and Steve Powis for their hard work, time given and passion to the Society over the years.

9 Close of Meeting

APPENDIX A: PRESIDENT'S REPORT

RULE 1
The Council of the British Transplantation Society shall be made up as follows:

President (2 year term)
Vice President (2 year term prior to becoming President)
Secretary (3 year term)
Treasurer (5 year term)
President of the Carrel Club (elected by Carrel Club members)
Archivist (appointed by Council)
Chairman of sub committees:

1. Ethics - elected by ethics sub committee
2. Training - elected by training sub committee
3. Research - appointed by Council
4. Standards - appointed by Council

Councillors without portfolio - 3 councillors, 1 elected per year for a term of 2 years each
Councillor with a particular constituency as follows:

Transplant surgery (1)
Transplant nephrology (1)
Liver transplantation (1)
Cardiothoracic transplantation (1)
Basic Science (1)
Histocompatibility (1)
Transplant Co-ordination (1)

Each of these to serve for a 2 year term.

Any member of the BTS in good standing can be proposed for any of the elected councillor positions but each nomination should be for a defined position i.e. without portfolio or to represent a particular constituency. All members will be entitled to vote in any category. *

**This rule is intended to remove the need for judgement or arbitration as to who is qualified to stand for particular posts – it is unlikely that a member standing to represent a sub group outside their own area would be supported by the membership.*

RULE 2
To be a BTS member of good standing, the individual must be registered with the professional body which is appropriate for their particular interest e.g. GMC, NMC etc. If a member is 'struck off' from their professional register, then they cease to have any of the rights and privileges of the Society and they cease to be members of the British Transplantation Society.

AMENDED
To be a BTS member of good standing, the individual must be registered with a professional body but only if this is appropriate for their particular interest e.g. GMC, NMC etc. If a member is 'struck off' from their professional register, then they cease to have any of the rights and privileges of the Society and they cease to be members of the British Transplantation Society.

REVIEW OF CERTAIN CONSTITUENT PARTS

- Basic Science
- Transplant Surgery
- Nephrology in Transplantation

- Liver Transplantation
- Transplant Co-ordination & Transplant Nursing Staff
- Histocompatibility and Immunogenetics
- Cardio-thoracic Transplant Surgery

APPENDIX B: GENERAL SECRETARY'S REPORT

NEW MEMBERS (to 5th March 2007)

Ali, Simi (J A Kirby, S Stamp): University of Newcastle, Newcastle
Amin, Irum (J A Bradley, G Pettigrew): Addenbrooke's Hospital, Cambridge
Bagia, Jai Seema (A D Mayer, D Mirza): Queen Elizabeth Hospital, Birmingham
Barcena, Leticia (P Morris, C J E Watson): Royal College of Surgeons, London
Behravesh, Susan (S Metcalfe, E M Bolton): University of Cambridge, Cambridge
Botha, Phil (J H Dark, J A Kirby): Newcastle University, Newcastle
Caborn, Sarah (M Evans, C Dudley): Southmead Hospital, Bristol
Carey, Sharon B (J Spencer, R Stoddard-Murden): Derriford Hospital, Plymouth
Carroll, Robert P (A Bushell, N D Jones): John Radcliffe Hospital, Oxford
Cartmel, Linda (B Camilleri, C J E Watson): Ipswich Hospital NHS Trust, Ipswich
Chandrasekar, Thangavelu (A Hammad, R Rustom): Liverpool University Hospital, Liverpool
Charif, Rawya (J Galliford, Dr K Chan): London
Clatworthy, Menna (A Wells, C J E Watson): Addenbrookes Hospital, Cambridge
Claughton, Joanna (K Jessop, K Tomlinson): University Hospital Staffordshire, Staffordshire
De Freitas, Declan (P A Dyer, M Picton): Manchester Royal Infirmary, Manchester
Dent, Paul C (AR Ready, P Cockwell): Warwickshire
Dhaliwal, Parveen (S Reddy, C Pattenden): Oxford
Didapur, R K (V Revenur, D Talbot): National University Hospital, Singapore
Dosani, Muhammed (N Kessaris, V Papalois): Hammersmith Hospital, London
Dudley, Tracey (D Mirza, S Bramhall): Queen Elizabeth Hospital, Birmingham
Evans, Martyn (A Asderakis, N Kumar): University Hospital Wales, Cardiff
Farid, Shahid (N Ahmad, K Menon): St James University Hospital, Leeds
Fraser, Sheila (K Menon, G Toogood): St James University Hospital, Leeds
Glover, Alison (J Lumsdaine, C Jansen): Royal Infirmary of Edinburgh, Edinburgh
Halazun, Karim (P Lodge, N Ahmad): St James University Hospital, Leeds
Hammad, Abdelqader (J Shallcross, A Sharma): Liverpool University Hospital, Liverpool
Harris, Bradley P (J Wallwork, Susan Johnstone): Wiltshire
Harris, Emma J (J Wallwork, S Johnstone): Wiltshire
Harrison, James Scott (A Broderick, R Stoddard-Murden): Derriford Hospital, Plymouth
Hiemstra, Thomas (C Watson, J A Bradley): Addenbrookes Hospital, Cambridge
Hutchison, Colin A (P Cockwell, R Hanvesakul): University Hospitals, Birmingham
Ismail, Mohammed (A Tavakoli, N R Parrott): Manchester Royal Infirmary, Manchester
Jukes, John-Paul (K J Wood, N D Jones): University of Oxford, Oxford
Kibondo, Aimee (D Vijayanand, H Wyrley-Birch): University of Sunderland, Tyne & Wear
Knight, Simon Robert (P Morris, R Jamieson): Northwick Park Hospital, Harrow
Laugharne, Matthew (D C Mitchell, J Morgan): Southmead Hospital, Bristol
Laurence, Jerome M (A George, A Bushell): University of Sydney, Australia
Lesh, Ailsa (E Moore, E Mowlem): Addenbrookes Hospital, Cambridge
Mallick, Mohammad (C Bhati, C Kubal): London
Moore, Jason (R Higgins, L Chin Tan): University Hospital Coventry & Warwick, Coventry
Morgan, Catherine (C Taylor, R Praseedom): Addenbrookes Hospital, Cambridge
Motallebzadeh, Reza (G Pettigrew, J A Bradley): Addenbrookes Hospital, Cambridge
Mowlem, Elizabeth (S Lawrence, M Ryan): Addenbrookes Hospital, Cambridge
Munro, Euan N (J D T Morgan, P Lear): Southmead Hospital, Bristol
Perrin, Moira (A D Mayer, S Bramhall): Queen Elizabeth Hospital, Birmingham
Rana, Tahawar (K Junejo, C Whittaker): Royal London Hospital, London
Reddy, Veena (R Baker, A Lewington): St James University Hospital, Leeds
Redshaw, Jane (R J Middleton, P Kalra): Hope Hospital, Salford
Roddam, Helen E (P A Dyer, S Sheldon): Manchester Royal Infirmary, Manchester

Russell, Neil (C Watson, P Morris): Addenbrookes Hospital, Cambridge
Sajid, Salman (M Welberry Smith, R J Baker): West Yorkshire
Sarney, Leanne (N Hamilton, C Dudley): Southmead Hospital, Bristol
Saxena, Rema (A Bakran, A K Sharma): Royal Liverpool University Hospital, Liverpool
Sivaganesh, S (E M Bolton, J A Bradley): University of Cambridge, Cambridge
Terrace, John David (J Lumsdaine, J Bradie): University of Edinburgh, Eginburgh
Tyler, Michelle (J Richardson, P Aubrey): Noth Thames Regional Coordinators, London
Udayaraj, Uday (C Dudley, D Ansell): Southmead Hospital, Bristol
Vass, David (A Adair, L Marson): Edinburgh Royal Infirmary, Edinburgh
Walter, Katie (P D Mason, S Sinha): Oxford Radcliffe Hospital, Oxford
Whittaker, Clare (M Yaqoob, R C Thuraisingham): The Royal London Hospital, London

British Transplantation Society Membership Statistics

(As of 7th March 2007)

Reduced Members	**114**
Normal Members	**601**
Consultant Members	**154**
Honorary Members	**13**
Retired Members	**6**
OVERALL CURRENT MEMBERSHIP	**888**

APPENDIX C: TREASURER'S REPORT

THE BRITISH TRANSPLANTATION SOCIETY - SUMMARY ACCOUNTS

Statement of Financial Activities for the year ended 31st October 2005

	Unrestricted	Restricted	2005 Total	2004 Total
Incoming resources				
Corporate subscriptions	114,000	-	114,000	114,000
Individual memberships	42,456	-	42,456	34,076
Meetings income	-	140,345	140,345	102,321
Contributions for fellowships	-	85,000	85,000	85,000
Donation from British Transplantation Society (unincorporated)	-	-	-	172,011
Bank interest	14,120	-	14,120	8,965
Donations and grants	600	220,117	220,717	12,300
Other income	6,021	-	6,021	4,013
Total incoming resources	177,197	445,462	622,659	532,686
Resources expended				
Cost of activities in the furtherance of the charity's objects	90,675	349,523	440,198	223,961
Grants payable	36,826	74,969	111,795	121,927
Management and administration	23,756	-	23,756	36,633
Total resources expended	151,257	424,492	575,749	382,521
Net movement in funds for the year	25,940	20,970	46,910	150,165
Accumulated funds brought forward	85,358	64,807	150,165	-
Accumulated funds carried forward	£111,298	£85,777	£197,075	£150,165

Statement of Assets and Liabilities at 31st October 2005

	2005	2004
Current assets		
	175,773	21,555
Cash at bank	377,586	258,777
Debtors	553,359	280,332
Creditors		
Amounts falling due within one year	356,284	130,167
Net assets	£197,075	£150,165
Unrestricted funds		
Designated funds	71,881	62,197
General funds	39,417	23,161
Restricted funds		
Fujisawa Fellowship Fund	46,954	45,286
Clinical Trials Fund	19,521	19,521
Novartis Fellowship Fund	8,033	-
Wyeth Travel Fellowship	330	-
American Transplantation Congress Bursary Scheme	1,836	-
European Society for Organ Transplantation Bursary Scheme	9,103	-
	£197,075	£150,165

- Income & Expenditure
- Cash flow
- Corporate par
- 2005-6
- Risk review

ABSTRACTS

Plenary Session 1

Access to Transplantation

Wednesday 28 March

10.00 – 11.30

O01

Establishing an In-House Coordinator Model – A Local Implementation

Sarah Caborn, Leanne Sarney, Kay Hamilton, Elaine Clarke, Diane Evans

Transplant Coordinators, Renal Unit, Southmead Hospital, Bristol, United Kingdom

Introduction; Following a successful donor liason scheme in a local neurosurgical intensive care unit (ICU), the regional team were keen to continue this approach and build upon its achievements. We reviewed the current American and Spanish models as well as pilot schemes in the UK and utilised the key elements from these programmes to implement a local solution.

Aims; To establish an in-house coordinator (IHC) whilst maintaining an integral role within the regional donor coordinator team.

- To maintain a consistent presence within the ICU and integration within the multi disciplinary team.
- To provide continued support and education for clinical staff.
- To achieve 100% referral rate of all potential heart beating donors.
- To maintain the profile of non heart beating donation
- To provide early family support in potential donation circumstances.

Method; With funding from UK Transplant it has been possible to recruit a new donor coordinator to the regional team and allow two experienced coordinators to adopt the in-house role from within the existing donor transplant coordinator team. The two IHCs worked on a job-share basis and maintained full regional on call commitments so as not to become isolated from the local team and wider coordinator community.

Results; The IHCs have become integral and valued members of the ICU team and are utilised daily as a specialist resource. Organ donation profile has been raised and donation has become a natural part of end of life care. 100% referral of all HB donors has been achieved. A collaborative approach has been introduced and in the first 6 months of the introduction of the in-house programme, the referral rate has increased by 97% compared to the same period in the previous year. Job-sharing the role has enabled greater flexibility and coverage.

Conclusion; Finding a solution that supports both the local team and the ICU has led to a seamless introduction of this in-house role. In the next 6 months we aim to build upon this successful referral rate and increase the ratio of potential to actual donors.

In-house coordinators can significantly improve the organ donation process through earlier involvement with families and by closer relationships with hospital staff.

O02

Are there Variations in the Assessment Practice for Renal Transplantation across the United Kingdom?

Deepika Akolekar, Gabriel C. Oniscu, John L.R. Forsythe

[1]Transplant unit, Royal Infirmary of Edinburgh, Edinburgh, Midlothian, United Kingdom,
[2]Transplant unit, Royal Infirmary of Edinburgh, Edinburgh, Midlothian, United Kingdom,
[3]Transplant unit, Royal Infirmary of Edinburgh, Edinburgh, Midlothian, United Kingdom

INTRODUCTION: There are well established guidelines for the assessment of adult candidates for renal transplantation.
AIM: The aim of this study was to investigate whether there are any variations in the evaluation of adult candidates for cadaveric renal transplantation among the transplant centres across the United Kingdom.
METHODS: An online questionnaire was sent to members of the multidisciplinary team (nephrologists, surgeons and transplant coordinators) from all adult transplant centres in the U.K. The questionnaire was designed and piloted in 4 centres prior to online distribution. Follow up contact was made to request completion of the questionnaire. Data was analysed comparing centres as well as according to the speciality of the person filling in the questionnaire.
RESULTS- A complete response was received from 20 out of the 23 centres (87%). 39 nephrologists, surgeons and transplant coordinators from these units responded to the questionnaire. In 30% of the units there is no multidisciplinary transplant assessment clinic and the majority of patients are identified and worked-up by nephrologists. There is no cut off age limit for assessment across the UK, but eleven centres (55%) exclude patients with a high BMI with an average cut off BMI of 35. Four centres have no specific policy regarding BMI.
8 out of the 20 centres do not give CMV negative patients the option to receive kidneys from a CMV positive donor. EBV status is checked in all patients in 80% of the units, whilst only 40% of the units perform routine Herpes zoster antibody testing. The investigation of cardiovascular disease follows no specific pattern across the country, but 35% of centres perform routine coronary angiography for all diabetic patients. Hepatitis C antibody positive donors are not utilized in 47% of the units. Five units had no consistent policy of re-evaluation patients once on the waiting list. There were significant differences in the responses provided by nephrologists and surgeons, sometime from the same units.
CONCLUSION- There is evidence, from this study, of significant variations in practice across the U.K. in the assessment of patients for renal transplantation. Further research, as well as clearly defined guidelines are required to ensure a uniform assessment process and equity of access to the renal transplant waiting list.

Plenary Session 2

Symposium with British Society for Gene Therapy

Wednesday 28 March

12:00 – 13:30

O03

Lentivirus-Mediated Gene Transfer of Bclxl Protects Aorta Endothelial Cells from Ischemia-Reperfusion Injury

Jing Zhao[1], Eleanor Bolton[2], J. Andrew Bradley[2], Andrew Lever[1]

[1]Department of Medicine, University of Cambridge, Cambridge, United Kingdom, [2]Department of Surgery, University of Cambridge, Cambridge, United Kingdom

Despite increasing success in organ transplantation, long-term graft survival is still limited by chronic rejection. Recent evidence indicates that endothelial cell (EC) dysfunction may contribute to the pathogenesis of this process. This is one of a series of studies attempting to deliver cytoprotective genes to EC to make them resist apoptotic stimuli with the aim of inhibiting chronic rejection. Bclxl is an anti apoptotic member of the Bcl2 family. Bclxl was delivered to rat aorta endothelial cells using a lentiviral vector to see if it could protect EC from apoptosis induced by ischemia-reperfusion (I/R) injury.

Lentiviral vectors containing Bclxl were generated from an HIV-1 construct, in which the viral promoter had been inactivated and virtually all the viral accessory proteins had been deleted in order to maximise safety. Bclxl gene expression was confirmed by Western blot. EC were prepared from rat aorta. I/R injury of EC was induced and apoptosis was assessed using caspase 3 activity and Tunel staining.

The *in vitro* I/R injury model in rat primary EC showed duration-dependent apoptosis (figure 1). Endogenous Bax expression increased with I/R injury while endogenous Bclxl remained constant (figure 2). When EC were transduced with a lentiviral vector expressing Bclxl, we showed significant protection from warm I/R injury (caspase 3 activity was 611587$\pm$308211 RLU for non-transduced EC vs. 137845$\pm$102586 RLU for EC transduced with Bclxl, n=6, $p<0.05$).
In conclusion, over expressing Bclxl in rat aorta endothelial cells using lentiviral vectors protects endothelial cells from I/R injury. We showed that Bax expression was upregulated during the I/R injury. The protective effect of over expression of Bclxl could be due to altering the balance of pro and apoptotic factors perhaps cancelling the effect of Bax during the ischemia reperfusion injury.

Figure 1

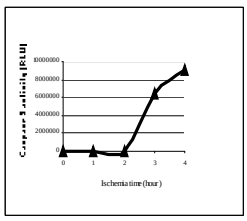


Figure 2

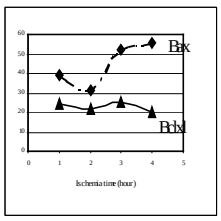


Fig 1 The degree of apoptosis correlates with the duration of I/R injury in EC.

Figure 2 Densitometry analysis for Western blot of endogenous expression of Bclxl and Bax in response to I/R injury in rat aorta EC.

O04

Lysine:Histidine Co-polypeptide Packaged siRNA For The Effective Knockdown Of Locally Expressed Pro-inflammatory Genes In The Donor Kidney

Marie D Parker, Claire L Corps, Patrick Lu, Martin Woodle, Frank Xie, J. Peter. A Lodge, Julian R Pratt

[1]Leeds Institute for Molecular Medicine, Leeds, United Kingdom, [2]Intradigm Corporation, Rockville, United States, [3]Department for Organ Transplantation, Leeds, United Kingdom

In vivo RNA interference offers an opportunity to diminish the expression of pro-inflammatory genes after transplantation. To enhance the transfection of siRNA, we have developed a self-assembling macromolecule where siRNA becomes incorporated into a cationic co-polypeptide consisting of Lysines and Histidines. To deliver the siRNA:co-polypeptide macromolecule, or nanoparticle, to the transplanted kidney, we used the flushing of donor kidneys with preservation fluid.

In a model of syngeneic rat kidney transplantation, 10□g of siRNA specific for C3mRNA, was packaged into the co-polypeptide and delivered to the kidney via Hyper Osmolar Citrate preservation fluid. Organs were exposed to 4 hours of cold ischaemia and then transplanted. After 48hrs of reperfusion, the kidneys were harvested and assessed for C3 gene expression by Real Time PCR. Off target effects of siRNA were examined by Real Time PCR for IFN□, IFN□ and IL-1□, and post transplant histopathology was assessed. To examine the efficacy of the cationic co-polypeptide to modify siRNA uptake, the w/w ratio of siRNA to co-polypeptide was altered, and the data compared against the efficacy of naked C3 siRNA to inhibit C3 gene expression.

Delivery of naked C3 siRNA did not produce significant C3 gene knockdown, however, using the the co-polypeptide at ratios of 4.5:1, 3:1 & 1.5:1 w/w with C3 siRNA did produce significant C3 gene knockdown (50% / 73% / 62% respectively: $P<0.05$, n=3/group) and reduced histopathological signs of ATN compared to untreated transplanted controls. Assessment of off-target effects so far indicates the siRNA sequence used did not itself induce an inflammatory response and analysis to date does not indicate any toxicity associated with the *in vivo* use of the co-polypeptide packaged siRNA.

In conclusion, packaging siRNA into the co-polypeptide nanoparticle provides a strategy to reduce pro-inflammatory gene expression in the transplanted kidney. Site specific delivery is made possible via the preservation fluid. The strategy offers clear clinical potential to reduce the local expression of genes contributing to post-transplant inflammation and in the future we will develop cocktails of siRNA specific for a range of genes to further modify the tissue response to transplantation to improve outcomes and support the induction of transplant tolerance.

O05

A Novel RNA Transcript Protects against Endothelial Cell Apoptosis during Ischemia Reperfusion Injury

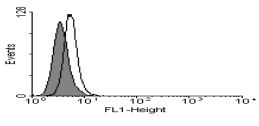
Jing Zhao[1], Jenny Houghton[1], John Sinclair[1], Eleanor Bolton[2], J. Andrew Bradley[2], Andrew Lever[1], Matthew Reebes[1]

[1]Department of Medicine, University of Cambridge, Cambridge, United Kingdom, [2]Department of Surgery, University of Cambridge, Cambridge, United Kingdom

Introduction: Ischemia-reperfusion (I/R) injury is associated with an increased risk of acute rejection, delayed graft function, and chronic graft rejection. The mitochondrion plays a central role in this process. Prolonged or even short periods of ischemia impair mitochondrial electron transport and can trigger mitochondrial-dependent apoptosis. A novel viral transcript used in this study is encoded by cytomegalovirus during the initial stages of infection. The function of this RNA molecule has only been identified recently and it appears to inhibit host cell apoptosis by direct physical interaction with Complex I in mitochondrial electron transport. In this study we examined the feasibility of using this viral RNA to protect vascular endothelial cells (EC) from I/R induced apoptosis using delivery via a lentiviral vector. Importantly, since the transcript is a non-coding RNA, it will not induce an immune response in the recipient.

Methods: Lentiviral vectors containing a full-length viral transcript expresser were generated from an HIV-1 construct. The viral transcript gene expression was examined by RT-PCR. EC were prepared from rat aorta. An *in vitro* I/R injury model was set up and apoptosis was assessed using Caspase 3 activity and Tunnel staining. Perturbation of respiratory chain function in mitochondria was assessed by the capacity to oxidize non-fluorescent DHR 123 to fluorescent rhodamine123 measured by FACS.

Results: This viral transcript could protect EC from I/R injury. After 4 hours I/R injury, caspase 3 activity for non-transduced EC was 351192±58661 RLU whereas caspase 3 activity for EC transduced with viral transcript was 198416 ± 41872 RLU (n=3, $p<0.01$). The protective effect of viral transcript was confirmed using FACS analysis for Tunnel staining (Figure).



Conclusion: The viral transcript is a novel method to protect rat aorta endothelial cells from I/R injury causing apoptosis. Further experiments are currently underway to confirm that the protective effect of this viral transcript was due to direct stabilization of the mitochondrial respiratory chain during I/R injury.

Fig Representative histogram of Tunel staining. The filled peak was EC transduced with viral RNA transcript and the overlay was non-transduced EC after 4 hours I/R injury.

Plenary Session 4

Best Abstracts

Wednesday 28th March

14:30 – 15:30

O06

SYMPHONY – Comparing efficacy of standard immunosuppression to low-dose cyclosporine, tacrolimus or sirolimus in combination with MMF, daclizumab and corticosteroids in renal transplantation.
Sub analysis of GFR in cases that completed one year within an intended regime.

Rafael Chavez[1], M Nicholson[2], J Grinyo[3], U Frei[4], Y Vanrenterghem[5], P Daloze[6], P Halloran[7], H Ekberg[8]

[1]University Hospital opf Wales, Cardiff, United Kingdom, [2]University Hospitals of Leicester, Leicester, United Kingdom, [3]Ciutat Universitaria de Bellvitge., Barcelona, Spain, [4]Virchow-Klinikum, Berlin, Germany, [5]KU Leuven, Leuven, Belgium, [6]Notre Dame Hospital CHUM, Montreal, Canada, [7]University of Alberta, Edmonton, Canada, [8]Lund University, Malmoe, Sweden

Introduction: SYMPHONY is a prospective, randomized, open trial comparing standard immunosuppression versus 3 regimens with low-dose or no CNI in de-novo renal transplant patients over 1 year.
Methods: This study has 4 parallel arms. 1645 patients in 15 countries were randomized to standard immunosuppression with normal-dose cyclosporine, MMF 1g BID and corticosteroids, or to one of three regimens consisting of daclizumab induction (2mg/kg followed by 4x1mg/kg every 2 weeks), MMF (1g bid) and corticosteroids, combined with a low-dose of either CsA (50-100 ng/ml), tacrolimus (TAC, 3-7ng/ml) or sirolimus (SRL, 4-8ng/ml).
Primary end point was renal function (Cockcroft-Gault GFR) at 12 months. Secondary end points were biopsy proven acute rejection (BPAR) rate, patient and graft survival rates and treatment failure.
Results: The low-dose TAC group was significantly superior to all other groups with respect to GFR ($p<0.01$) and BPAR ($p<0.0001$) and to normal-dose CsA and low-dose SRL for graft survival ($p<0.05$). GFR after exclusion of premature withdrawals (per protocol; PP), shows a similar distribution of results.

	n	GFR (12 mo) (ITT)	**n**	**GFR (12 mo) (PP)**	BPAR (6 / 12 mo)	Graft Survival	Patient Survival
	(ITT)	mean (SD) [ml/min]	**(PP)**	**Mean (SD) [ml/min]**	[%]	[%]	[%]
Control (CsA)	390	57.1 (25.1)	**305**	**61.1 (23.9)**	24.0 / 25.8	89.3	96.5
Low-dose CsA	399	59.4 (25.1)	**318**	**63.0 (23.4)**	21.9 / 24.0	93.1	98.2
Low-dose TAC	401	65.4 (27.0)	**340**	**68.0 (26.0)**	11.3 / 12.3	94.2	97.2
Low-dose SRL	399	56.7 (26.9)	**258**	**60.8 (26.6)**	35.3 / 37.2	89.3	96.8

Conclusion: Combination of daclizumab, MMF, low-dose TAC and corticosteroids offers optimal balance of efficacy and toxicity. The study shows comparable functional results (GFR) in the Intention to Treat and the Per Protocol populations.

O07

An open, prospective, randomised, controlled, study comparing Fixed Dose vs Concentration Controlled MMF regimens in renal transplantation (the FDCC trial)

Stephen Powis[1], Iain MacPhee[2], James Pattison[3], Teun van Gelder[4]

[1]Royal Free Hospital, London, United Kingdom, [2]St George's Hospital, London, United Kingdom, [3]Guy's & St Thomas's Hospital, London, United Kingdom, [4]Erasmus Medical Centre, Rotterdam, Netherlands

Introduction. MMF is effective in the prevention of acute rejection following solid organ transplantation at fixed dose. Several studies have shown a relationship between MPA plasma concentrations and the likelihood of acute rejection. The FDCC trial was therefore designed to assess whether therapeutic drug monitoring (TDM) could further improve outcomes in *de novo* renal allograft recipients.
Methods. A total of 901 patients, from 65 centres in 19 countries, were randomised 1:1 to either fixed-dose (FD) or concentration-controlled (CC) MMF therapy. All patients were treated with a calcineurin inhibitor (either tacrolimus (Tac) or ciclosporin (CsA)) and corticosteroids (± induction therapy) according to centre protocol. In the CC group, abbreviated AUCs (3 samples within the first 2 hours after administration) were measured on day 3, day 10, week 4 and months 3, 6 and 12 and used to predict the $AUC_{0\text{-}12}$. MMF dose was adjusted to reach a target value for MPA $AUC_{0\text{-}12}$ of 45 mg•h/l.
Results. Patients treated with CsA (*n* = 483) or Tac (*n* = 418) were evenly distributed between the CC (*n* = 449) and FD groups (*n* = 452). Similar incidences of biopsy-proven acute rejection (BPAR) were observed at 12 months [14.9% (67/449) in CC patients vs 15.5% (70/452) in FD patients]. Treatment failure at 12 months (defined as either BPAR, graft loss, death or discontinuation of MMF) was also similar (25.6% CC group vs 25.7% FD group). Adverse events were equally distributed among the two groups, and there were no significant differences in the incidences of anaemia, diarrhoea, leukopenia, thrombocytopenia or weight loss. A significant proportion of patients in the CC arm did not have dose adjustments performed correctly (particularly when larger dose adjustments were required), resulting in similar MPA exposures in the FD and CC arms. There was a significant relationship between early exposure on days 3 and 10 and efficacy during the first year after transplantation. However, in around 30% of patients in both arms (and up to 50% in the CsA-treated patients), MPA AUC was below 30 mg•h/l up to day 10.
Conclusion. TDM may help optimise efficacy only if dose adjustments are performed correctly. Excellent efficacy is correlated with correct early exposure to MPA. Initial doses of 3 g MMF in combination with CsA or 2 g MMF with Tac, adjusting doses to the therapeutic window thereafter, may provide optimal MPA exposure early post-transplantation.

O08

The Use of Rituximab to Successfully Treat Refractory C4d Positive Chronic Allograft Nephropathy

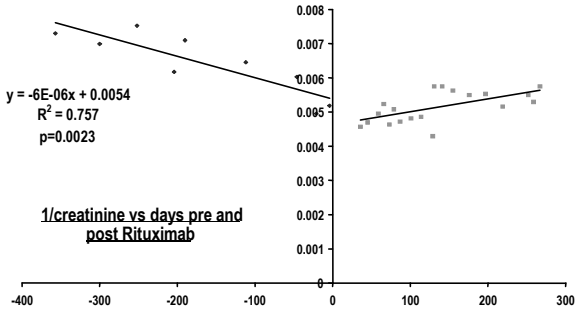
Kakit Chan, Jack Galliford, Terence Cook, David Taube, Anthony Dorling

West London Renal and Transplant Centre, Hammersmith Hospital, London, United Kingdom
We present the first reported use of Rituximab in chronic allograft nephropathy [CAN].

Introduction: CAN is a common and significant cause of renal allograft failure, with no established treatment. A significant proportion of those identified with CAN have an immune pathogenesis, with evidence of chronic humoral rejection [CHR] on renal biopsy and detectable circulating donor specific antibodies [DSA]. Staining for the complement split product C4d in allograft biopsies has been useful in distinguishing immune from non-immune injury. Rituximab can be effective in the treatment of acute humoral rejection but there are no reports of its use in CHR.

Methods: 11 patients [5m, 6f; mean age 49.6 ± 8.95 years] who underwent allograft biopsy for significant graft deterioration [mean graft age 11.43 ± 6.9 years] +/- proteinuria had histopathological evidence of CAN with C4d deposition in peritubular capillaries and/or glomeruli. All were treated with optimisation of immunosuppression using tacrolimus [12 hr trough level 5-7 ng/L (LCMS)], and Mycophenolate Mofetil [12 hr trough level 1.5 – 3.0 mg/ml]. Steroids have not been used. Rituximab [1g twice: Day 0 and 14] was administered to 6 patients who failed to stabilise after 3 months; these were designated 'refractory C4d + CAN'.

Results: 2/4 patients with >3 months follow up have stabilised following rituximab administration [example in figure], with a quantifiable reduction in proteinuria if present. A further 2 have < 3 months follow-up. 5 have not required Rituximab as graft function stabilised on MMF and tacrolimus, so they have continued on this optimised conventional immunosuppression. DSA analysis will be presented.



Discussion: This study is the first to show that Rituximab can stabilise allograft function in patients with 'refractory' CAN with an immune aetiology.

O09

Influence of lifestyle and pharmacological modification in renal transplant recipients with abnormal glucose metabolism: a prospective study to prevent development of de novo diabetes after transplantation

Adnan Sharif, Richard Moore, Keshwar Baboolal

University Hospital of Wales, Cardiff, United Kingdom

Background. Transplantation is associated with glucose dysregulation which can progress to new onset diabetes after transplantation (NODAT) or impaired glucose tolerance (IGT). No data exists to demonstrate the efficacy of lifestyle modification for these complications. The aim of this study was to assess the benefit of lifestyle/steroid modification in renal transplant recipients with NODAT or IGT.

Methods. An oral glucose tolerance test (OGTT) stratified patients into 2 groups:

- Group 1: Glucose intolerance group, IGT (n=23) and NODAT (n=7), was managed with lifestyle modification ± reduction in steroid dosage

- Group 2: The control group had normal glucose tolerance and were counselled regarding risk of IGT & NODAT with leaflet advice alone (n=60)

Both groups had a follow up OGTT after 6 months to compare the benefits of intervention in Group 1 against the natural history of glucose regulation in Group 2.

Results. Lifestyle/steroid modification in Group 1 resulted in 13% improvement in 2hr glucose metabolism versus 13% deterioration observed in Group 2 (Table 1):

Table 1: Change in glucose metabolism (mean in mmol/L ± standard error)

OGTT	Group 1 – Glucose intolerance		Group 2 - Control	
	0hr Glucose	2hr Glucose	0hr Glucose	2hr Glucose
Baseline	6.2 ± 0.1	10.1 ± 0.4	5.8 ± 0.1	6.0 ± 0.1
Repeat	5.9 ± 0.2	8.8 ± 0.6	5.6 ± 0.1	6.8 ± 0.3
Change	-5% (p=0.06)	-13% (p=0.03)	-3% (p=0.08)	+13% (p<0.01)

In Group 1, 52% (n=12) of IGT patients had complete normalisation of glucose tolerance with lifestyle modification after 6 months while only 4% (n=1) developed NODAT. 58% (n=4) of NODAT patients also improved their glucose tolerance (29% to IGT and 29% to normal). Only 6 patients (5 IGT and 1 NODAT) in Group 1 attempted steroid withdrawal and all had normal OGTT and stable graft functions at follow up. In contrast glucose metabolism deteriorated in control Group 2 with 14% (n=8) developing IGT and 3% (n=2) developing NODAT after 6 months.

Discussion. This study demonstrates the natural progression of glycaemic dysregulation post-transplantation. Lifestyle/steroid modification can attenuate and even reverse glycaemic dysregulation in renal transplant recipients with glucose intolerance. This study highlights the importance of early recognition of glucose intolerance as early intervention can halt the progression of glucose dysregulation.

O10

How Safe is Laparoscopic Donor Nephrectomy in the United Kingdom? – data from the UK Transplant Registry in 2509 patients

Vassilis Hadjianastassiou, Nizam Mamode, Roberto Cacciola, Rachel Johnson

[1]Renal and Transplantation Unit, Guy's & St. Thomas' NHS Trust, London, United Kingdom, [2]Department of Statistics, UK Transplant, Bristol, United Kingdom

INTRODUCTION: The nationwide increase in living donation has coincided with the growth in laparoscopic/hand-assisted living donor nephrectomy rates. It is imperative for the transplant community to be informed of the safety of these procedures relative to the tried and tested open approach. We conducted an analysis of the clinically important outcomes in living donors to compare Laparoscopic and open donor nephrectomy.
METHODS: The UK Transplant registry collecting mandatory information on all living donations in the country was analysed, for all operations performed between 11/2000 (the start of mandatory reporting of laparoscopic data) to 06/2006. Outcome variables analysed were classified into: major morbidity [intra-operative splenectomy, deep vein thrombosis, pulmonary embolism, pneumothorax necessitating chest drainage, pneumonia, re-operation] and minor morbidity [wound infection, urinary tract infection, constipation, prolonged ileus, blood transfusion, nausea and others]. The open approach (OPEN) was compared to laparoscopic/hand-assisted (LAP) techniques using Pearson's Chi-Square tests (Fisher's test when appropriate) for categorical variables and independent t-tests for continuous variables.
RESULTS: 2509 donors were reported (601 LAP; 1800 OPEN, 108 (4.3%) missing). 46.5% Male, 53.5% Female. The mean donor age was 46 years old (No significant gender ($p=0.545$) or age ($p=0.277$) bias between LAP and OPEN). There was 1 death 3 months post-discharge (OPEN) and a further 5 deaths beyond a year post-discharge. The mean length of stay was 4.5 days (LAP) and 6 days (OPEN) ($p<0.001$). Major morbidity was 3.5% for both LAP and OPEN approaches ($p=0.949$), but minor morbidity was significantly less ($p<0.001$) for LAP (7.4%) than OPEN (13.3%). The overall rate of any (major and/or minor) morbidity was 14.3% (LAP=10.3%, OPEN=15.7% $p=0.001$).
DISCUSSION: Living donation has remained a safe procedure during this period of the learning curve associated with adopting the LAP approach in the UK. The latter offers measurable advantages to the living donor in terms of reduced length of stay and morbidity associated with the procedure. We acknowledge the help of UK Transplant, which has kindly supplied the data.

O11

Indo- Asian Ethnicity is Associated with Poor Outcome After Renal Transplantation in the United Kingdom.

Sonal Asthana, Chris Rudge, Niaz Ahmad

[1]St James's University Hospital, Leeds, United Kingdom, [2]UK Transplant Authority, Bristol, United Kingdom

Introduction: The Indo-Asian population in the United Kingdom is more likely to develop end-stage renal disease than the native British population. They are also less likely to receive cadaveric organs under an HLA based organ allocation scheme. Analysis of data from our own centre has previously shown a poor post-transplant outcome in this group. This study was conducted using national data to validate our earlier findings.
Methods: All patients who had undergone renal transplant in the United Kingdom between 1995 and 2005 were included in the study. Data was from the prospective national database maintained by UK Transplant. Donor variables studied included age, sex, blood group while recipient data included age, sex, blood group, diabetic nephropathy, type of transplant, HLA mismatches and previous transplants . Patients with no recorded ethnicity on the database were excluded from the analysis. Statistical analysis was performed using the chi-square test,'t' test, KM analysis using the log-rank test and a Cox regression analysis for independent predictors of graft survival. Graft failing in the first 30 days were excluded from the analysis.
Results: 17105 renal transplants were carried out nationally during this 10-year period, of whom 15180 were eligible for the study. Asian and black patients received a significantly higher proportion of non-heart beating (NHB) kidneys. The mean HLA mismatch, DR mismatch and waiting time were significantly higher for these ethnic groups. Recipient ethnicity, donor age, DR mismatch and previous grafts affected graft survival for cadaveric heart-beating (CHB) kidneys, while recipient ethnicity and previous transplants affected outcome for NHB kidneys. The one, three and five-year survival rates for the white, asian and black recipients were 94.5%, 90.3%,84.9% ; 94.5%,89.2%, 83.1% ; 94%, 89.7%, 78.3% ($p<0.001$).
Conclusion: Graft outcomes after renal transplantation were worse among Asian and black recipients of CHB and NHB organs in this study. Effect of ethnicity was greater than the effect of HLA mismatches. Increasing awareness for organ donation within ethnic communities may improve waiting time and graft outcome.
Acknowledgement: UKT for providing the data and all the UK transplant centres whose patients have been included in analysis.

Parallel Session 5

Pharmacogenomics

Wednesday 28 March

16:00 – 17:30

O12

Does cyclosporine C2-level monitoring confer clinical benefit when compared with conventional trough-level monitoring? A systematic review.

Simon Knight[2], Peter Morris[1]

Does cyclosporine C2-level monitoring confer clinical benefit when compared with conventional trough-level monitoring? A systematic review.[1]Centre for Evidence in Transplantation, Royal College of Surgeons of England and London School of Hygeine and Tropical Medicine, London, United Kingdom, [2]Transplant Unit, Churchill Hospital, Oxford, United Kingdom

Introduction Cyclosporine has a narrow therapeutic window so that close monitoring of blood levels is required to ensure adequate immunosuppression whilst avoiding side effects, especially nephrotoxicity. Pharmacokinetic and indirect clinical studies have suggested a potential benefit of monitoring cyclosporine levels at 2-hours post dose (C2) in comparison to trough levels (C0). We have reviewed clinical outcomes in studies directly comparing solid organ transplant recipients monitored either with C2 or C0 levels

Methods A systematic literature search of the Cochrane Central Registry of Controlled Trials, Ovid Medline, Embase, Pubmed Medline and clinical trial registries was performed from 1990 to present. Bibliographies of identified studies were examined for further references, and the principal investigators of ongoing trials were contacted. Primary outcomes assessed were renal function and acute rejection.

Results 5907 potentially relevant citations were initially identified but only 29 studies met the inclusion criteria. 10 of these were randomised controlled trials; the remainder were a mixture of observational and experimental cohort studies. Overall quality was poor and this precluded meta-analysis.

The most consistent finding in *de novo* renal, hepatic and cardiac transplant recipients is a higher mean cyclosporine dose in the early postoperative period in C2 monitored patients. There is no clear evidence that this leads to impaired renal function. In the majority of studies, the monitoring strategy appeared to have no effect on the rate of acute rejection. In stable transplant recipients, the majority of studies show a reduction in mean cyclosporine dose with adoption of C2 monitoring. No clear clinical benefit was derived from this reduction in doseage..

Conclusion Evidence in support of C2 monitoring is sparse and of limited quality. In *de novo* transplant patients there is difficulty reaching initial target levels which may explain why the theoretical benefits of C2 monitoring are not supported by prospective studies. Potential dose reductions in stable patients may reduce costs, but no clear clinical benefit is seen. The practical limitations of C2 monitoring outside of the clinical trial setting mean that more evidence is required before adoption of a strategy for the administration of cyclosporine based on C2 levels can be recommended.

O13

Does The Use Of MMF To Enable Calcineurin Inhibitor Reduction Or Withdrawal Result In Better Kidney Graft Function? A Meta-analysis.

Neil Russell[1], Andrew Bradley[1], Peter Morris[2]

[1]Cambridge University Department of Surgery, Cambridge, United Kingdom, [2]Centre for Evidence in Transplantation, Royal College of Surgeons of England, London, United Kingdom

Introduction: The nephrotoxic side effects of calcineurin inhibitors (CNI) can result in decreased kidney graft function and may impact on long term graft survival. The use of Mycophenolate Mofetil (MMF) to enable reduction or withdrawal of CNI's, to minimise their nephrotoxicity, may be of potential benefit to graft function and long term graft survival.
Methods: Detailed literature searches of the Medline, Embase and Cochrane databases were performed to find all the randomised controlled trials (RCT's) of CNI reduction or withdrawal. RCT's that met the inclusion criteria were identified.
Primary outcome of the meta-analysis was renal function. Secondary outcomes were patient and graft survival, acute rejection rate, blood pressure, lipid profile and diabetes. The results were analysed using the meta-analysis software Review Manager. All groups were analysed with a random effects model and confidence intervals (CI) were set at 95%.
Results: 14 RCT's met the inclusion criteria. 1438 patients were enrolled in these trials. 6 month creatinine (Cr) was lower in the CNI reduction group (Mean Weighted Difference (MWD) = -8.81 CI -17.33 to -0.28, 5 studies 623 participants). Further benefit was seen in Cr at 12 months (WMD -11.54, CI -19.52 to -3.55, 3 studies 324 participants). 6 month creatinine clearance (CrCl) was higher in the CNI reduction group (MWD 7.21, CI 3.82 to 10.60, 5 studies 623 participants). Again further improvement was seen in CrCl at 12 months (MWD 10.58, CI 5.01 to 16.16, 4 studies 381 participants).
There was no difference in patient survival at 6 months (9 studies, 823 participants) or 12 months (5 studies, 637 participants) nor was there any difference in graft survival at 6 months (7 studies, 715 participants) or 12 months (5 studies, 637 participants). There was no difference in acute rejection at 6 months (5 studies, 466 participants) but there was a significant increase in acute rejection in the CNI reduction group at 12 months (Odds Ratio = 3.69, CI 1.53 to 8.85, 4 studies 505 participants). Diastolic BP was reduced in the CNI reduction group (MWD -5.37, CI -2.45 to -8.28, 3 studies 118 participants), but there was no difference in systolic blood pressure, number of BP medications, lipid profile or incidence of diabetes.
Conclusion: The use of MMF does allow CNI reduction resulting in improved renal function at 6 and 12 months, but at the expense of an increase in AR.

O14

Maintenance of Bone Mineral Density With Complete Steroid Avoidance After Renal Transplantation

Richard Baker, Veena Reddy, Stephen Tibble, Dorothy Littler, Andrew Lewington, Chas Newstead.

Renal Unit, St James's University Hospital, Leeds, United Kingdom

Introduction: Since January 1st 2004 we have been using a complete steroid avoidance regime in our renal transplant programme. Here we demonstrate the effects on bone mineral density (BMD) during the first twelve months after transplantation.

Methods: 27 patients had dual-energy x-ray absorptiometry (DEXA) (GE/Lunar Prodigy) scans soon after hospital discharge and again 12 months later (median 419.8±9.2 days). All patients were low or medium risk recipients of a renal transplant and were immunosuppressed with basiliximab 20mg (day 0 and day 4), tacrolimus (levels 9-14 ng/ml for 3 months and 5-9ng/ml thereafter) and mycophenolate mofetil (750mg bd). A single intraoperative injection of methylprednisolone 1g was given but no further steroids unless deemed clinically indicated.

Results: At 12 months patient and graft survival was 100%. All patients were steroid free. Median creatinine level was 166.7 ± 9.2 at discharge and 150.4 ± 7.9 after 12 months. Calcium and phosphate levels were within the normal range in all patients at both time points and the mean PTH level was 18.3 ± 2.9 at discharge and 20.0 ± 5.1 at 12 months. 4 patients suffered an episode of rejection and were treated with steroids. BMD levels shown in the following table were unchanged:

mean±sem	**Bone Mineral Density (g/cm^2)**		
	spine	**R hip**	**L hip**
Discharge (n=27)	1.24±0.04	0.98±0.03	0.99±0.03
12 months (n=27)	1.26±0.03	0.98±0.03	0.98±0.03

Discussion: In contrast to previous studies which show a consistent decrease in BMD of around 10% in patients treated with steroid-containing immunosuppressive regimes, our results show essentially unaltered bone mineral density after 12 months of steroid avoidance. It is hoped that this improved bone strength will translate into meaningful clinical benefits.

O15

Significance Of Acute Rejection In A Steroid Avoidance Regime After Renal Transplantation

Richard Baker, Aravind Cherukuri, David Border, Niaz Ahmad, Krish Menon, Stephen Tibble, Harish Shetty, Chas Newstead, Andrew Lewington

Renal Unit, St James's University Hospital, Leeds, United Kingdom

Introduction: Since January 1st 2004 we have been using a complete steroid avoidance regime in our renal transplant programme for low and medium risk patients. We have observed a small increase in rejection rates during this period and we were concerned whether this was detrimental to transplant outcome at one year. Here we study the effects of rejection episodes in terms of function.

Methods: All low or medium risk adult recipients of a renal transplant and were immunosuppressed with basiliximab 20mg (day 0 and day 4), tacrolimus (levels 9-14 ng/ml for 3 months and 5-9ng/ml thereafter) and mycophenolate mofetil (750mg bd). A single intraoperative injection of methylprednisolone 1g was given. Patient records were analysed to assess outcomes.

Results: 12 month follow up data was available for 195 patients and there was an overall rejection rate of 16.9% (33/195). Rejection was associated with poor HLA matching but no other pre operative parameter.

	Rejection	No Rejection	P value
N	33	162	
1 year eGFR	40.5±2.7	48.8±1.2	**0.008**
Graft Survival	78.8%	96.3%	**0.0002**
Patient Survival	97.0%	98.0%	0.66
DGF	48.5%	28.1%	**0.02**
Antibody treatment	15.2% (5/33)		

BANFF grade 1 rejection occurred in 24/33 (72.7%) and was associated with a 38.6±3.9 mls/min 1 year GFR, 87.5% graft survival and 100% patient survival compared to 48.5±7.6 mls/min, 55.6% and 88.9% respectively in BANFF grade 2 or 3 rejection.

Discussion: Even milder grades of rejection are associated with significantly adverse outcomes. If those patients who are likely to undergo rejection, e.g. those who are poorly matched, can be identified preoperatively then they might benefit from the addition of steroids. More work is required to try and identify such patients.

O16

Forewarned is Forearmed: Patients' Views on Pharmacogenetics

Emily A Fargher, Katherine Payne, Karen Tricker, William Newman, Faieza Qasim

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Introduction: Despite theoretical advances in tailoring medication for individuals, the use of pharmacogenetics has not yet been widely integrated into clinical practice. There is limited evidence on patients' and healthcare professionals' views of pharmacogenetic test (PGx) services. It is vital to explore these views prior to widespread implementation, as they may provide useful information that can be used to inform future service development. The aim of this study was to explore patients' and healthcare professionals' views of NHS PGx services.
Methods: Semi-structured interviews were conducted with 25 patients (10 male) with a history of taking azathioprine (7 post-renal transplant, 11 gastroenterology; 6 rheumatology; 1 dermatology). Four focus groups were conducted with 18 healthcare professionals (genetics and non-genetics). A topic guide was developed using published literature. Show cards were used to offer a lay definition of PGx. A PGx that identifies thiopurine methyltransferase (TPMT) status to identify the risk of developing neutropaenia in individuals prescribed azathioprine was used as a case study. Interviews and focus groups were recorded and transcribed verbatim. Data were analysed using the constant comparative method.
Results: Patient experience and knowledge of PGx varied considerably. Renal patients had a vast amount of knowledge about their condition and were most keen to explore their understanding of PGx. All healthcare professionals had limited experience of PGx and found the concept difficult to explain. PGx was perceived to be of benefit to both patients and healthcare professionals. Patients gave opinions about PGx services based on their experiences of illness, taking medicines and using the NHS. Healthcare professionals based their opinions on existing services and limited resources. Patients had strong feelings about how this service should be delivered and expected high standards of explanation about PGx. Renal patients appeared to value the test most highly and were most concerned with the level of explanation that would be provided about the test and subsequent treatment decisions. They did not feel that this test would be provided outside of their usual clinic. Health care professionals did not expect to have a role in the future delivery of PGx services.
Conclusion: There is no clear model of how PGx and results will be explained to patients. Patients are willing to receive pharmacogenetic services from any health care professional that is able to explain the test and results with confidence. Patients with long term illness wanted pharmacogenetics to be fully integrated into their usual service. These opinions may be used to shape the development of PGx services in the NHS.

Parallel Session 6

Developments in Immunosuppression

Wednesday 28 March

16:00 – 17.30

O17

A Randomised Prospective Trial of Daclizumab Induction Followed by Sirolimus in Association with Mycophenolate Mofetil and Steroids Versus Standard Cyclosporin Based Triple Therapy for Rejection Prophylaxis in Renal Transplantation

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Background. Although cyclosporin (CsA) is an effective immunosuppressant, the benefits of CsA therapy observed for renal graft survival at 1 year post-transplant (Tx) are not sustained over the longer term (≥5 years). This may be due, in part, to the drug's well documented nephrotoxicity. Both the therapeutic and nephrotoxic effects of CsA are related to its properties as a calcineurin inhibitor (CNI). The failure of CsA to prevent late graft loss has directed new therapeutic initiatives, such as the study presented here. The aim of this study was to compare the effects on post-Tx renal function of a CNI-free immunosuppressive regimen versus conventional CsA-based triple therapy.

Methods. This was a randomized, prospective, open-label, comparative, two centre study in which patients received either standard triple therapy with CsA, MMF and prednisolone (CsA group) or daclizumab induction followed by sirolimus (Sir), MMF and prednisolone (Sir group). The primary efficacy endpoint was the comparison of renal function at 6 and 12 months post-Tx, assessed via calculated GFR (Cockcroft-Gault). Various secondary endpoints were evaluated, including patient and graft survival and BPAR.

Results. A total of 80 patients were randomized into the treatment groups; CsA n=39 versus Sir n=41. Renal function at 6 and 12 months post-Tx, patient survival and graft survival were comparable between the two groups; however, more cases of BPAR were observed in the Sir group (Table).

Table: Efficacy endpoints for patients receiving CsA versus Sir regimens.

Endpoints	**CsA regimen (n=39)**	**Sir regimen (n=41)**
MeanGFR (mL/min)		
+ 6 months	61.77(SD17.59)	60.27(SD15.49)
+12 months	60.60 (SD17.47)	61.03(SD20.11)
Graft survival	38/39	40/41
Patient survival*	38/39	40/41
BPAR	8	16

**One patient from each group died with a functioning graft (patient from Sir group had discontinued study 5 months previously)*

Conclusions. These 12mth data demonstrate that a CNI-free immunosuppressive regimen appears to be feasible and offers equivalent graft survival to standard CsA-based therapy. The Sirolimus group patients who did not suffer acute rejection had better graft function. The results of the three years extension study is awaited.

O18

A Simple Tool to Assess Concordance with Immunosuppressive Drug Therapy

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An important factor governing long-term renal allograft survival is concordance with immunosuppressive therapy. Hitherto this has been difficult to measure quantitatively and most investigators have relied on questionnaires or electronic monitoring of drug containers. We hypothesized that the degree of variability in repeated measures of ciclosporin (CyN) concentration during out patient follow up of recipients of renal transplants would be a marker of concordance with therapy. To assess this variability we have calculated the coefficient of variation (CV) of sequential CyN drug concentrations obtained during routine follow up. CV is a simply calculated measure that can be applied to any repeated data to give a quantitative reproducible assessment of variability. To test if the CV was correlated with graft survival we carried out a logistic regression analysis using graft failure as the primary outcome measure.
The database used for this study was the Long Term Efficacy and Safety Surveillance of Transplant Patients (LOTESS) made available by Novartis Pharmaceuticals. CV was calculated for each individual patient from the CyN trough concentrations measured between day 30 and day 365 using the formula 100x(standard deviation/mean). The absolute value of serum creatinine (SCr) at 12 months and the occurrence of acute rejection in the first 12 months were also included as potential predictive variables. A receiver operator curve (ROC) analysis was used to test if the CV could be used to categorise patients in to groups with a high or low risk of graft failure.
Data from 1658 patients from the total of 2011 was included in this analysis. The CV was highly significantly associated with graft failure (Wald ChiSq $p<0.0001$). SCr at 12 months was also highly significant (Wald ChiSq $p<0.0001$). The ROC analysis showed that both the CV and the SCr at 12 months were equally predictive of long term outcome (AUC values of 0.63 and 0.68 respectively).
This analysis suggests that increased variability in ciclosporin blood concentrations in the first year after renal transplantation is predictive of shorter graft survival. The coefficient of variation of measurements of ciclosporin concentration can be repeatedly calculated automatically during follow up after transplantation and used to identify patients at increased risk of premature graft loss. These patients could be offered an enhanced level of support and monitoring and avoidable graft loss reduced.

O19

An Electronic Transplant Library (TL) Of Randomised Controlled Trials (RCTs) In Organ Transplantation Simplifies Searching For Level 1 Evidence

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Introduction: Searching the literature for RCTs using electronic resources such as PubMed are both time consuming and need professional expertise.
Methods: An electronic TL has been developed in collaboration with LWW which includes all RCTs in organ transplantation from 1995 to simplify searching so that the relevant level 1 evidence can be obtained in minutes. We assessed the efficacy of the TL compared to PubMed in retrieving relevant level 1 references in solid organ transplantation. Using two examples we employed the term "precision" as a measure of efficacy. This is defined as "the proportion of all retrieved documents that are relevant divided by the number of documents retrieved".
Results: In the first example we used a Cochrane systematic review to compare the results obtained from the TL and PubMed. This review on the use of ureteric stenting in kidney transplantation was published in 2005. It included seven RCTs and quasi-RCTs. A search in the TL using the term "stents" and limiting the results to kidney transplant retrieved 11 references which included all the 7 relevant RCTs identified in the Cochrane review resulting in a precision of **0.60 (60 %)**. The search took aprox. 3 minutes. A professional PubMed search strategy which included a filter to identify RCTs, terms for kidney transplantation and stents retrieved 109 references using the same publication date range. Six out of the seven relevant RCTs were included (one of the references identified in the TL was not indexed in PubMed). The precision for this search was **0.05 (5%)** and sifting through these 109 references would have taken aprox. 2 hours.
In the second example we searched for level 1 evidence to evaluate the role of biliary stents in liver transplantation. A simple search in the TL retrieved 11 references of which 7 were relevant to the question. The precision for this search was **0.6 (60%)** and this took 5 minutes. A professional search strategy in PubMed retrieved 208 potential relevant references. After sifting through these references 5 RCTs were identified which were also identified in the TL (two references identified in the TL were not indexed in PubMed). The precision for this search was **0.02 (2%)** and this took 3,5 hours.
Conclusion: These examples illustrate the power of the electronic TL of RCTs in that it is accurate and easy to use and does not require professional search skills. This should prove an invaluable time saving tool for the transplant community.

Parallel Session 7

Basic Science

Wednesday 28 March

16:00 – 17:30

O20

Vimentin Autoantibodies Induce Formation of Platelet-Leukocyte Conjugates and Blood Agglutination via Platelet-Activating Factor.

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Introduction: Anti-vimentin antibodies (AVA) are produced by about 30% of transplant recipients and are associated with graft vasculopathy. Whether they actively contribute to disease pathology is unknown. In view of the recent observation that activated platelets express vimentin, we have examined the interaction between AVA and platelets in whole blood and its separate components. **Methods**: Normal whole blood (from individuals who were HLA A2 positive and HLA A3 negative) was treated with patient sera or monoclonal antibody (mAb) AVA for 30-45mins, and platelet :leukocyte conjugates assessed by flow cytometry for CD41:Hoechst + cells, for deposition of fibrinogen and C3d on leukocytes, generation of platelet microparticles and blood agglutination. **Results**: Normal blood treated with patient sera containing high AVA-IgM titres or with a vimentin-specific IgM mAb led to formation of platelet:leukocyte (P:L) conjugates (24.7% vs 2.9% for patient sera, 14.9% vs 2.1% control for the mAb), a reduction in platelet counts, and macroscopic blood cell agglutination. Depletion of AVA's from patient sera with vimentin-coated agarose beads or addition of recombinant vimentin to the blood mixture, abrogated theses effects. The IgM mAb to A2, but not A3, also produced platelet/leukocyte conjugates, but not agglutination, demonstrating the effect of the IgM antibodies to be antigen specific. Flow cytometry demonstrated that AVA do not bind to resting platelets in whole blood but they bind to approximately 10% of neutrophils, these are senescent neutrophils. An in vitro cytotoxicity test revealed that binding of AVA to neutrophils results in complement dependent cytolysis (50%) and nuclear condensation. Supernatant derived from AVA activated neutrophils, transferred to fresh purified platelets, caused platelet activation as measured by generation of platelet microparticles. Experiments performed in the presence of CV-6209, a PAF receptor inhibitor, prevented blood cell agglutination and platelet depletion, suggesting that PAF is one of the mediators released from AVA activated neutrophils. **In conclusion**, we propose a novel pathogenic mechanism whereby AVA, binding to vimentin expressing neutrophils, results in platelet activation, and may contribute to atherogenesis and thrombosis, in patients with AVA.

O21

NK cell and macrophage infiltration into organ xenografts is absolutely dependent on thrombin-mediated production of MCP-1 through protease activated receptor-1

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Introduction; Effective inhibition of thrombin (FIIa) generation inside mouse heart xenografts completely suppresses acute humoral rejection (AHR) after transplantation into rats, despite deposition of anti-mouse antibody (Ab) and complement on graft endothelial cells (EC). In contrast, preventing intravascular thrombosis by depletion of fibrinogen fails to prevent AHR. Instead, hearts are rejected by NK cells and macrophages (MØ). This study investigated how FIIa influenced cellular infiltration into xenografts.
Methods; Wild-type (WT) C57BL/6 heart xenografts were transplanted into the abdomen of LEW rats. Recipients received ANCROD to deplete fibrinogen and protease activated receptor (PAR) antagonists. In separate experiments, hearts from transgenic (Tg) animals expressing hirudin on EC were transplanted and the recipient treated with PAR agonists and /or Ab against monocyte chemotactic protein-1 (MCP-1). Circulating cytokines were measured by ELISA.
Results; Antagonists against PAR-1 but not PAR-4 prolonged the survival of WT hearts in ANCROD-treated recipients (3.8 ±0.3 vs. 5.8 ± 0.31 days), which showed no infiltration by NK cells or MØ. In separate experiments, agonists for PAR-1 but not PAR-4 shortened survival of hearts from hirudin-Tg mice (6.3± 0.58 vs. 4± 0.26 days), which were infiltrated with NK cells and MØ. In both series, ELISA studies revealed that circulating levels of interferon-gamma (a marker of NK cell activation), interleukin-6 and tumour necrosis factor (markers of macrophage activation) and MCP-1 were dependent on signalling through PAR-1. A blocking Ab against anti-MCP-1, but not an isotype control, inhibited the actions of the PAR-1 agonist when used in recipients of hirudin-Tg hearts, prolonging survival (5.3±0.21 vs. 3.8±0.17 days) and inhibiting NK cell and MØ infiltration.
Discussion; These data explain the discrepancy between experiments in which the intravascular thrombosis of AHR is prevented by inhibition of FIIa generation vs. depletion of fibrinogen. FIIa, through PAR-1, is absolutely required for significant production of MCP-1, which is necessary for infiltration by, and subsequent activation of, NK cells and MØ. These results demonstrate for the first time that FIIa is necessary for inflammatory cell recruitment into transplanted xenografts, and illustrate that targeting PAR-mediated signalling can have a profound influence on mode of rejection.

O22

Predictive Preservation: Toward An Evidence Based Organ Retrieval Strategy

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In renal transplantation the choice of preservation strategy for the various donor types is not evidence based. This study is a first attempt to match the efficacy of preservation fluids to the period of cold ischaemia using an in-depth assessment of functional parameters. The aim of this work is to investigate the effects of preservation fluids over time to predict which fluid should be used in any particular clinical scenario, so- called "***Predictive Preservation***".

Male Wistar rat kidneys were flushed with a preservation solution (PBS140, LS, SLS, HOC or UW) and were stored at 4^{o}C for 0-72 hours (n = 6 per group). The kidneys were then maintained for 2 hours on an optimised *ex vivo* reperfusion circuit at 37^{o}C. Physiological analyses of reperfusion fluid and urine were performed at 30 minute intervals to assess ischaemia / reperfusion injury (I/RI) to components of the nephron.

Using the optimised *ex vivo* model, preservation with LS produced significantly improved urine flow rate, GFR and % Na^{+} reabsorption (29, 44 and 25% increase respectively) when compared to organs preserved in PBS140, HOC, SLS or UW (P<0.05) after 24 hours of preservation. Compartmental assessment suggested LS attenuated tissue damage in the glomerulus, the proximal tubules and the collecting system that was supported by histological observation. Using ***100% Stacked Column Analysis*** the data showed differential effects of time on cold ischaemic damage in the different nephron compartments. In effect, the cumulative data rank scores showed that from 24 to 48 hours, LS was optimal, but not at either extreme. At time 0, PBS140 was best, and beyond 48 hours, SLS or PBS140 was optimal.

In conclusion, a global assessment of functional parameters has enabled an in-depth assessment of fluids used in experimental renal cold storage. The data suggests different fluids should be applied where a short (living donation), or longer (cadaveric) cold ischaemic time is anticipated, i.e. ***Predictive Preservation***. Importantly, all fluids which best protected the kidney from I/RI were based on PBS140 and outperformed UW across the duration of cold ischaemia. To diminish I/RI and maximise post-transplant functional recovery, we advocate an evidence-based approach to preservation be developed in the future and that consideration be given to PBS based preservation for clinical renal transplantation.

O23

Critical Role for C3 in transplant tolerance

Richard Phillips, Julieta Karegli, Kathryn Brown, Steven Sacks, Wilson Wong

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Introduction The third component of the complement system (C3) has been shown to play opposing roles in graft rejection and tolerance. Mouse renal allografts deficient in C3 are rejected in a delayed fashion in allogeneic recipients. By contrast, absence of C3 prevents the induction of anterior eye chamber induced tolerance. If inhibition of C3 is to be employed as a therapeutic strategy in transplantation, it is critical to deduce whether C3 facilitates or hinders the induction of transplantation tolerance.

Methods and Results We have used a model of male to female trunk skin transplantation, in which donor and recipients are mismatched by the HY minor antigen. Wild type (WT) C57BL/6 male skin grafts were rejected by WT female recipients acutely (MST=15 days, n=19). $C3^{-/-}$ male skin grafts were rejected by $C3^{-/-}$ female recipients at a similar tempo (MST=16 days, n=7, P>0.05). Intravenous infusion of 35×10^6 WT male splenocytes (DLI) into WT female recipients on the day of transplantation resulted in indefinite survival in 11/13 WT male skin grafts (MST >100 days, n=6, $p < 0.0001$). By sharp contrast, infusion of $C3^{-/-}$ male splenocytes into $C3^{-/-}$ female recipients failed to prolong survival of $C3^{-/-}$ male skin grafts (MST=12 days, n=9, $P > 0.05$). To determine which pool of C3 is important in the induction of tolerance, the DLI protocol was performed using either a) $C3^{-/-}$ donor lymphocytes, WT graft, and WT recipient b) WT donor lymphocytes, $C3^{-/-}$ graft and WT recipient or c) WT donor lymphocytes, WT graft and $C3^{-/-}$ recipient. While donor lymphocyte derived C3 was dispensable for tolerance (MST > 80 days, $p<0.001$), absence of either graft derived or recipient C3 prevented tolerance induction (MST = 14 and 19 days respectively, $p>0.05$). Given the inability to induce tolerance in $C3^{-/-}$ animals, we analysed the natural regulatory T cell compartment in these animals. On the basis of $CD4^+CD25^+$ enumeration, foxp3 expression, and in vitro suppressive capability, there appeared to be no inherent defect in regulatory T cells derived from $C3^{-/-}$ animals.

Conclusions C3 plays a non-redundant role in this model of tolerance induction. Absence of C3 does not appear to affect the thymic generation of $CD4^+CD25^+$ T cells and further experiments will determine whether C3 is important for peripheral regulatory T cell generation. This data suggests complement inhibition must be used with caution in tolerance protocols involving donor lymphocyte infusion.

O24

Widespread Exchange of MHC Between Donor and Recipient Cells In Vivo Following Transplantation: Extent of Semi-Direct Antigen Presentation Pathway

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Introduction Cells have the ability to exchange surface molecules with their neighbours, including intact MHC molecules. The functional significance of this is unknown. Transplantation is the only example in which foreign MHC molecules are deliberately transferred between individuals. However, the extent of this phenomenon in vivo after a solid organ graft is unknown. If donor MHC molecules are transferred whole to the surface of recipient antigen present cells (APC) such as dendritic cells, they will be recognised by recipient T cells that would normally recognise them via the direct antigen presentation pathway, despite being presented by recipient APC. These recipient APC will also express self MHC molecules that can present donor derived peptides, which are recognised by recipient T cells via the indirect pathway. Thus, this "semi-direct" antigen presentation pathway can potentially link allospecific T cells of the direct and indirect pathways to enable bystander activation or regulation (linked suppression).
Methods Vascularised BALB/c or DBA/2 (both H-2^d) kidney or heart allografts were transplanted into BL/6 (H-2^b)recipients. Recipient spleens were harvested at 1, 2, 4 or 8 days post transplantation. Tissue sections were stained for the donor (I-A^d) and recipient (I-A^b) class II MHC molecules using immunofluorescent histochemistry. Cells expressing both donor (stained red) and recipient (green) class II MHC molecules were identified using digital overlay.
Results Following transplantation of BALB/c, DBA/2 kidneys or DBA/2 hearts, the number of donor I-A^d positive cells within recipient spleen rose to a maximum of 16.24$\pm$3.44 cells per high power field (hpf). After staining for recipient I-A^b, followed by digital overlay, cells positive for both donor and recipient class II MHC molecules could be clearly seen. This rose to a peak of 32.92$\pm$13.95% and 11.98$\pm$10.01% of all donor I-A^d positive cells 8 days post transplantation for BALB/c and DBA/2 kidney graft recipients respectively.
Conclusions MHC transfer between donor and recipient cells is a common occurrence following transplantation with up to 30% of cells expressing both donor and recipient MHC molecules, representing a potentially novel and major route of T cell activation which may link allospecific T cells of the direct and indirect pathways.

O25

Therapeutic control of immune responses in pre-sensitized transplant recipients

Stipo Jurcevic, Nicola Gardner, Roseanna Hargreaves, Steven Sacks, Conrad Farrar,
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It is increasingly evident that primed/memory T cells play a major role in the immune response of a transplant recipient to allogeneic graft tissue. Furthermore, primed T cells are resistant to most treatments, which are effective in controlling naive T cell responders.
We have investigated whether we can selectively control the response of pre-sensitised (primed) T cells using the synergistic combination of CD154-specific antibody plus rapamycin. Notably, the naive response to the male (HY) minor histocompatibility antigen is amenable to treatment with either CD154-specific antibody or rapamycin when used as a monotherapy. However, pre-sensitisation with HY antigen (male splenocytes given i.p. to syngeneic females) resulted in a dramatic change in the nature of the anti-HY response. As a result CD154-specific antibody with or without rapamycin failed to extend male (HY) skin graft survival.
The phenotype of the target T cell population (HY-primed CD4+ and CD8+ T cells) was investigated to enable the design of a therapeutic strategy based on increasing the quantity of antibody bound to the activated T cells, such that it reaches a threshold required for their Fc-mediated depletion. It comprised rapamycin together with a combination of antibodies specific for activated T cells, anti -CD154 and -CD70, and a CD8-specific antibody. The latter was used at a very low dose which, as a monotherapy, has only modest and transient depleting effects on the CD8+ T cell population. Rapamycin functioned to contain the expansion of the activated, target T cell population.
This approach, which we termed multi-hit therapy, showed striking effects in the pre-sensitised HY model significantly ($P<0.03$) prolonging skin graft survival (median survival time (MST)=59 days) compared to untreated pre-sensitised controls, which rapidly rejected their grafts (MST=9 days). Furthermore, male skin graft survival in the pre-sensitised multi-hit therapy group was of greater duration than that of untreated, naive recipients (MST=39 days). These data suggest treatment has resulted in the recipient's primed T cell repertoire being depleted of HY-specific immunological memory so that its response to re-challenge is similar to a first set (primary) rejection. This is supported by the absence of primed, HY-tetramer+ T cells in the multi-hit therapy group.

O26

Modulation of dendritic cell function by tissue factor and coagulation proteases

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Introduction; The elements that cause blood to clot have been well understood for many years. More recently it has been realised that these same proteins are involved in other biological processes by direct effects on a family of receptors called protease activated receptors (PARs). Evidence that the coagulation proteases (CP) play a role in the highly specific adaptive immune response includes data from a transplantation model, in which inhibition of coagulation led to indefinite survival of fully MHC mismatched murine cardiac allografts. We hypothesise that CP play a specific role in T cell activation through several potential mechanisms.
Methods; *In vitro,* murine bone marrow-derived dendritic cell (DC) and purified CD4+ T cells are used in primary and two step allogeneic mixed leukocyte reactions (MLR), assessing proliferation and cytokine production. Flow cytometry is used to assess surface expression of molecules and RT-PCR is used to detect expression at mRNA level. *In vivo* experiments comprise intravenous injection of different subsets of DC into mice and re-challenge of the harvested T cells, after 2 weeks, with unmanipulated DC.
Results; Tissue factor (TF) is the main initiator of the coagulation cascade leading to generation of thrombin. We have found a subpopulation of DC express TF with procoagulant activity in a clotting assay using re-calcified mouse plasma. *In vivo* work is underway to further assess the role of TF on DC. When thrombin, one of the activated CP, is added to DC culture 12 to 48 hours prior to harvest, these DC promote an enhanced T cell response in an allogeneic MLR (compared to unmanipulated DC), without detectable changes in surface expression of MHC II, CD80, CD86, CD40, PDL1, PDL2 or ICAM. Work is underway to define differences in resulting cytokine profiles. PARs are expressed on DC suggesting a mechanism through which these cells are able to respond to thrombin and other coagulation proteases. Thrombin has no direct effect on mouse T cell proliferation when activated by CD3/CD28 beads.
Discussion; This is the first report of TF expression on murine DC and the first showing that thrombin has a direct effect on DC. In support of the hypothesis that CP have a specific effect on T cell activation, this work suggests that DC have the ability to generate and respond to CP. These data provide the basis for further work with the potential for new therapeutic approaches to promote allograft survival.

O27

Modification Of Dendritic Cells For The Induction Of Tolerance

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Stimulation of allogeneic T cells requires not only antigen specific signals but also costimulatory signals. The most important of these interactions are between CD80/86 on the antigen presenting cell (APC) and CD28 and CTLA4 on the T cell. Engagement of the T cell receptor in the absence of costimulation can lead to anergy and the subsequent induction of $CD4^+CD25^+$ regulatory T cells (Tregs). T cell activation is also controlled by expression of the tryptophan-catabolising enzyme indoleamine 2,3-dioxygenase (IDO). Depletion of this essential amino acid, and/or the production of tryptophan metabolites inhibits T cell proliferation. We are exploring the potential for using a genetic approach to confer tolerogenic properties on murine dendritic cells (DCs). An intracellular approach, that prevents costimulation, has been developed: A fusion protein, which consists of CTLA4 and KDEL [an endoplasmic reticulum (ER) retention signal], is expressed in APCs. The CTLA4-KDEL binds to CD80/86 in the ER, and in previous work in a human *in vitro* system, this has prevented CD80/86 expression on the DC surface resulting in anergy in antigen-specific T cells. We are now repeating this strategy in the murine system and determining whether CTLA4-KDEL or IDO can prevent allograft rejection. Lentiviral vectors (based on EIAV- equine infectious anaemia virus) containing the murine CTLA4-KDEL construct or the IDO enzyme have been generated. These lentiviruses are capable of efficiently transducing murine bone marrow-derived DCs. The specific downregulation of CD80/86 expression in DCs transduced with EIAV CTLA4-KDEL has been demonstrated, and EIAV CTLA4-KDEL- or EIAV IDO-transduced DCs are unable to induce and/or sustain allogeneic T cell proliferation. Using new two-stage DC:T cell co-culture assays, we are determining whether these EIAV transduced DCs can induce anergy *in vitro* and *in vivo*. Furthermore, using EIAV CTLA4-KDEL, IDO double-transduced DCs, we are assessing whether DCs that express IDO whilst lacking CD80/86 ligation by CTLA4 (CTLA4-CD80/86 ligation upregulates IDO but down-regulates T cell activation) are able to generate new Tregs. The ability of EIAV transduced DCs to induce tolerance to alloantigens is being assessed in a corneal graft model: We are using a murine CBK→CBA strain combination in which rejection results specifically from the indirect pathway of allograft recognition, the predominant pathway of recognition during the chronic phase of allograft rejection.

Plenary Session 2

Medawar Medal

Thursday 29 March

11:00 – 12:30

O28

Antivimentin Antibodies Cause Acute and Chronic Damage In MHC-Matched Allografts

Balakrishnan Mahesh, Hon Leong, Ann McCormack, Angela Holder, Padmini Sarathchandra, John Smith, Marlene Rose

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Introduction: Antivimentin antibodies (AVA) are strongly associated with chronic rejection in human cardiac and renal allograft recipients. Using murine models, we examine the mechanisms of damage caused by AVA.
Methods: C57Bl6 mice (B6; H2b) were immunised with 400μg murine recombinant vimentin in 100μl Complete Freund's Adjuvant (Vim/CFA) to develop an antivimentin response, characterised by high titres of AVA. Controls received 200μg hen-egg lysozyme in CFA (HEL). They then received a 129/sv cardiac allograft (H2b; multiple minor-mismatches). Other vim/CFA B6 recipients were immunosuppressed with 500μg monoclonal anti-CD4 and CD8 antibodies (GK1.5, GK2.43; ATCC) administered intraperitoneally 3 times prior to implantation of allograft to abrogate acute rejection; these allografts were harvested on the 30^{th} and 45^{th} postoperative days. To prove that AVA were pathogenic, B-cell knockout mice on B6 background (IgH6) lacking AVA were adoptively transferred AVA on days -1, 0, 6 following transplantation.
Results: Vim/CFA B6 Recipients showed significantly accelerated rejection of 129/sv allografts [8.4(±1.5) days; n=18] compared to HEL controls [13(±2) days; n=10; P<0.0001]; isografts in Vim/CFA B6 Recipients were not rejected at 90 days. This was mediated by AVA, because passive transfer of AVA restored accelerated rejection in IgH6 recipients [AVA serum: 8.5±2.4days; n=4] [normal serum: 12.3±1.3 days; n=4;p=0.009]. Eluates of allografts from vim/CFA recipients showed greater AVA in Western Blots, and significantly greater complement C3d deposition [31(±8)vs14(±4.5)pixel units;P<0.05] than controls at 2-8 days following transplantation. Confocal microscopy of rejected hearts co-localized vimentin expression and C3d deposition on apoptotic leukocytes, platelet-leukocyte conjugates and activated endothelial cells. In presence of immunosuppression, allografts from vim/CFA recipients showed greater Graft Vasculopathy-GV [% luminal occlusion 49±22%; n=5; controls 31±18%; n=5; p<0.0001].
Conclusions: AVA lead to accelerated rejection in the absence of immunosupression and increased GV when acute rejection is attenuated. This provides evidence of pathogenic role for autoantibodies, and suggests that these autoantibodies may play a major role in acute and chronic rejection of heart and kidney allografts in humans. Endothelial activation and platelet-leukocyte interactions play an important role in this autoimmune process.

O29

Hemeoxygenase-1 is required for Kupffer cell differentiation and cellular survival of hepatic ischaemia

Luke Devey, Stephen Wigmore

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BACKGROUND. Ischaemia reperfusion injury (IRI) arises from the necessary interruption of the hepatic blood supply.during liver retrieval and transplantation. Hemeoxygenase-1 (hmox-1) catalyzes degradation of heme into biliverdin, Fe2+ and carbon monoxide. It has been shown to protect animals and cells from IRI. Hmox-1 is localized within Kupffer cells (KCs). GdCl3 is used to inhibit macrophage phagocytosis, and Liposomal Clodronate (LC) is used to selectively ablate macrophages. METHODS.. Genetically altered littermate hmox-1 +/+, +/-, -/- mice and wildtype C57/B6 animals were treated with GdCl3, liposomal clodronate (LC) or vehicle. Under isoflurane anaesthesia, animals underwent 40 or 50 minutes' hepatic left lobar ischaemia followed by recovery and kill at 24 hours. Blood was analysed for ALT: results are presented as mean +/- SEM. Western blots of liver lysates were performed for hmox-1. Immunohistochemistry was performed for hmox-1 and macrophage markers CD68, CD11b, and F4/80.
RESULTS. 1. Hmox-1 -/- but not hmox +/- mice are susceptible to hepatic IRI and exhibit abnormal KC phenotype. Following 40' hepatic ischaemia, mean ALT was 9515 +/- 1437 (hmox-1 -/-), 403+/- 99 (hmox +/-), 214 +/- 28 (hmox-1 +/+) ($p=0.<0001$). KCs in hmox +/+ and +/- animals were CD11b+ CD68+, F4/80+ whereas KCs in hmox-1 -/- animals were CD11b+, CD68+, F4/80- with aberrant morphology. 2. GdCl3 treated mice are protected from hepatic IRI and have hmox-1 upregulation. Following 50' hepatic ischaemia, mean ALT was 1929 +/- 404 (GdCl3 treated mice) and 4467 +/- 532 (untreated) ($p=0.007$). hmox-1 was upregulated in the GdCl3 group. KCs were CD11b+, CD68+, F4/80+ and of normal number. 3. KC ablated mice have downregulated hmox-1 and are susceptible to hepatic IRI. Following 50' hepatic ischaemia, mean ALT was 19300 +/- 3523 (LC treated mice) and 4467 +/- 532 (untreated mice, as above) ($p<0.0001$). Western blotting demonstrated complete loss of hmox-1 expression in the LC treated group. KCs were entirely ablated.
DISCUSSION. **Hmox-1 is required for hepatic survival from ischaemia reperfusion insults. Furthermore, cellular localization of hmox-1 with KCs is critical: hmox-1 is required for normal differentiation of KCs and conversely, KCs are required for normal hmox-1 stress responses.**

O30

Mononuclear Cell Modulation of Endothelial Cells in Renal Allograft Rejection

Anya Adair, Feng Qi, Tiina Kipari, David Mitchell, Chris Bellamy, Jeremy Hughes, Lorna Marson

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Introduction: Our recent work indicates that cytokine-activated macrophages (Mø) induce nitric oxide (NO)-dependent apoptosis of endothelial cells (EC) *in vitro* and that human renal allograft tissue from kidneys affected by Chronic Allograft Dysfunction (CAD) exhibit increased Mø infiltration, reduced microvascularity and increased numbers of interstitial lymphatics (BTS 2006). In this study we have extended our analysis of human allograft tissue exhibiting CAD by investigating possible mediators of the changes described, and have undertaken Mø depletion experiments in a murine model of acute renal allograft rejection.
Methods: Transplant nephrectomy specimens affected by CAD (n=28) and control kidney (n=19) were studied by immunohistochemistry and immunofluorescence. We performed renal transplants between donor Balb/c mice and either CD11b-DTR mice transgenic for the diphtheria toxin receptor (DTR) under the CD11b promoter or control non-transgenic FVB/N mice. Diphtheria toxin (DT) was administered on days 3 and 5 to induce macrophage depletion and mice sacrificed at day 7. Isograft controls were performed between FVB/N mice.
Results: Human CAD tissue exhibited interstitial expression of vascular endothelial growth factor (VEGF)-A and the lymphatic growth factor, VEGF-C, with double labelling studies indicating CD68 +ve Mø expression of VEGF-C and striking B220 +ve B cell expression of VEGF-A, when compared with controls.
Murine allografts exhibited marked interstitial F4/80+ve Mø infiltration with expression of inducible NO synthase present only in the allografts. There was significant loss of peritubular capillaries (PTC) in allografts compared to isografts, indicating microvascular injury (PTC per 100 tubules reduced by 56.2%, $p<0.01$). DT treated CD11b-DTR mice exhibited 75% reduction in Mø infiltration (1.37±0.6 % area vs 4.93±1.6 %, Mø depleted vs control allografts, $P<0.03$). Mø depletion was associated with dramatic microvascular protection (isograft 130±10 PTC per 100 tubules, FVB/N allograft 90±10, CD11b-DTR allograft 131±10, $p<0.03$) and preservation of normal PTC morphology.
Conclusion: Mø directly injure the microvasculature in experimental acute rejection through action of nitric oxide. Our recent work on human CAD suggests a role for Mø and B cells in promoting lymphangiogenesis through the production of VEGF-C and –A. Targeting these cells may provide therapeutic strategies in CAD.

O31

Pathways of CD4 T Cell Help For Autoantibody Production In Chronic Allograft Rejection

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Introduction:
Recent studies suggest that allo- and auto-antibody are involved in the development of chronic rejection. Although production of alloantibody requires help from indirectly-activated CD4 T cells, it is unclear how help is provided for generating autoantibody. This study examines the pathways of T helper cell activation in the development of autoantibody in chronic cardiac allograft rejection.
Methods:
B6 mice were grafted with Bm12 hearts, a strain combination that differs at only 3 a.a residues within the I-A MHC CII antigen. Serial development of allo- and auto-antibody was assessed by incubating sera with either target Bm12 dendritic cells or nuclear-antigen-expressing HEp2 cells. The role of indirect allorecognition was examined by immunizing B6 mice, 14 days prior to transplantation, with a synthetic 20mer peptide that corresponds to the disparate region of $I\text{-}A^{bm12}$ antigen.
Results:
B6 mice rejected Bm12 hearts slowly (MST=95, n=13). Histological examination of hearts harvested at day 50 revealed a vascular humoral component (C4d staining and arteriolar fibrinoid necrosis). Surprisingly, only autoantibody, but not alloantibody, was detected in the sera of transplanted animals. Neither MHC CII KO, CD4 T cell deficient recipients nor syngeneic controls developed autoantibody, suggesting its development is dependent upon CD4 T cell allorecognition. To test this, B6 mice were primed for indirect allorecognition by immunizing with Bm12 allopeptide. Although subsequent heart grafts were rejected more rapidly (MST=35, n=6), autoantibody responses were comparable to WT. Interestingly, treating Bm12 mice with depleting anti-CD4 monoclonal antibody prior to donation abrogated autoantibody responses in B6 recipients, suggesting that help for autoantibody production is provided by graft resident donor CD4 T cells that recognise allogeneic MHC CII on recipient B cells.
Conclusions:
Humoral vascular rejection may be effected by autoantibody in the absence of a demonstrable alloantibody response. Recipient CD4 T cell allorecognition is not responsible for providing autoreactive B cell help; help is instead provided by donor CD4 T cell allorecognition of recipient B cells in a graft-vs-host response.

O32

DRI and MELD trends in a decade of Liver Transplantation: A single centre experience

Glenn Bonney, Sonal Asthana, John Davies, Peter Lodge, Stephen Pollard, Giles Toogood, Raj Prasad

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Introduction

Schaubel et al and unpublished data from our centre has shown that the transplantation of high Donor Risk Index (DRI)organs in low and intermediate MELD categories (MELD <15 and 15-30 respectively) results in poorer graft survival rate. We aimed to analyse the trend in DRI and MELD scores at our centre.

Methods

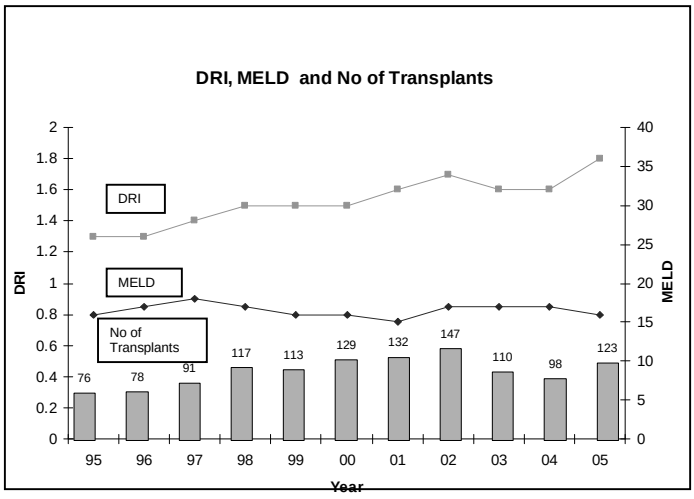
Prospectively collected data of all patients transplanted at our centre between 01/95 and 12/05 were included in this retrospective analysis (n=1213). The DRI and MELD at transplantation were calculated using published methods. The trend of these scores were tabulated over the 10 year period.

Results

From 01/95 to 12/05, 1213 liver transplantations were performed at our centre. The trend of DRI and MELD at transplantation was as shown in graph below. There was an overall trend towards a rising DRI (median=1.54), with the highest score being 1.8 in 2005. However, with a median of 17, there was a generally unchanged MELD score at transplantation over the 10 year period.

Conclusion

The increasing need for organs to serve the waiting list has resulted in a trend towards the transplantation of grafts with a higher DRI, which might have a negative affect on graft survival. The Donor Risk Index needs to be taken into account when comparing outcomes of transplantation.



O33

Ex Vivo Generation of Regulatory T Cells that Prevent Skin and Islet Allograft Rejection: A Novel Role for IFN-γ

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Background Regulatory T cells (Treg) play an important role in models of autoimmunity, GVHD and transplantation and offer potential as a cellular therapy. In rodent models, in vivo generated $CD25^+CD4^+$ T cells can prevent allograft rejection but therapeutic exploitation of Treg will more likely depend on protocols that allow generation or selection of Treg ex vivo.

Methods and Results Ex vivo alloantigen stimulation in the presence of the pro-inflammatory cytokine IFN-γ results in a population of T cells (IFN-γ conditioned cells) that prevent skin graft rejection in an adoptive transfer model. IFN-γ conditioned CBA ($H2^k$) $CD4^+$ T cells were harvested after two rounds of stimulation with B10 ($H2^b$) bone marrow derived DCs in the presence of 5ng/ml recombinant IFN-γ and transferred (2×10^5) into CBA-$Rag^{-/-}$ mice with 1×10^5 naive $CD25^-CD4^+$ cells as effectors. Mice were transplanted with B10 skin grafts 1 day later. Reconstitution with $CD25^-CD4^+$ cells resulted in acute graft rejection (MST=22 days, n=4), but this was prevented completely by co-transfer of IFN-γ conditioned cells (MST>100 days, n=20 in 5 independent experiments). IFN-γ conditioning results in increased activation induced cell death (24% vs. 15%, presence and absence of IFN-γ respectively) and inhibition of proliferation correlates with stable up-regulation of Foxp3 expression within the responding population (27% vs. 3%, presence and absence of IFN-γ respectively). IFN-γ conditioned Treg can be generated from $Foxp3^-$ $CD25^-$ precursors but pre-existing $CD25^+$ T cells contribute to this process. As with in vivo generated Treg, regulation mediated by IFN-γ conditioned Treg is dependent on CTLA-4 as CTLA-4 blockade abolished regulation (MST=16 days, n=3). Importantly, co-transfer of IFN-γ conditioned Treg also prevents the rejection of islet allografts under physiological load in an STZ-induced diabetes model ($CD25^-CD4^+$ cells only, MST=18 days, n=2; co-transfer $CD25^-CD4^+$ cells and IFN-γ conditioned Treg, MST>100 days, mean blood glucose 7.9 mmol/L, n=3).

Conclusion Alloantigen-reactive Treg can be generated/expanded ex vivo using IFN-γ, a cytokine more usually associated with allograft rejection. The fact that these cells regulate the rejection of both skin and islet allografts without further enrichment or sorting indicates a potential route for the generation of Treg in numbers sufficient for therapeutic use.

Parallel Session 4

Joint symposium with British Society for Histocompatibility and Immunogenetics

Thursday 28 March

14:30 – 18:30

O34

The Frequency and Cause of Unexpected Positive Deceased Donor Crossmatches

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Defining HLA antibody specificities for patients on the transplant list is intended to predict positive crossmatches (XMs) and thus prevent unnecessary shipping of organs. However, despite comprehensive antibody identification protocols a number of unexpected positive XMs occur. This study investigated positive flow cytometry XM results with the aim of identifying the causes of the positive results and any improvements which could be made to antibody testing protocols.

A total of 110 consecutive deceased donor XMs were analysed. These were split into 2 groups, 12 months prior to and 6 months following the change in the National kidney allocation scheme in April 06. Results were classified as negative, irrelevant positive (not regarded as a contra-indication to transplantation e.g. auto-antibody) and unexpected positive. Unexpected positive samples were further investigated using single antigen beads to identify additional HLA specificities.

There were 66 XMs between April 05 and March 06 of which 6 (9%) were unexpected positives. From April-Sept 06 11/44 XMs (25%) were unexpected positives. The 17 positive XMs involved 14 patients, all with HLA class I and/or class II specific antibodies with an average peak reaction frequency of 89%. Single antigen bead testing identified donor specific antibodies that conventional Luminex and ELISA analysis had been unable to define in most patients. In 4 cases allele specific antibodies to antigens within the same broad antigen group as the patient were found to be responsible for the positive XM. Antibodies specific for HLA-DP antigens were also found in 4 patients.

This study shows that the change to the national allocation scheme has resulted in an increase in positive XMs due to offers to highly sensitised patients. The use of single antigen beads improves the specificity definition for HLA antibodies in these patients and, if introduced into routine testing, should help reduce the occurrence of positive XMs. Detection of allele specific antibodies emphasises the importance of meeting the UK Transplant minimum reporting criteria for HLA in order to eliminate inappropriate offers from donors with offer types lacking sufficient resolution. The detection of HLA-DP specific antibodies raises the question of whether donor typing should include HLA-DP. Without sufficiently detailed information on donor HLA types the level of accuracy afforded by single antigen beads cannot be utilised to the full in preventing unexpected positive XMs.

O35

Kidney after cardiothoracic or liver transplant: the effect of repeat mismatches on outcome

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This study examines the effect of repeat HLA-A, B and DR mismatches on the outcome of renal allografts in patients that have previously received a non-renal solid organ transplant.
All heart, lung or liver transplant patients who received a first deceased or living donor renal transplant, between 1.1.99 and 31.12.03 were included. Subjects were censored at death, kidney graft failure or end of follow-up, 31.12.05. The listing of unacceptable antigens together with the tissue type of the recipient, the previous solid organ transplant and the sequential renal allograft were reviewed. Individualised questionnaires were also sent out to transplant centres to supplement UKT data.
The cohort comprised 87 patients, median age 46 years, male gender 72%. Twenty-five percent received living donor kidneys. Patients who had unacceptable antigens listed (n=21) waited no longer to receive a renal transplant than those without unacceptable antigens (median wait 268 v 363 days, respectively, p=n.s., recipients of living donor kidneys excluded). Exposure to a repeat HLA mismatch occurred in 20 (23%) renal allograft recipients. There was no difference between the groups with and without a repeat mismatch in terms of recipient age, donor age, recipient-donor age difference, gender, donor type or cold ischaemia time. Recipients of kidneys with a repeat mismatch were more likely to receive a non-favourably matched allograft than those receiving a kidney that had no repeat mismatch (75% vs. 37%, respectively, p=0.007). There were no differences in initial or 12-month immune suppression therapy between the two groups. Kidney allograft function at 2 years was significantly better in recipients with no repeat mismatch (eGFR 52.7 vs. 42.0 ml/min/1.73m^2, p=0.02), but graft survival was not significantly different between the two patient groups (85% and 95%, respectively, p=n.s.).
This is the first study to examine the association between repeat mismatches and outcome in non-renal solid organ transplant patients receiving sequential kidney allografts. In this cohort of all sequential renal transplants over a 6-year period, listing previously exposed antigens as unacceptable does not appear to be associated with longer waiting times. Repeat mismatches are associated with poorer kidney allograft function, but not survival, at two years.

O36

Flow-PRA characterisation of de novo anti-HLA class I donor specific antibodies in patients with apparent 'transplant accommodation'.

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Introduction; Some patients maintain good transplant function despite the presence of circulating donor-specific antibodies (DSA). The graft in these cases may show evidence of 'transplant accommodation'. So far, this has only been investigated in patients who have been through a desensitisation procedure prior to ABO incompatible or HLA-sensitised transplantation. This study was to define the characteristics of de novo anti-HLA DSA in a group with stable graft function and apparent accommodation.
Methods; 35 renal transplant recipients attending clinic met the following inclusion criteria and were recruited to this pilot study; >1 year post transplantation; all pre-transplant PRAs negative; grafts mismatched for at least one HLA class I; stable function as assessed by reciprocal creatinine plots. Serum was tested by FlowPRA screening test followed by single class I-coated beads. Serum from16 HLA-A2-neg recipients of A2+ grafts was also tested by flow cytometry on C1R-A2, a human lymphoma line expressing A2 as the only class I HLA antigen.
Results; 8/35 (22%) samples were positive on FlowPRA screening test although only 2/35 (6%) were positive for DSA on single antigen beads. One of these was strongly positive for anti-HLA A2 DSA and therefore underwent characterisation on C1R-A2 cells. By flow cytometry, the serum showed no specific binding, indicating that the DSA were unable to bind intact, native A2. Serum from a third patient (which according to the manufacturer's criteria had 'undetermined' binding to HLA-A2 FlowPRA beads) showed specific binding to C1R-A2 but not parental C1R cells. Follow-up samples, obtained >1 year later from both patients with anti-A2 DSA have shown the same pattern of staining. Both have stable graft function.
Discussion; The 22% prevalence of circulating de novo anti-HLA class I antibodies is consistent with data from other studies. Only 3 (9%) had evidence of anti-HLA class I DSA, consistent with accommodation. However, in the 2 patients where further analysis was possible, comparing binding to beads with that to native, membrane-expresssed HLA-A2, we found that only 1 patient had DSA that could bind intact graft antigens. This study confirms the existence of patients with de novo circulating DSA and stable graft function (apparent accommodation), but indicates that only some of these DSA having binding characteristics consistent with 'true' accommodation.

O37

Rejection Rates in HLA Antibody Incompatible Renal Transplantation.

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Quantification of the rejection risk in HLA antibody incompatible (HLAi) transplantation would reduce the risks and costs.
Thirty patients received HLAi transplants in our centre from 2003-6. Age range was 22-66 yrs, 21 were regrafts and 9 first grafts. 4 had deceased and 26 had living donors. 9 were complement dependent cytotoxic (CDC) crossmatch (XM) +ve before treatment, 14 were flow cytometric (FC) XM +ve, and 7 had donor specific antibodies (DSA) detected by Luminex bead only. Pre-transplant plasmapheresis was used in 25 patients. Daily monitoring of DSA by Luminex was performed post-transplant. Two patients died in the first week, 28 were evaluated.
The incidence of rejection was associated with DSA levels; 5/9 (56%); 5/12 (42%); 1/7 (14%) in CDC XM; FC XM; bead +ve respectively. 3/13 (23%) with HLA Class 1 (but not HLA DR) DSA had rejection.7/11 (64%) with HLA DR DSA had rejection (many of these also had Class 1 and DP/DQ or DRB3/4/5 DSA). In those with only DQ, DP or DRB3/4/5 DSA, 2/4 (50%) had rejection. 2/8 (25%) first grafts had rejection, and 9/21 (43%) regrafts. All rejection episodes were vascular. In 100 ‘standard’ transplants in our unit in the same time period, 9% had vascular and 15% had cellular rejection.
Five patients were dialysed for severe rejection. 2 had Class 1 DSA, 2 had Class 1 + HLA DR DSA, 1 had HLA DR DSA. 3 were FC XM +ve pre-treatment, one was bead only +ve and 1 was CDC XM +ve. All 5 were regrafts. Nine rejection episodes were fully reversed, using high dose steroids and antibody therapy (usually OKT3) in the majority of patients. One rejection episode partially reversed, further dysfunction was caused by a thrombotic microangiopathy, and the graft failed at 3 months.
In summary, the occurrence of rejection in HLAi transplantation was associated with antibody level and specificity, and this assists patient selection and treatment. However, severe rejection occurred in regrafted patients irrespective of antibody specificity or level.

O38

Alloantibody and Proteinuria After Kidney Transplantation

William McKane[1], Badri Shrestha[1], Carole Angel[2], John Goodwin[3], Andrea Harmer[3]

[1]Sheffield Kidney Institute, Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, United Kingdom, [2]Department of Histopathology, Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, United Kingdom, [3]Histocompatibility and Immunogenetics, National Blood Service, Sheffield, United Kingdom

Introduction: Alloantibody detected after kidney transplantation is associated with a poor outcome. Some authors have proposed that non-donor specific alloantibody (NDSA) and donor-specific alloantibody (DSA) are equally hazardous for the graft and not all centres determine antibody specificity after transplantation.

Method: Transplant patients in our institution have been tested at least annually since 2000 by a combination of ELISA, Flow PRA and Luminex to screen for alloantibody and determine specificity. Data from 524 prevalent patients transplanted 1985-2005 with grafts surviving after 2000 were available for analysis. Patients who were allosensitised at the time of transplantation were excluded.

Results: Twenty-seven (5.2%) patients developed DSA prior to graft failure and 19 (3.6%) developed NDSA. 46% had class I antibody, 48% class II antibody and 6% both, with no difference in species distribution between the two groups (p=0.52). Anti-DQ antibodies were common (30% DSA, 16%NDSA, p=0.32). The mean time to antibody detection was 6.1 years DSA and 6.8 years NDSA. Characteristics of the two groups are shown in the table below.

	Female	**Regraft**	**HLA mismatch**	**AR**	**Mean peak proteinuria**	**Graft loss**
DSA	44%	11%	2.6	74%	3.8g/l	26%
NDSA	53%	16%	2.6	42%	1.0g/l	11%
p value	0.765	0.68	0.996	**0.04**	**0.001**	**0.04**

The most striking difference between the two groups was the maximum degree of proteinuria, with over half of the DSA group developing nephrotic syndrome. Significant proteinuria pre-dated detection of alloantibody in 59% of DSA patients. Although a prior rejection episode was common, acute humoral rejection was only seen in 22% of DSA cases and many presented in a sub-acute manner with glomerulopathy. Nevertheless, graft losses were common in the DSA group.
Discussion: DSA is associated with heavy proteinuria and poor outcome but this is not necessarily the case for NDSA. The prognostic value of post-transplant alloantibody surveillance is improved by accurate determination of specificity.

Parallel Session 5

Liver Transplantation

Thursday 29 March

14:00 – 15:30

O39

Incidence and risk factors associated with early hepatic artery thrombosis in patients undergoing orthotopic liver transplantation: a multivariable analysis.

Giuseppe Fusai[1], Parveen Dhaliwal[1], Nancy Rolando[1], Caroline Anne Sabin[2], David Patch[1], Andrew Kenneth Burroughs[1], Keith Rolles[1], Brian Ritchie Davidson[1]

[1]Liver Transplantation & Hepatobiliary Unit, Royal Free Hospital, London, United Kingdom, [2]Department of Primary Care & Population Sciences, Royal Free Hospital, London, United Kingdom

Hepatic artery thrombosis (HAT) is a dramatic complication which is reported in up to 10% of patients undergoing orthotopic liver transplantation (OLT). The consequences are dramatic and inevitably cause graft loss. Knowledge and correction of the predisposing factors might reduce the incidence of early HAT.

The database included 914 consecutive patients undergoing OLT between 1988 and 2005 in a single institution. Early HAT was diagnosed if occurred within the first 30 days postoperatively. Donor and recipient arterial anatomy and the number of arterial anastomoses were documented. Aetiology of liver disease, graft number, donor and recipient blood group, CMV status, intraoperative use of blood products, cold ischaemia and reperfusion times were also recorded.

The incidence of early HAT was 4.6%. Graft number, abnormal arterial anatomy, number of arterial anastomoses, arterial bench work, reperfusion time and number of units of blood received intraoperatively were significantly associated with early HAT in univariate analysis ($p<0.10$). These variables were included in a multiple regression model which suggested that the need for bench arterial reconstruction is associated with a 4-fold risk of early HAT [$p<0.0001$, Risk Hazard 3.55 (95% CI 1.89-6.66)], whereas each additional 10 minutes of reperfusion correlates with a 27% increase in the risk of early HAT [$p<0.04$, Risk Hazard 1.27 (95% CI 1.02-1.60).

Early HAT is primarily associated with surgical risk factors. Selective anticoagulation and strict surveillance protocols with arterial Doppler for patients at risk might be beneficial.

O40

Hepatic Venous Outflow Obstruction after Orthotopic Liver Transplantation – A Single Centre 10 Year Experience.

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Introduction: Hepatic venous outflow obstruction is rare but significant complication post orthotopic liver transplantation (OLT). We report our experience of hepatic venous outflow obstruction after orthotopic liver transplantation and evaluate outcome of endovascular treatment.
Methods: A retrospective analysis of the period from 1996 to 2006 of adult patients confirmed to have hepatic outflow obstruction and referred for endovascular treatment. Grafts were all whole livers and transplanted either with or without preservation of the retrohepatic inferior vena cava (IVC). Pressure gradients before and after venoplasty were compared using Mann-Whitney test. Patients in whom obstruction recurred were reassessed and treated with repeat venoplasty with or without insertion of expandable stents. Technical success was measured by pressure gradient reduction, angiographic and clinical improvement.
Results: 1096 liver transplants were carried out in the study period. 21 patients (1.9%) were confirmed to have hepatic outflow obstruction and treated endovascularly. 48% of patients had stenosis of the IVC alone and 48% involving both vena cava and hepatic veins (HV). The single most common presenting clinical feature was ascites 82%. The time from transplant to first intervention ranged from 13-941 days (median 178). Median interventions per patient was 2. The interval between interventions was 9-3274 days (median 221). The mean pressure gradients fell from 12mmHg to 4mmHg post primary intervention ($p=<0.001$). 90% of patients had resolution of ascites at 3 months. Re-intervention rate at 6 months was 53% and 90% at 12 months. 10/21 patients (48%) ultimately required stents and 9/21 patients (43%) were treated with repeated venoplasty. Equal numbers of patients with IVC and IVC and HV stenosis required stenting but there was difference in time to reintervention post-primary venoplasty between these two groups; 759.9days (17-3311) vs. 69.8 days (40-148) respectively. No significant stenosis occurred after stent placement.
Conclusion: Hepatic outflow obstruction remains an uncommon complication following OLT. Venoplasty is an effective treatment for post transplant hepatic venous outflow obstruction and stent placement reserved for patients with restenosis or resistant to venoplasty. Stenosis of IVC and hepatic veins required reintervention earlier compared to isolated IVC stenosis.

O41

Long term outcome following liver transplantation for paracetamol overdose in Scotland

Lucy Khan, Gabriel Oniscu, James Powell

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Background: Paracetamol overdose (POD) is a major cause of fulminant hepatic failure (FHF) requiring liver transplantation in the United Kingdom.
Aim: To characterise the early and late outcome after orthotopic liver transplantation (OLT) for paracetamol overdose in the Scottish Liver Transplant Unit over a 14 year period (1992-2006).
Methods: Of 127 liver transplants performed for FHF, 44 (20 male) were undertaken for paracetamol overdose. The median age was 32 (range 18-51). Data were obtained from a prospective database supplemented by case-note review.
Results: 18 patients (63.7%) overdosed in association with alcohol or other drugs, 9 (20.5%) had a staggered overdose and only 4 patients (9.1%) had an accidental overdose. 19 patients (43.2%) had a history of previous overdose or psychiatric illness. The mean time interval between admission and transplantation was 50 hours (range 12.5-156). The mortality rate during the index admission was 30% (13 patients), whilst 5 died during follow-up. The cause of death is shown in the table. The 5 year patient survival was 59%, whilst the graft survival was 54%. Biliary complications occurred in 7 (27%) patients. Re-transplantation was required in 6 patients (3 patients one OLT and 3 patients 2 OLTs). To date, 9 patients (35%) patients continue to have social/psychiatric issues. Only 3 patients (12%) have no complications or ongoing problems at follow up.
Conclusion: OLT for POD is associated with significant early and late morbidity and mortality. Few return to normal. Options such as auxiliary transplantation should be explored to minimise organ usage and long term transplant related morbidity.

Cause of death	Index admission (n=13)	During follow-up (n=5)
Cardiac intra-operative	2	1 (2^{nd} transplant)
Sepsis/organ failure	4	2
Cerebrovascular	3	
Hepatic artery thrombosis	1	1
Primary non-function	1	
Peritonitis	1	
Pulmonary haemorrhage	1	
Immunosuppression related		1

O42

Sixty minutes of warm ischaemia: resuscitation of livers by normothermic perfusion.

Debabrata Roy, Karl Morten, Shantanu Bhattacharya, Russel Jamieson, Laura Vay, Dino Guerreiro, David Hughes, Richard Taylor

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Background: Livers from non-heart-beating-donors (NHBD) are an important approach to alleviating the donor organ shortage. However, the liver does not tolerate prolonged warm ischaemia followed by cold preservation and, as a result, the application of non-heart-beating-donors has had limited impact in clinical liver transplantation to date. The aim of this study is to investigate whether addition of normothermic recirculation prior to retrieval complements the already proven benefit of normothermic preservation.
Material & Methods: Porcine livers were subjected to 60 minutes of warm ischaemia and assigned to the following groups. Group NR (Normothermic recirculation, n=5), had in situ oxygenated perfusion (NR) for 1 hour followed by normothermic preservation for 23 hours. Group C (Control, n=5) did not receive NR, but were otherwise treated in the same way. Both groups were subjected to transient cooling during the bench work prior to warm preservation. We assessed liver viability both during preservation and during 24 hours of subsequent reperfusion (a surrogate for transplantation). Serum transaminases, bile production, base deficit and ATP levels were measured. The apoptotic and necrotic changes after reperfusion were examined by TUNEL and haematoxylin staining.
Results: Cellular ATP levels declined sharply during 60 minutes of warm ischaemia (by 90% of the basal level, $p<0.01$). NR improved mitochondrial function (mitochondrial respiratory control ratio, 6.05 ± 0.60 vs. 3.09 ± 0.24, $p<0.05$) and ATP levels significantly ($p< 0.01$). This effect was maintained throughout the period of warm preservation and associated with greater functional recovery of the Group NR livers with superior bile production ($p<0.05$), base deficit ($p<0.05$) and reduced hepatocellular ($p<0.01$) damage. Both apoptosis and necrosis were attenuated in the NR group with significantly greater destruction of architecture on histology in group C livers.
Conclusion: The resuscitation of NHBD livers (60 minutes of warm ischaemia) is improved significantly by a combination of normothermic recirculation and normothermic preservation. This may have important clinical implications.

Parallel Session 6

Cardio – Thoracic Transplantation

Thursday 29 March

14:00 – 15:30

O43

Improved renal function after switch from ciclosporin to mycophenolate-sirolimus immunosuppression: experience with 2 regimens after heart transplantation

Haifa Lyster, Neil Leaver, Iman Hamour, Andrew Palmer, Nick Banner

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Calcineurin inhibitors (CNIs) are the mainstay of immunosuppression after heart transplantation but are associated with nephrotoxicity. We compared 2 ciclosporin (CsA) elimination protocols in 37 heart transplant recipients with renal impairment. CsA was stopped and sirolimus (SRL) commenced immediately. In protocol A, 14 patients (13 male, mean age 56±12 years) were switched from July 02 to August 03, SRL target level was16 (12-20)ng/ml. Those on mycophenolate (MMF) continued; those on azathioprine (AZA) were transferred to MMF 1g bd. The transfer period was covered with 30mg prednisolone (PRED) daily which was subsequently tapered. As a result of our experience with protocol A, a second protocol was introduced. In protocol B, 23 patients (all male, mean age 54±15 years) were switched March 04-06. Those patients who were receiving AZA were transferred to MMF two weeks prior to the switch; SRL target level was 7 (5-10)ng/ml. The switch was covered with 10mg PRED daily. Graft function was assessed clinically, by echo and, when indicated, biopsy. Baseline eGFR (MDRD) (A 21±7 vs B 26±12 ml/min/1.73m^2, p=0.18), 24 hour proteinuria (0.41±0.34 vs 0.74±1.5 g, p=0.84) and ciclosporin level (155±58 vs 126±57ng/ml, p=0.16) were similar in both groups, but those in protocol B were later after their transplant (mean of 37.2 vs 90.1 months, p=0.006). Early improvement in eGFR was similar in protocol A and B, with a mean increase in eGFR of 14.5±19 vs 15.8±20 ml/min/1.73m^2, p=0.96 respectively at 1 month post-switch; this was maintained subsequently. Proteinuria increased following the switch to SRL with a mean increase of 0.57±0.9 vs 0.27±0.6 g/24 hours p=0.67. Seven patients discontinued SRL in protocol A: 2 experienced grade 3A rejection, 1 a fall in LVEF without histological rejection, 1 progressive renal failure and 3 had serious side-effects (leucopenia and thrombocytopenia in 1, pneumonitis in 1 and severe acneform rash complicated by an axillary abscess in 1). Seven discontinued in protocol B: heavy proteinuria in 1, diarrhoea and acne in 2, pulmonary thromboembolism in 1 and there were 3 deaths (1 PTLD, 2 graft vascular disease). There were no acute rejection episodes in protocol B. 13 out of the 14 discontinuations occurred within 6 months. MMF-SRL substitution resulted in a prompt improvement in renal function that was maintained. 50% remained on protocol A long term and 70% remained on protocol B.

O44

Decreased Utility of Routine Surveillance Endomyocardial Biopsies after Heart Transplantation with Contemporary Immunosuppression In The First Year

Iman M Hamour, Mathen G Panicker, Rajasi Banerjee, Alex D Bell, Margaret M Burke, Nicholas R Banner

The Royal Brompton and Harefield NHS trust, Harefield Hospital, Harefield, Middlesex, United Kingdom

Routine surveillance endomyocardial biopsies (EMBx) are used in most centres for the early detection of acute cardiac allograft rejection. Biopsy protocols became standardised in an earlier immunosuppression era. We compared the yield of such a protocol with azathioprine (AZA) or mycophenolate mofetil (MMF) immunosuppression.
We studied 258 patients following heart transplantation [207 (80%) male; mean age 50 yrs (range 18-68)] comparing 135 patients immunosuppressed by MMF with 123 patients treated by AZA (both with ciclosporin (Neoral) and corticosteroids after induction therapy with RATG). Survival at 1-year in the MMF group was 81.5% and the AZA 80.5%. Fifteen EMBx were scheduled per patient in the first year. Additional EMBx were performed for suspected rejection, following treatment or inadequate samples. The MMF group had 1875 EMBx performed within the first year vs 1854 in the AZA group.
The yield of ISHLT grade $\geq$3a biopsy-proven acute rejection (BPAR) was 37 (1.9% of biopsies) MMF vs. 56 (3%) AZA. In the MMF group 26.8% (n=11) of BPAR were symptomatic vs. 33.3% (23) AZA group. The proportion of biopsies associated with treatment for rejection was 3.6% (65) MMF vs 4.4% (82) AZA. Symptomatic low-grade rejection (ISHLT grade <3a) were similar; 21(1.1% of biopsies) MMF vs. 22 (1.2%) AZA, while clinically diagnosed, biopsy-negative rejection was 28 (1.5% of biopsies) MMF vs. 15 (0.8%) AZA. The number of asymptomatic BPAR that lead to change in treatment (the true yield of routine surveillance) was 30 (1.6% of biopsies) MMF vs. 46 (2.5%) AZA. The incidence of any complication per biopsy was 1.1% (42). However, the total number of patients experiencing a complication within 1-year was 16.2%. The number of serious complications requiring intervention or with long term sequelae was only 0.13 % (5). There was no biopsy-related mortality.
The yield of BPAR per biopsy was low. The incidence of complications and serious complications per EMBx was low but repeated biopsies led to a higher rate of complications per patient. The role of routine surveillance EMBx and the frequency of such biopsies should be re-evaluated in the light of their low yield under current immunosuppression protocols

O45

Chronic Kidney Disease After Heart Transplantation A 10-year Perspective

Iman M Hamour, Fazir Omar, Haifa S Lyster, Andrew Palmer, Nicholas R Banner

The Royal Brompton and Harefield NHS Trust, Harefield Hospital, Harefield,Middlsex, United Kingdom

Chronic kidney disease (CKD) is a recognised complication of organ transplantation. We analysed the renal function of 352 patients who underwent heart transplantation (HTx) at our centre between January 1995 and January 2005. There were 282 males (80%); the mean age was 48 years (range 18-71). Ischaemic heart disease was the indication for HTx in 185 (53%) and dilated cardiomyopathy in 147 (42%). Actuarial patient survival was 78.7% at 1-year, 77.4% at 3 years and 62% at 10 years.

Three immunosuppression protocols were used;[1]full dose ciclosporin (Neoral or Sandimmune aiming for C12 levels of 250-350 ng/ml initially) , azathioprine and corticosteroids, only using antithymocyte globulin (ATG) in cases where ciclosporin (CsA) was temporarily omitted because of postoperative renal failure;[2] full dose Neoral ciclosporin after ATG induction therapy, azathioprine and corticosteroids;[3] ATG induction followed by lower dose Neoral CsA (aiming for C12 levels of 200-300 ng/ml initially), combined with mycophenolate mofetil (MMF) and corticosteroids.

Pre-transplant estimated glomerular filtration rate (eGFR) by MDRD was 63.7 ml/min per 1.73m², inter-quartile range (IQR) 54-78. After transplantation the eGFR was 48(IQR 37-61) at year-1, 45(33.5-63) at year-5 and 40.6(35.1-56.9) at year-10. The cumulative probability of renal dysfunction with eGFR <45 ml/min per 1.73m² was 45.5% at 1-year, 71% at 5 years and 83.3% at 10 years. Seventeen patients required long-term renal replacement therapy. A multivariable logistic regression model was constructed for the development of eGFR<45 ml/min per 1.73m² by 3 years The risk factors that were identified were post-operative acute renal failure, p=0.0001; pre-transplant diabetes mellitus, p=0.005; increased recipient age, p=0.0001; female recipient, p=0.03 and a female cardiac donor, p=0.04. The cumulative probability of developing stage 5 CKD (eGFR<15) was 3% at 5 years and 12 % at 10 years. Although lower CsA levels coupled with MMF use was associated with less renal dysfunction at 1-year (p=0.03), there was no significant effect by 3 years (p=0.6).

The incidence of eGFR<45 increased with time and more than 80% of patients were affected at 10 years. Risk factors were postoperative acute renal failure, pre-transplant diabetes mellitus, increasing recipient age together with female organ donor and recipient. Although calcineurin inhibitors play a role in CKD post HTx other factors are also important Measures to reduce the incidence of post-operative acute renal failure may help reduce the burden of CKD.

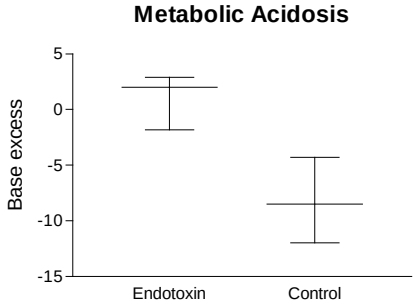
O46

Endotoxin tolerance: protection against the haemodynamic injury of brain death

Anthony Rostron, Vassilios Avlonitis, David Cork, John Dark, John Kirby

School of Surgical and Reproductive Sciences, University of Newcastle, Newcastle upon Tyne, United Kingdom

Introduction: Brain death (BD) induces transient hypertension and sustained hypotension which leads to suboptimal organ perfusion. Ischaemia of the gut compromises its barrier function leading to increased endotoxin translocation which potentially enhances the systemic inflammatory response (SIRS) and exacerbates the hypotension observed after BD. Importantly, repeated sub-lethal doses of lipopolysaccharide (LPS) induce tolerance to endotoxin. This series of experiments was designed to determine whether endotoxin tolerance (ET) can protect against the haemodynamic injury associated with BD.
Methods: ET was induced in a group of rats (n=7) by daily intraperitoneal injection of 0.5mg LPS (*E.coli* O55:B5) for 5 days. Matched control animals were injected with equal volumes of apyrogenic saline. The endotoxin-treated animals showed an initial 11.8% weight loss ($p<0.001$). On day 8, rats were anaesthetized, ventilated and BD was induced by intracranial balloon inflation. The haemodynamic response to BD was monitored for 5h. Arterial blood gases were measured and flow cytometry was used to assess the expression of CD11b/CD18 by peripheral blood neutrophils.



Results: Haemodynamic deterioration following the sympathetic storm associated with BD was more marked in the control group and led to a complete haemodynamic collapse in one control animal. After 1h the mean arterial pressure of ET was significantly higher than in control animals ($p<0.05$); this difference was maintained over 5h and prevented the development of metabolic acidosis (Figure; $p<0.005$). Blood neutrophil integrin expression increased progressively with time in both groups, and by 3h the expression of CD11b was 30% higher in the controls.
Conclusions: ET slows the haemodynamic deterioration following BD, prevents the development of metabolic acidosis and affords some protection against cardiac arrest. Furthermore, ET prevents systemic neutrophil activation in the brain dead donor, suggesting modulation of SIRS.
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Session 7

New Initiatives in Donor CoOrdination
UKTCA

Thursday 29 March

16:00 – 18:15

O47

Unit Based Time Strategy Has Improved Donor Identification And Referral Rate

Andrew Broderick

Plymouth University, Plymouth, Devon, United Kingdom

Introduction
Implementing the unit based time strategy will aid the donor co-ordinator in becoming a functioning part of the Intensive Care Unit (ICU) team in each hospital and re-educating the medical and nursing staff in donor identification and referral.
Methods
The strategy was based on the role of the In House Co-ordinator but was adapted to meet the needs of each unit. The Donor Co-ordinator would attend the ICU once each week and attend the ward round, undertake ad-hoc and formal education of staff, complete the Potential Donor Audit (PDA), aid staff in the identification of potential organ donors, participate in the approach of relatives for consent for organ donation and provide debrief sessions for staff involved in caring for organ donors. The strategy was piloted in two referring ICU's referred to as ICU P and ICU B. Evaluation would be by knowledge questionnaires and review of PDA data.
Results
Between 1st September 2004 and 31August 2005 data from the PDA showed ICU B had 3 patients likely to be Brain Stem Dead (BSD) 2 were not identified as potential donors The third was identified but the family refused consent. ICU P had 11 patients in whom BSD was likely 3 became organ donors of the others 4 families refused consent, 3 had cardiac arrest 1 not identified.
In the 12 months following implementation of the strategy on 1st September 2005, ICU B had 4 patients likely to be BSD All 4 patients were identified and referred to the DTC Team. 2 families gave consent to donation. ICU P had 7 patients likely to be BSD. All 7 patients were identified and referred to the DTC Team.5 families gave consent to donation. In both ICU's the knowledge questionnaire showed increased knowledge of issues surrounding organ donation each respondent knew how and when to contact the DTC team and was able to identify a potential BSD patient.
Discussion
The unit based time strategy has been successful in increasing the knowledge of staff on both ICU's. This is reflected in the knowledge questionnaire and in the increase of potential donor identification and referral from 36% on ICU P and 33% on ICU B to 100% on both units and an increase family consent on each unit.

O48

Increasing The Supply Of Organs For Transplant: A Retrospective Audit of Deaths From Within The Accident And Emergency Departments

Paula Aubrey

North Thames Regional Donor Transplant Coordinators, London, United Kingdom

Background
In the last eighteen months there has been a significant increase in the number of solid organ donors in the Region. This is due to the increase in donors referred from Accident and Emergency (A&E) departments. This abstract outlines the audit and educational programme being carried out within the A&E departments across this region.

Method
Between October 2004 and December 2005 we undertook a retrospective audit of deaths within ten A&E departments. Our aim was to determine the potential number of controlled non heart beating donors and heart beating donors available from this clinical area.

Results
The Audit identified twenty potential organ donors from within the ten units and it is believed that these numbers could be replicated over the thirty two A&E departments, which would suggest as many as two potential donors from each A&E.

Discussion
The audit findings have provided the basis to develop an education programme in each of the A&E departments within this region. This involves assessing the educational needs of nursing and medical staff, and developing programmes aimed at helping the A&E clinicians to identify potential donors. This includes lecture sessions for key A&E nursing and medical staff. Non identification of potential donors is the major barrier to organ donation from the A&E departments.

We acknowledge the programme is in its infancy and we have a long way to go before we achieve a desired 100% referral rate. However, as demonstrated below, the significant increase in donor referrals rates from the A&E is very encouraging. In the first seven months of this financial year, seventeen potential donors have been referred from the A&E departments, nine of which have resulted in solid organ donation.

A&E donor referrals 2001-2006

A&E	2001	2002	2003	2004	2005	2006		
Donor referrals			1	9	9	7	17	17
Actual donors	1	2	1	0	6	9		
No goes	0	7	8	0	11	8		

O49

How Many Extended Criteria Should We Accept In Renal Transplant Donors?

Matthew Laugharne, Diane Evans, Kay Hamilton, Justin Morgan, Christopher Dudley

[1]Department of Surgery, Southmead Hospital, North Bristol NHS Trust, Bristol, United Kingdom, [2]Department of Renal Medicine, Southmead Hospital, North Bristol NHS Trust, Bristol, United Kingdom

INTRODUCTION: Reduced availability of renal allografts from deceased donors has stimulated interest in more marginal donors. The use of donors who satisfy extended criteria is now established. However, there is a limit to the acceptability of a marginal donor and therefore the number of extended criteria in each donor.
PATIENTS: We performed a retrospective review of our recipients of deceased donor kidneys from January 2002 to December 2005. Donor extended criteria included age over 60; malignancy; cerebral infarct; history of hypertension; diabetes; anatomical anomaly or retrieval damage; positive hepatitis serology; creatinine over 120 μmol/L; cold ischaemia time over 20 hours; non-heart beating donor. A point was scored for each of these criteria. Recipients were unselected and categorised as no extended criteria (EC 0), one (EC 1), two (EC 2) and three or more (EC 3+). Estimated GFR was calculated at 3 months, 1 year and 3 years (MDRD-4) comparison by ANOVA with Bonferroni post-test analysis. Patient survival and graft survival were compared by Kaplan-Meier with logrank statistic.
RESULTS: There were 259 recipients (EC 0 n=49; EC 1 n=98; EC 2 n=62; EC 3+ n=50). There were no differences in age or gender between the recipient groups. The table shows mean eGFR during follow-up. Estimated GFR was significantly lower in EC 3+ at all time points and also declined over time. In contrast eGFR improved with time in groups EC 0, 1 and 2. Graft survival was significantly worse in EC 3+ in comparison to the other groups (p=0.0359). Patient survival was lower in EC 3+ but this did not reach significance (p=0.0969).

	EC 0	EC 1	EC 2	EC 3+
3 month eGFR	51 ml/min	53 ml/min	53 ml/min	**41 ml/min**
1 year eGFR	56 ml/min	54 ml/min	51 ml/min	**41 ml/min**
3 year eGFR	55 ml/min	56 ml/min	56 ml/min	**36 ml/min**
4 year graft survival	*100%*	*90%*	*91%*	***74%***
4 year patient survival	*94%*	*92%*	*96%*	***75%***

DISCUSSION: Renal grafts from donors with one or two extended criteria performed similarly to grafts from standard donors. These donors are therefore an excellent source of kidneys. However, grafts from donors with three or more criteria had worse graft survival and lower estimated GFR. We suggest that grafts with three or more extended criteria should be accepted with great caution.

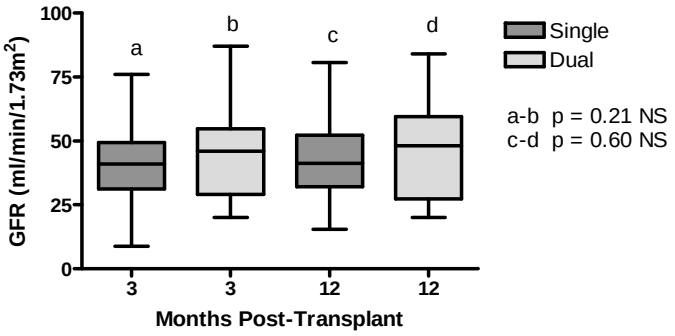
O50

Dual Transplantation of 'Marginal' Kidneys from Non Heart Beating Donors

Alex Navarro, Soroush Sohrabi, Hugh Wyrley-Birch, Dhakshinamoorthy Vijayanand, Aliu Sanni, Mettu Reddy, Naeem Soomro, David Rix, Bryon Jacques, Derek Manas, David Talbot

Liver and Renal Transplant Unit, Freeman Hospital, Newcastle-upon-Tyne, United Kingdom

INTRODUCTION. Viability testing can be used to avoid transplantation of NHBD organs that are likely to have PNF. Such testing also identifies a second group of kidneys which although unsuitable for solitary transplantation may be considered for dual transplant. In kidneys of this group solitary transplants would be unlikely to produce a sufficient glomerular filtration rate (GFR) to support the recipient. However, when used together as a dual transplant they could potentially produce sufficient renal function for one patient.
METHODS. Our unit has performed 17 dual NHBD renal transplants from 2003 to date. Using 3 and 12 month post-transplant recipient GFRs as functional outcome measures, we compared our dual transplant group with our series of 115 single NHBD transplants (1998-2006).
RESULTS. One dual transplant resulted in PNF (5.9%), compared with 11 single transplants (9.6%). Of the 16 functioning dual transplants the mean GFR after 3 months was 45.61 +/-18.15. In the single transplant group (n=115) after 3 months mean GFR was 40.73 +/-13.71. At 12 months post-transplant the mean GFR in the dual group was 46.02 +/-20.66 vs 43.03 +/15.66 in the single group.



DISCUSSION. We have demonstrated that a subset of NHBD kidneys, which do not satisfy the criteria for single organ transplantation, may become successful dual organ grafts producing early recipient renal function statistically comparable to that of their single organ counterparts. The use of machine perfusion and perfusate enzyme viability testing identifies NHBD kidneys suitable for dual transplantation, avoiding unnecessary organ non-use is and maximising organ resources.

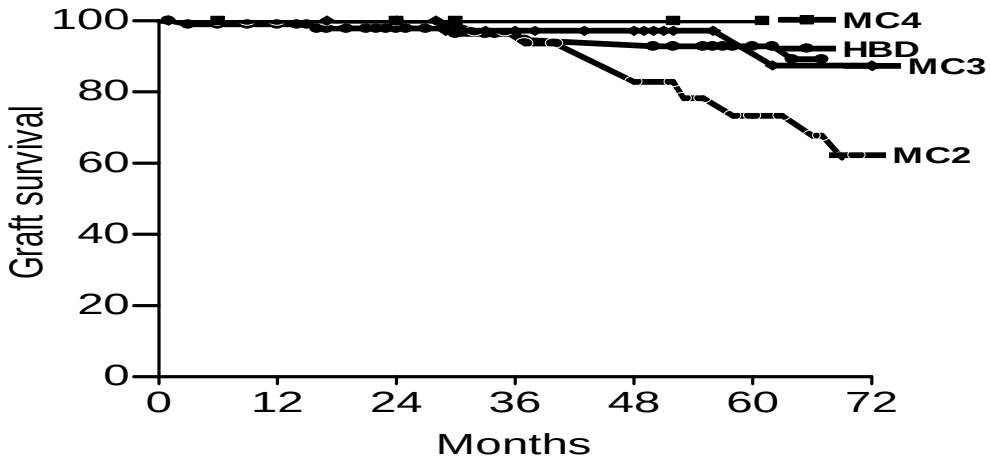
O51

Six Year Outcomes Following Non Heart Beating Kidney Transplantation

Aliu Sanni, Hugh Wyrley-Birch, Dhaksinomoorthy Vijayanand, Alex Navarro, Soroush Sohrabi, Mettu Reddy, David Talbot

Regional Liver/Renal Transplant Unit, Freeman Hospital, Newcastle upon Tyne, United Kingdom

Introduction: Non-heart beating donor kidneys (NHBD) are being employed to increase the donor pool following the exponential increase of patients on the renal transplant waiting list and scarcity of cadaveric heart beating donors (HBD).
We evaluated the long-term outcomes of renal transplantation using NHBD kidneys (Maastricht Categories [MC] 2-4).
Methods: We compared the first 100 NHBD kidneys transplanted at our facility to the next consecutive cadaveric HBD kidneys for graft survival, recipient survival and quality of graft function. All NHBD kidneys were machine perfused prior to transplantation.
Results: Recipient survival (p=0.22) and graft survival (p=0.19) at 6 years did not differ between recipients of NHBD (83%, 80%) and HBD (89%, 87%) kidneys respectively. Quality of graft function using the mean GFRs were significantly lower in the NHBD group up to 3 months following discharge (41±2 vs. 47±2, p=0.007) but then comparable beyond this period up to 6years following transplantation (43±5 vs. 46±4, p=0.55).
Conclusion: Overall graft function, recipient and graft survival at 6 years of the NHBDs are comparable to that of HBD kidneys. However in isolation, the MC2 donor kidneys had poor long-term outcomes when compared to the HBDs, MC3 or MC4- see survival curve below. .



O52

Effect of Ethnicity on Primary Non-Function Following Renal Transplantation – Analysis of National Databases

Sonal Asthana, Rachel Johnson, Chris Rudge, Niaz Ahmad

St James's University Hospital, Leeds, United Kingdom, UK Transplant Authority, Bristol, United Kingdom

Introduction: Primary non-function (PNF) following renal transplantation is rare. Concerns about PNF are increasing due to increasing use of allografts from extended criteria donors, which carry an increased relative risk of non-function compared to standard cadaver kidney grafts. This study was performed to assess the potential factors affecting the risks of primary non-function after renal transplantation.
Methods: All renal transplants performed within the United Kingdom over the last 10 years were included in this study. Data was collected using the prospective database maintained by UK Transplant. Primary non-function was defined as the grafts which never functioned and excluded graft loss from identifiable causes. Variables studied included: donor age, sex and type, recipient age, sex and ethnicity, number of HLA mismatches, previous grafts, cold ischemia time and time on the waiting list. The study group was analysed as two separate 5 year periods, the most recent 5 year period indicating increasing use of marginal donors. Statistical analysis was performed using chi-square tests and 't' tests as appropriate. Logistic regression analysis was used to determine independent predictive factors for PNF.
Results: One per cent of transplants (175 of 17105 grafts) had PNF in the 10-year period. The median donor age, recipient age, HLA mismatches, cold ischemia time and waiting time were higher in these patients (Table-I). The era of transplant did not affect the incidence of PNF. Patients of Asian or black ethnicity as well as those receiving NHB transplants were more likely to develop PNF (1.4% and 2.3% of all grafts, as compared to 0.4% of white recipients, $p<0.001$. The donor age, type of donation, recipient age, and recipient ethnicity independently predicted PNF on regression analysis.
Conclusion: Primary non-function following renal transplantation is associated with several predictable variables. Recipient of Black or Indo-asian ethnicity are more likely to develop PNF.
Acknowledgement: UKT for providing the data and all the UK transplant centres whose patients have been included in analysis.

O53

Use of kidneys with small renal tumours for renal transplantation- Attitude, beliefs and opinions of the transplant society

Aliu Sanni, Colin Wilson, Hugh Wyrley-Birch, Dhaksinamoorthy Vijayanand, Alex Navarro, Soroush Sohrabi, David Rix, David Talbot

Regional Liver/Renal Transplant Unit, Freeman Hospital, Newcastle upon Tyne, United Kingdom

Introduction: Demand for organs outstrips supply. A potential source of organs for transplantation is kidneys removed for the treatment of renal cell carcinoma (RCC). The Cincinnati group (Buell *et al 2005*) have safely transplanted kidneys with small RCC's after back table excision. This study will survey the attitude, beliefs and opinions of the transplant society on this ground breaking subject.
Methods: Structured questionnaires were administered or sent to focus group of patients on the North east renal transplant waiting list, post-nephrectomy patients for small renal cancer, Urologists, Nephrologists & Transplant Surgeons in the UK.
Results: Potential recipients: Of the 116 questionnaires sent, 113 were returned (97%). Mean participant age was 52yrs (range 20-76). With a median time of 17 months (range 1-105 months) on the renal transplant waiting list. The use of kidneys with small renal tumours (after excision) for transplantation was a favoured choice in 59% (67/113) of these patients.
Potential donors: There was a 100% response rate (15/15) with 93 % (14/15) accepting secondary use of their organs following radical nephrectomy for renal transplantation.
Nephrologists: 58 % (94/161) response rate with 78% (73/94) supporting the use of kidneys with small tumour (after removal) for renal transplantation.
Transplant Surgeons: 66 % (43/65) of the surgeons responded with 72% (31/43) supporting the use of these kidneys for transplantation. Interestingly, 21% (9/43) of the respondents have faced a clinical scenario of a donor kidney with small renal tumour.
Urologists: 44% (11/25) response rate with 64%(7/11) supporting this concept.

Respondents	Response rate	Support use of kidneys
Potential recipients on waiting list	**97%(113/116)**	**59%(67/113)**
Potential donors (previous nephrectomy)	**100%(15/15)**	**93%(14/15)**
Nephrologists	**58%(94/161)**	**78%(73/94)**
Urologists	**44%(11/25)**	**64%(7/11)**
Transplant Surgeons	**66%(43/65)**	**72%(31/43)**

Conclusion: There is a universal acceptance of this concept among the transplant society. With careful selection and appropriate immunosuppression; it should be safe to transplant kidneys with small renal tumours.

O54

A Posthumous Diagnosis Of Hereditary Haemochromatosis In An Organ Donor And Donor Family Care – A Case Study

Guy Heathcote

Cardiff and Vale NHS Trust, Cardiff, United Kingdom

The study outlines the case of a 69 year old male who donated liver and kidneys, which were all subsequently transplanted. Three weeks following transplant, results of a time zero biopsy of the donated liver showed signs of iron overload suggestive of a diagnosis of hereditary haemochromatosis. There had been no suspicion raised of this diagnosis at the time of donation from the family interview or donor assessment. It was, therefore, assumed that the donor and his family had been unaware of this condition.

Hereditary haemochromatosis is a common genetic disorder amongst Caucasians. It is an autosomal recessive disorder leading to abnormal absorption of iron from the diet. Excess iron can accumulate in the organs and tissues causing damage. Onset is insidious but symptoms of the disease are potentially serious and life threatening. It is easily treated and symptoms reversible if treated in the early stages. The donor's immediate family and future generations could unknowingly be affected or genetically predisposed to this condition.

Knowledge of this diagnosis presented the donor transplant co-ordinator team with a dilemma. Should we break patient confidentiality and inform the donor's family of the possible health implications?

This situation was outside the team's experience and specific guidelines on how to proceed were unavailable. The study outlines the use and adaptation of the UK Transplant UK Policy for the Management of Potential Organ/ Tissue Donors with confirmed positive virology results as guidance in this case.

Following this guidance, the diagnosis was confirmed using genetic testing, expert advice sought from haematologists and the actual risk to the donor family assessed. The multi-disciplinary team assembled decided that not informing the family would be a gross omission and a breach of duty of care. A meeting was arranged with the family to sensitively disclose the diagnosis, discuss the health implications and offer genetic counselling and screening. Consent was gained for specialist care.

The main aspect of this case study was the decision to breach patient confidentiality by adapting the positive virology policy for guidance out of consideration for the safety of the donor family. In light of this experience, a requirement for a national policy for the management of hereditary conditions identified in the donor population becomes clear as a similar situation could arise again in future.

Parallel Session 3

Kidney and Pancreas Transplantation

Friday 30 March

11:00 – 12:30

O55

Outcome Of Patients Who Travel To Pakistan For Living Kidney Transplant

Andrew Henderson, Pamela Mackenzie, R Stuart C Rodger, Colin C Geddes

[1]Ninewells Hospital, Dundee, United Kingdom, [2]Western Infirmary, Glasgow, United Kingdom

Aim: The aim of this study was to analyse single centre experience of patients travelling from United Kingdom (UK) to Pakistan for living kidney transplantation. Reports from elsewhere in the UK have led to patients being advised that this approach is associated unacceptably high risks.
Methods: Using the electronic patient record (EPR) and review of case sheets in our centre we have identified all patients who travelled to Pakistan for living donor kidney transplant since 2000 (PT group). A control group of living unrelated donor transplants (LUD) performed in centre from a similar period of time was also identified. The outcomes analysed were patient survival, graft survival, transplant function at one, three and twelve months, incidence of acute rejection and infective complications.
Results: 12 patients were identified in the PT group and 24 patients in the LUD group. 1 patient in the PT group died in Pakistan and therefore no follow-up data are available. There was one early graft loss due to renal vein thrombosis in the LUD group.
There was no significant difference in age, sex, prevalence of diabetes or incidence of pre-emptive transplant between the 2 groups. 1 year actuarial patient survival was 91% in the PT group and 100% in the LUD group (p=0.33). 1 year actuarial graft survival was 91% in the PT group and 96% in the LUD group (p=0.56). Mean serum creatinine in the PT and LUD groups was similar at 1 months (151.6 v 159.65 respectively; p=0.68), 3 months (130.9 V 144.65 p=0.34) and 12 months (128.8 V 141.25; p=0.44). The incidence of acute rejection in the first year was 36% in the PT group and 46% in the LUD group (p=0.46). There was greater use of tacrolimus and mycophenolate mofetil as primary immunosuppression in the LUD group. One PT group patient developed malaria on his return from Pakistan. There were no instances of hepatitis B, hepatitis C or HIV infection in either group.
Conclusions: These data do not support the view that the outcome of patients travelling from UK to Pakistan for living kidney transplantation is worse than LUD transplantation in UK. A national study is warranted to inform discussion with patients about this approach.

O56

Renal transplantation in identical twins in USA and UK between 1988 and 2004

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Introduction: The aim of this study was to review the graft and patient survival, as well as immunosuppression, of all recipients of a living identical twin donor renal transplant in the USA and UK from 1988-2004.
Methods: Data of all patients who underwent living identical twin donor renal transplantation in the USA and UK during the study period were retrieved from UNOS (OPTN data, 16 Nov 2006*) and UKT (22 Dec 2005) respectively.
Results: There were 120 living identical twin donor renal transplants in USA and 12 in UK during the study period. Graft and patient survival data are shown below:

Months after Tx	**Graft survival USA**	**Patient Survival USA**	**Graft survival UK**	**Patient Survival UK**
12	99.17%	100%	83.3%	100%
36	91.87%	97.01%	83.3%	100%
60	88.96%	97.01%	75%	100%

Some 30 patients in the USA group were on steroids, 27 on MMF, 17 on FK506, 7 on rapamycin, 4 on azathioprine and 2 on CYA for maintenance immunosuppression. In the UK, 3 patients were on steroids, 3 on MMF, 1 on FK506, 2 on azathioprine and 2 on CYA at last follow up. Results were missing from one patient in the latter group.
Discussion: Patient survival was excellent after living identical twin donor renal transplantation in both countries. Graft survival was better in the USA group but the UK sample was small. Furthermore, all 3 graft failures from the UK were from cases transplanted before 1995. Immunosuppression is still widely used despite identical twin transplantation. The most common type of immunosuppression was steroid based. Whilst phenotypic differences in monozygotic twins can exist (Gringras et al 2001) immunosuppression may be unnecessary in all these patients.
*This work was supported in part by Health Resources and Services Administration contract 231-00-0115. The content is the responsibility of the authors alone.

O57

Outcomes of Kidney Grafts Refused By One or More Centres and Subsequently Transplanted at a Single UK Centre.

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Introduction
The rate limiting factor for kidney transplant is the shortage of donor organs with resultant steady increase in transplant waiting list. Recent years has seen an expansion of kidney donor eligibility and utilisation of suboptimal grafts in an effort to meet the increasing demand for transplantation. In our centre we have seen an increase in the use of kidneys refused as suitable by one or more centres in the UK. This study was conducted to analyse the outcome of transplant from kidneys refused by one or more centres and subsequently transplanted by our institution.
Methods
A retrospective analysis using the UK Transplant database of donor grafts refused by one or more centres and subsequently transplanted at our centre from January 2000 to December 2005. The reason for refusal, donor and recipient factors, graft rejection, primary and delayed function, post operative complications, graft and patient survival at three years were studied.
Results
During the period, January 2000 to December 2005 a total of 623 renal transplants were carried out of which 60 (9.6%) donor grafts were refused by one or more centres. The main reasons for initial refusal included: elderly donor 26.6% (mean age 59.7 yrs), better HLA match required 36.6%, anatomical 5%, past medical history 6.6%, prolonged cold ischaemia time 3.3% (median 1091mins), organ damage 1.6%, and "centre criteria not met" 1.6%. 1 and 3 year creatinine were, 120μmol/l (56-599), 126μmol/l (62-566) respectively. Acute rejection occurred 8.2% of cases. Three-year graft and patient survival was 88.3% and 96% respectively. None of the above variables were significant predictors of 3-year graft survival on multivariate analysis.
Conclusions
9.6% of transplants in our center in the studied period were performed with graft refused by one or more centers as 'unsuitable' with graft and patient survival similar to other standard grafts. None of the factors for refusal of kidneys by other centers were found to predict for graft failure at 3 years. There may be an element of subjective assessment of these kidneys and a 'cascade effect' involved in refusal of these kidneys. **Acknowledgement: UK Transplant for providing data.**

O58

Kidneys from older donors: Does the outcome justify their use

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Aims:
The progressively widening gulf between number of patients on the waiting list and available organs has amongst other things contributed to more marginal donors being accepted as kidney donors. Organ allocation rules and possible bias within the transplant community may be resulting in organs from older donors being allocated to / accepted for only older recipients. We undertook this study to evaluate if kidneys from older donors were more likely to be accepted for older recipients and if so was there any difference in post transplant outcome.
Methods:
The data set comprised of consecutive 4,701 adult first kidney only deceased donor transplants carried out in the UK between 01 January 2000 and 31 December 2004. Patients were followed up from date of transplantation to 06 August 2006 or death or graft failure if earlier. Transplants were divided into four groups based on donor age as <50years, 50-59years, 60-69years and >70years.
Results:
There was no difference in CIT or diabetes as cause of ESRD or waiting time on transplant list for recipients between the four groups. There was a significant difference in the median age of the recipient in each of the four groups [p = <0.0001] with older recipients getting kidneys from older donors. As expected graft and patient survival was better with kidneys from younger donors. However, in-spite of the bias in recipient selection with older donor kidneys, 5 year graft and patient survival in the recipients of older donors (>70 yrs) was 64% and 69% respectively.
Conclusions:
Current allocation rules and clinical practise of transplant teams tend to favour transplantation of kidneys from older donors into older recipients. Our work suggests that the current allocation policy is a pragmatic use of a scarce resource with acceptable graft and patient survival. Further work is needed to analyse if this outcome is superior to remaining on dialysis.

O59

Factors Affecting Long-term First Renal Graft Survival Identified in a 10-year, 5-centre Retrospective National UK Study

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Introduction: Long-term renal graft survival has progressively improved, but more slowly than improvements in acute rejection. This long term transplant outcome study will collect detailed information on 3000 first renal transplant recipients. This is a presentation of graft survival in those transplanted between 1992 and 2001.
Methods: All patients who had a first renal transplant were identified in five UK transplant centres. Data pertaining to: transplant centre, patient age, sex, ethnic group, time on dialysis pre-transplant, transplant donor type (live/cadaver), year of transplant (1992-1996/1997-2001) and diabetes as the attributed cause of renal failure were collected. Patients were considered to be at risk of graft failure until they died, or until the end of December 2001 if death had not occurred by this point. 1659 patients were included in the final analysis, 403 (24%) of whom had experienced graft failure by this time. Univariable analysis was initially performed using Log-Rank tests. Factors significantly affecting graft survival were then included in a Cox multivariable analysis.
Results: 2373 patients have been identified to date. Mean age at transplant 44.3yrs (SD14.4), 1491 Male, 882 Female. 1158 were transplanted 1992-1997, 1215 were transplanted 1998-2002. Ethnic gp was known in 1830(1583 white, 247 non-white).
Univariable analysis showed differences in graft survival between transplant centres ($p=0.001$), year of transplant (1997-2001 > 1992-1996, $p=0.003$), donor type (live survival > cadaver, $p=0.002$) and ethnic group (white > non-white $p<0.001$). Significant differences also existed between recipient ages; patients aged 40-49 had significantly better graft survival than either younger (<40yrs) or older recipients (≥60yrs). Multivariable analysis showed that recipient middle age, live donor type, recipient white ethnic group, 1997-2001 time cohort, and certain sites predict longer graft survival. There was a significant interaction between time-on-dialysis and donor age ($p=0.0008$), such that at age <30yrs a longer period of time on dialysis predicted better graft survival, whilst at older ages the opposite is true.
Conclusion: There were significant graft survival differences in the study cohort associated with donor and recipient characteristics, and between centres. Detailed data collected over the next two years will allow investigation of quality of life, and other patient reported outcomes, other important donor and recipient characteristics, treatment, and models of care affecting patient and graft survival.

O60

Prevalence of chronic kidney disease 1 year after living kidney donation

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Background. The aim of this study was to explore the implication for previous living kidney donors of the widespread use of the 4-variable MDRD equation that uses age, sex and serum creatinine (SCr) to calculate estimated glomerular filtration rate [eGFR(MDRD)].
Methods. We analysed eGFR(MDRD) 1 year after living kidney donation in 90 consecutive donors at our centre since 2000 who had isotopically measured GFR > 80ml/min/1.73m^2 pre-donation (mean 103.4±15.6mL/min/1.73m^2). We also calculated an estimate of 1 year GFR [eGFR(calc)] based on the fact that if muscle mass is unchanged, 1 year after donation the ratio of pre-donation GFR(measured isotopically):post-donation GFR will be the same as [reciprocal pre-SCr]:[reciprocal post-SCr].
Results. Mean donor age (±SD) was 44.8(±10.3) years and 53.3% of donors were female. Mean SCr (±SD) pre-donation was 90.2(±15.1)µmol/L. One year after donation mean SCr was 114.3(±18.4)µmol/L ($p<0.0001$). This equated to a mean eGFR(MDRD) of 56.1(±9.0) mL/min/1.73m^2 compared with mean eGFR(calc) 1 year after donation of 83.1(±16.3)mL/min/1.73m^2 ($p<0.0001$). 65.6% of donors had eGFR<60ml/min/1.73m^2, ie. Stage 3 chronic kidney disease (CKD) using eGFR(MDRD), compared with only 3.3% if eGFR(calc) was used ($p<0.0001$). There was no significant correlation between age and pre-donation GFR ($r = -0.14$; $p=0.19$), and no correlation between age and 1 year eGFR(calc) ($r = -0.194$; $p=0.068$). However, there was a correlation between age and 1 year eGFR(MDRD) ($r = -0.39$; $p<0.0001$). This discrepancy is likely to be explained by the use of age in the MDRD eGFR formula, rather than by true loss of renal function in older donors.
Conclusions. Using eGFR(MDRD) a large proportion of living donors are labelled as having stage 3 CKD after donation. Our data demonstrate this likely relates to the poor validity of the MDRD formula in a healthy population with near normal renal function rather than genuinely low renal function. The simple eGFR(calc) formula we describe is likely to be re-assuring in this setting, although validation against formal GFR measurement is required.

O61

Increased Incidence of Monoclonal Gammopathy of Undetermined Significance and Elevated Free Light Chains in Renal Transplant Recipients

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Introduction: Monoclonal gammopathy represents a paraproteinaemia secondary to clonal proliferation of plasma cells. Further, polyclonal elevation of free light chains (FLCs) may be seen in renal impairment and systemic inflammation. When present, these abnormalities may contribute to renal damage. To address the hypothesis that there is high prevalence of aberrant monoclonal disease and elevated FLC levels in transplant recipients we have performed a large prospective study in a cohort of renal transplant recipients.
Methods: 258 patients were recruited from transplant clinics at our institution. Serum protein and immunofixation electrophoresis (SPE and IFE; Sebia, UK) were performed to detect monoclonal immunoglobulins (Ig). FLC concentrations were measured in serum and urine samples using the immunoassay FREELITE^{TM} (The Binding Site, UK). The Cockcroft-Gault equation was used to estimate glomerular filtration rate (eGFR) based on serum creatinine. Serum cystatin-C levels and ACR were also measured. Results were compared with 282 normal controls.
Results: The mean age of the renal transplants recipients was 48.6 (18-82). Mean biochemical markers are as follows: Cystatin C 2.5mg/L (0.88-6.25); Creatinine 180.2umol/L (12-913); eGFR 51.7mls/min/1.73m2; ACR 43.5 (0.2-627). **SPE revealed that 8.5% of patients with renal transplants had a monoclonal component confirmed by serum IFE as immunoglobulin, compared with <1% of normal age-matched individuals.** Mean serum polyclonal kappa and lambda FLC levels in the patients with renal transplants were significantly higher than in the control group (30.9mg/L **vs** 8.4mg/L for kappa $p<0.0001$ and 34.3mg/L **vs** 13.4 mg/L for lambda $p<0.0001$). The mean FLC ratio was 0.93 **vs** 0.63 $p<0.0001$ (normal range 0.26-1.65). 5 (2%) patients had abnormal FLC ratios suggesting clonal sFLC production. FLC concentrations in the urine were significantly higher in transplant recipients than in the normal population (kappa 62.7mg/L vs. 7.49mg/L $p<0.0001$; lambda 12.1mg/L vs. 0.79mg/L $p<0.0001$).
Discussion: Renal transplant patients have a greater than eight fold increased incidence of MGUS. In addition serum and urine polyclonal FLC concentrations are markedly increased in patients with no evidence of a paraprotein. Prospective work now needs to be undertaken to determine whether these abnormalities are mechanistically involved in renal transplant outcomes.

O62

Encapsulating Peritoneal Sclerosis following Renal Transplantation

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UK EPS Study Group, Manchester, United Kingdom

Encapsulating peritoneal sclerosis (EPS) is a rare but severe complication of patients who have undergone peritoneal dialysis. It is characterised by progressive intra-abdominal fibrosis resulting in compromised motility and function of the bowel. Little is known about the incidence, pathophysiology and management of EPS because of its rarity. with Treatment options discussed in case reports include enteric rest, Tamoxifen and immunosuppression. Case reports and small case series have suggested that immunosuppression is associated with clinical improvement and improved survival. However, here we report UK EPS Registry data of EPS occurring early post renal transplantation between 1999 and 2006 in 7 UK units.

This multi centre series of 23 cases of EPS following immunosuppression, of whom 16 were male and 7 were female. 11/23 cases occurred in the first 3 months (earliest at 1 week), with 11/23 between 3 and 8 months and only one case >1 year post transplant. Clinical presentation included vomiting, altered bowel habit, abdominal pain and ascites. EPS was diagnosed following clinical suspicion and abdominal CT scans in 22 patients. The mean age of the patients at time of diagnosis was 44 yrs (IQR 32 - 54) and the mean time on peritoneal dialysis prior to transplant was 71months (IQR 41 - 96). All patients had received Mycophenolate Mofetil (MMF) and a calcineurin inhibitor prior to diagnosis. 8 patients underwent peritonectomy and adhesiolysis, all of whom are still alive. 6 patients had adhesiolysis and cocoon resection, of which 4 are alive. 7 of the 9 patients who were treated conservatively are still alive. One patient developed the condition, while on maintenance Tamoxifen.

This is the first multicentre case series to report the occurrence of EPS early in the post transplant period in patients previously treated with peritoneal dialysis. A high clinical suspicion is required to make the diagnosis during this time period as treatment with MMF may result diagnostic delay, due to gastrointestinal symptom overlap. Reduction in MMF dose, due to these symptoms, may predispose to rejection episodes. Further research needs to be performed to further define the role of immunosuppression in EPS progression.

O63

Detrimental Effects Of Sirolimus on Islet β-cell, Podocyte and Renal Tubular Cell Viability And Vascular Endothelial Growth Factor (VEGF) Production

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INTRODUCTION. Sirolimus is used as immunosuppression in solid organ and islet transplantation. Islet allograft recipients exhibit a fall in insulin-independence with only 10% off insulin at 5 years (Ryan et al. *Diabetes* 2005; 54: 2060). Sirolimus has been associated with proteinuria and reduced renal function following both solid organ and islet transplantation. We have examined whether sirolimus is responsible for these effects through the inhibition of vascular endothelial growth factor production (VEGF).
METHODS. We investigated the *in vitro* effect of sirolimus on the viability and VEGF production by human islets, conditionally-immortalised human podocytes and human HK2 renal proximal tubular cells. The effect of sirolimus and VEGF blockade was further investigated in murine MIN6 β-cells. Finally, the effect of VEGF over-expression on murine islet viability was characterised.
RESULTS. Sirolimus reduced human islet viability by 36% ($p=0.001$) and human renal tubular cell viability by 65% ($p=0.006$). This toxicity was associated with a 44% reduction of VEGF release by islets ($p=0.0001$) but not the proximal tubular cells. Sirolimus did not affect human podocyte viability with a trend towards reduced VEGF production ($p=0.087$). Sirolimus reduced both viability (78%, $p=0.012$) and VEGF production (70%, $p=0.009$) by MIN6 β-cells. Antibody blockade of VEGF reduced viability by 67% ($p<0.0001$). Transfection of murine islets with adenoviral VEGF improved islet viability by 100% ($p=0.012$).
DISCUSSION. Sirolimus was toxic to human islets and murine β-cells. This may explain the loss of insulin-independence in islet transplant recipients treated with sirolimus. Sirolimus reduced VEGF production by islets and β-cells. Moreover, blockade of VEGF reduced β-cell viability whereas VEGF over-expression improved islet viability. Sirolimus may impair VEGF production from transplanted islets, reducing β-cell survival and also graft neo-angiogenesis. Sirolimus reduced tubular cell viability and may therefore induce renal tubular damage. However, sirolimus had no significant effect on podocyte viability or VEGF production. This suggests that sirolimus may induce proteinuria through an alternative mechanism on glomerular function. Further investigations into sirolimus are warranted before it may be concluded that it is an ideal long-term agent in islet transplantation.

Parallel Session 4

Stem Cells

Friday 30 March

11:00 – 12:30

O64

The Potential of Umbilical Cord Blood-derived Stem Cells for Neural Repair

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Introduction. Human umbilical cord blood (hUCB)-derived stem cells have been reported to possess a greater degree of plasticity than previously thought, but results suggesting differentiation along the ectodermal lineage are still inconclusive. Interestingly, hUCB-derived stem cells have been found to secrete neurotrophic factors and are not immunogenic, indicating these cells may be suitable for the protection of damaged neural tissue. To test this possibility, we have derived mesenchymal stem cells (MSC) from hUCB and tested their potential to promote the survival of damaged neurons in an animal model.

Methods. MSCs were isolated by plastic adherence following depletion of cells expressing haematopoietic markers, and were characterised as CD34-, CD45-, CD73+, CD105+, HLA-I+ and HLA-II-. Interestingly, some of the MSCs also expressed the neural precursor markers nestin and PSA-NCAM, and the early neuronal marker Tuj1. To investigate whether MSCs can survive and/or trigger immune responses in an injured animal, they were first grafted into the vitreous humour of the eye. To determine if the axotomised retinal ganglion cells (RGCs) could be rescued, the MSCs were transplanted into a lesion of the optic tract in a model of neural degeneration,

Results. Few MSCs survived in the eyes of immunocompetent hosts, so immunosuppression was employed for 2 weeks post-grafting in subsequent experiments. Three weeks after grafting the immunosuppressed animals, a host immune response to the MSCs was observed through the presence of rat MHC Class II+ cells, correlating with decreasing MSC numbers. The neuroprotective effect of the MSCs was then examined by transplanting them into a lesion in the optic tract region of newborn rats. Survival of the transplanted cells was assessed 2 weeks post-grafting, whilst after 4-8 weeks the survival of the RGCs was examined using retrograde Fast Blue labelling. Preliminary results suggest the MSCs can promote the survival of the RGCs for at least 4 weeks following injury. Little evidence of migration or differentiation into neural subtypes was seen.

Discussion. Human MSC are subject to a xenogeneic response, therefore immunosuppression is required. Although the hMSC did not appear to differentiate into neural cell types, they do appear to be neuroprotective. These results suggest that MSCs might be a useful source of cells to limit damage to the CNS.

O65

Generation of hepatic and biliary cells from a common pancreatic adult stem cell population.

Karen Stevenson, Jimi-Carlo Bukowski-Wills, Alan MacIntyre, W David George, R Wayne Davies, Paul Shiels

Div. Cancer Sciences & Molecular Pathology, University of Glasgow, Dept of Surgery, Glasgow, United Kingdom, . IBLS, University of Glasgow, Glasgow, United Kingdom

Introduction

We have previously isolated a stem cell population (PDPCs) from adult rat pancreatic ductal tissue. These cells are characterised by expression of Nestin, GFAP, NCAM, Thy-1 and are negative for expression of PDX-1. *In vitro* differentiation, in media containing nicotinamide, results in the production of functional, insulin secreting islets. We have assessed the plasticity of PDPCs to determine if they have the potential to differentiate into a functional hepatic / biliary lineage, given that during embryonic development the liver and pancreas both originate from the ventral foregut. Other putative pancreatic progenitors have been described, which after differentiation in vitro, express alpha-fetoprotein, c-Met and HGF, although they have not been demonstrated to produce functional hepatic cells.

Methods

PDPCs were differentiated in serum free media with FGF-4. Differentiation to hepatocyte like cells in vitro was assessed by RT-PCR analysis for Albumin, CK19, alpha-feto protein, CK18, cytochrome P450(2B1) and hepatocyte transcription factors HNF 1-alpha, HNF 3-beta, GATA-4 on days 7, 14, 21and 28.Immunocytochemistry using monoonal antibodies to albumin, CK7, CK19 and vimentin was performed. Albumin production was assessed by Western blot. Glycogen storage, a functional characteristic of hepatocytes, was assessed using Periodic –Acid Schiff staining.

Results

PDPCs cultured with FGF-4 demonstrated a phenotypic change from fibroblastoid to epithelioid cell type. Undifferentiated PDPCs expressed early endoderm specification markers HNF3 beta, GATA 4 and alpha-feto protein, but did not express later markers of hepatocyte differentiation, HNF 1-alpha and Albumin, until day14. Albumin production was confirmed by western blot analysis. CK19 expression, a biliary marker, was also induced (Day 7-28). Differentiated PDPCs demonstrated staining indicative of production and storage of glycogen (Day21). Interestingly, in vitro, during differentiation vimentin positive ductal like structures surrounded by hepatic cells, typical of in vivo architechture were formed.

Discussion

We have derived a from adult rat pancreas, a cell population that demonstrates the potential to differentiate into functional pancreatic, hepatic and biliary lineages. Further characterisation of this population may provide insight into the potential identification of a common precursor cell for liver and pancreas in development. Significantly, it provides candidate cell populations for transplantation and toxicology screening.

O66

The Characterisation Of Adult Rat Pancreatic Stem Cells and Differentiated Insulin-Secreting Cells.

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Introduction: Pancreatic Derived Pathfinder Cells (PDPCs) isolated from adult rat pancreatic ducts, are a putative adult stem cell population, that has been shown to mitigate the effects of diabetes in a STZ diabetic rodent model. PDPCs also display the capacity to form islets through in-vitro differentiation. We have assessed the capacity of these islets to produce insulin under glucose stimulation, with a view to providing proof of principle for the production of insulin-producing cells for the treatment of diabetes, derived from human PDPCs.
Aim: To establish whether PDPC derived islet clusters can secrete insulin in response to glucose stimulation.
Methods: The Static Insulin Secretion Test (SIST) was used as an in-vitro model to compare insulin release in response to different glucose concentrations, from PDPCs versus islet clusters derived from PDPC differentiation. A rat insulin ELISA kit was used to determine insulin concentration. Cellular protein was extracted from all wells using Triton-HEPES (TH) buffer and then protein concentration quantified using the Roche Diagnostics turbidimetric protein assay. The measured insulin concentration was then expressed as insulin released (pg) per mg protein per minute.
Results: At all three different glucose concentrations (3, 10 and 20 mM), the islet clusters secreted significantly more insulin per mg of protein than the undifferentiated PDPCs ($p < 0.001$). However, a biphasic release of insulin was not observed with the concentrations of glucose used.
Conclusion: Islet clusters derived from PDPCs successfully produce insulin in response to glucose stimulation, though a bi-phasic release was not observed. This experiment provides proof of principle for the derivation of human islets from human PDPCs, as a source of beta cells for the treatment of diabetes.

Wednesday 28 March

Moderated Poster Session

Basic Science

P01

Leukocyte recruitment to endothelial cells following hypoxia reoxygenation is regulated by reactive oxygen species via MAPK signalling

Tim Millar, Van Phan, Lee Anne Tibbles

University of Calgary, Calgary, Canada

Ischaemia reperfusion injury in transplanted organs causes recruitment of leukocytes and eventual graft failure. Using isolated human endothelial cells and leukocytes in a dynamic flow based adhesion assay we show slow rolling and neutrophil adherence following hypoxia reoxygenation (H/R) at 1dyne cm^{-1}. Mitochondrial membrane potential measured by JC-1 fluorescence was lost during endothelial hypoxia. Leukocyte recruitment was mimicked by rotenone or FCCP, compounds which cause mitochondrial depolarisation and also increase intracellular reactive oxygen species (ROS). Leukocyte recruitment was inhibited by the antioxidants Vitamin C, N-acetyl cysteine or specific enzyme inhibitors Allopurinol and Apocynin. Interactions of the leukocyte to the endothelium as measured by rolling velocity was also inhibited by Vitamin C and Apocynin suggesting reactive oxygen species involvement in regulating inflammation in our model of ischaemia reperfusion. Recruitment was also blocked with a specific anti P-selectin blocking antibody. The mitogen activated protein kinases (MAPK) ERK 1/2, SAPK/JNK and p38 were phosphorylated during hypoxia and showed a further round of phosphorylation during reoxygenation. Inhibition of MAPKs by small molecule inhibitors showed a significant reduction in H/R mediated recruitment. This was also seen in adenoviral-transfected cells expressing a dominant negative MKK7 protein which specifically blocks SAPK phosphorylation. These results suggest a P-selectin mediated recruitment during early reoxygenation stimulated by mitochondrial and non mitochondrial sources of ROS. These results indicate the MAPK cascades in early, P-selectin mediated, H/R induced leukocyte recruitment and show the potential use of specific gene therapy, antioxidant and targeted inhibition as methods to reduce acute post transplant inflammation.

P02

The Effect Of Ischaemic Preconditioning On The Production Of Regenerative Mediators In Human Liver Sinusoidal Endothelial Cells

Dhanwant Gomez[1], Anne Graham[2], Nicholas Orsi[1], Uma Ekbote[1], Lance Burn[3], Shervanthi Homer-Vanniasinkam[1], Rajendra Prasad[1]

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Introduction: The effect of ischaemic preconditioning (IPC) on liver regeneration following liver transplantation and resection is still undetermined. We aimed to assess the cytokine and growth factor production by human liver sinusoidal endothelial cells (HLSEC) and evaluate the effect of IPC on these mediators in an *in vitro* hypoxia-reoxygenation (H-R) model mimicking ischaemic-reperfusion injury.
Methods: Confluent culture flasks of HLSEC were subjected to H-R (1 hour hypoxia + 1 hour reoxygenation), IPC with H-R (10 minutes hypoxia + 10 minutes reoxygenation + 1 hour hypoxia + 1 hour reoxygenation) and compared to untreated Controls. Production of interleukin (IL)-1 beta, IL-1 receptor antagonist (IL-1ra), IL-6, IL-8, tumour necrosis factor (TNF)-alpha, transforming growth factor (TGF)-alpha, granulocyte-colony stimulating factor (G-CSF) and hepatocyte growth factor (HGF) were determined over a 48 hour period.
Results: IL-6, IL-8, G-CSF and HGF were produced by HLSEC, while IL-1 beta, IL-1ra, TGF-alpha and TNF-alpha were not. IPC prior to H-R increased IL-6 (36% and 38%), G-CSF (31% and 85%) and HGF (130% and 12%) production compared to H-R alone after 36 and 48 hour respectively. IPC prior to H-R decreased IL-8 output by 9% and 7% compared to H-R alone after 36 and 48 hours respectively. Although there was a trend in increased IL-6 and G-CSF production, there was no significant difference in IL-6, IL-8 and G-CSF production between the IPC-treated group and non-IPC-treated groups. HGF production was significantly higher in the IPC-treated group compared to the non-IPC-treated group at the 36 hour time-point only ($p=0.05$).
Conclusion: HL-SEC produces pro-regenerative mediators such as IL-6, IL-8, G-CSF and HGF. Although IPC influences IL-6, IL-8 and G-CSF release in HLSEC between 24 to 48 hours following H-R, this was statistically not significant. HGF profile was significantly influenced by IPC after 36 hours. The final effect on liver regeneration would depend on the interaction of various liver cells and studies on co-culture models are required.

P03

Ischaemic Preconditioning Versus Intermittent Clamping On Human Liver Sinusoidal Endothelial Cells: Effects On Cytokines And Growth Factors

Dhanwant Gomez[1], Anne Graham[2], Nicholas Orsi[1], Uma Ekbote[1], Lance Burn[3], Shervanthi Homer-Vanniasinkam[1], Rajendra Prasad[1]

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Introduction: Ischaemic preconditioning (IP) with continuous clamping and intermittent clamping (IC) of the portal triad are distinct protective strategies against ischaemic-reperfusion injury (IRI) following liver surgery but their effect on liver regeneration is still undetermined. Therefore, we aimed to evaluate the effect of IP and IC on cytokine and growth factor production by human liver sinusoidal endothelial cells (HLSEC) in an *in vitro* hypoxia-reoxygenation (H-R) model to mimic IRI.
Methods: Confluent culture flasks of HLSEC were subjected to H-R (1 hour hypoxia + 1 hour reoxygenation), IP with H-R (10 minutes hypoxia + 10 minutes reoxygenation + 1 hour hypoxia + 1 hour reoxygenation), IC (15 minutes hypoxia + 5 minutes reoxygenation x3 + 1 hour reoxygenation) and compared to untreated Control. Differences in production of interleukin (IL)-1-beta, IL-1 receptor antagonist (IL-1ra), IL-6, IL-8, tumour necrosis factor (TNF)-alpha, transforming growth factors (TGF)-alpha, granulocyte-colony stimulating factor (G-CSF) and hepatocyte growth factor (HGF) were determined over a 48 hour period.
Results: The production of IL-1-beta, IL-1ra, TGF-alpha and TNF-alpha was undetectable in all groups. IP prior to H-R featured increased levels of IL-6 (36% and 38%), G-CSF (31% and 85%) and HGF (130% and 12%) compared to H-R alone after 36 and 48 hours, respectively. IP prior to H-R exhibited a decrease in IL-8 profile by 9% and 7% compared to H-R alone after 36 and 48 hours, respectively. By contrast, IC increased IL-6 production (22% and 42%), G-CSF (57% and 107%) and HGF (124% and 25%) compared to H-R alone after 36 and 48 hours, respectively. IC decreased IL-8 release by 8% and 1% compared to H-R alone after 36 and 48 hours, respectively. There was no significant difference in IL-6, IL-8, G-CSF and HGF production between IP-treated and IC-treated groups.
Conclusion: Both IP and IC appear to equally influence the expression of pro-regenerative mediators such as IL-6, IL-8, G-CSF and HGF in HLSEC. Both IP and IC seem to influence the release of IL-6, IL-8, G-CSF and HGF between 24 to 48 hours following H-R. These results suggest that both IPC and IC could potentially affect the liver regeneration signaling cascade. Hence, both strategies require further evaluation using co-culture models to determine their final effect on these mediators of liver regeneration.

P04

Tolerisation of donor specific memory T cells by kidney grafts deficient in C3

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Introduction Memory T cells are detrimental in transplantation as they have enhanced capabilities to destroy allografts. Furthermore, tolerance induction protocols fail when applied to pre-sensitised recipients. Thus, establishing means to induce tolerance in the context of pre-existing memory is of paramount importance. It has been previously shown that C3 synthesised within kidney allografts is involved in the primary alloresponse. Given the expression of complement receptors on antigen experienced T cells, and the well established influence of the complement system on the T cell response, we hypothesise that C3 synthesised within renal allografts might influence the efficacy of the memory T cell response.

Methods and results We have used the male to female combination on the BL/6 strain, in which donor and recipients differ by a single minor antigen HY. No antibody is generated against this minor antigen, thus, rejection is T cell dependent. Female recipients were transplanted with male trunk skin, which were rejected acutely (MST=15 days). FACS analysis of peripheral blood using HY tetramer identified a population of donor specific CD8+ cells that also express the memory marker CD44. 60 days following skin transplantation, female recipients were transplanted with either $C3^{-/-}$ or WT male kidney grafts followed by bilateral native nephrectomies, leaving the transplanted organ life sustaining. Despite having rejected male skin grafts and the development of demonstrable donor specific CD8+ memory T cells, not all male kidney grafts were rejected. A higher proportion (40%, n=10) of $C3^{-/-}$ grafts were accepted when compared to WT renal grafts (11%, n=9). Animals that did not reject male kidney grafts had normal creatinine. Additionally, when recipients who had accepted $C3^{-/-}$ grafts long term were challenged with male skin grafts, instead of rejecting the grafts with accelerated second-set kinetics, these recipients accepted male skin grafts indefinitely, despite the persistence of donor specific CD8+ T cells.

Conclusions Memory T cell responses may be impaired in the absence of C3 within the donor graft. Acceptance of $C3^{-/-}$ grafts is associated with generation of tolerogenic processes which abrogate T cell memory. The persistence of donor specific CD8+ T cells suggests a non-deletional mechanism such as anergy or regulation. Targeting the complement system may be a promising approach to overcome the problem of immunological memory in renal transplantation.

P05

Migration of Donor Passenger Leukocyte Subsets in Tolerance and Rejection

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Introduction Donor passenger dendritic leukocytes play a vital role in allo-sensitisation, while on the other hand, persistence of passenger leukocytes is associated with tolerance. Using a mouse kidney transplant model, we compared the fate of donor dendritic leukocytes in tolerance and acute rejection.

Results Kidneys from DBA/2 mice enjoy prolonged survival, with 80% surviving over 80 days in BL/6 mice (MST=101 days), compared with only 17% of BALB/c donor kidneys (MST=8 days); despite both donor strains being MHC identical ($H\text{-}2^d$). Immunohistochemical analysis of dendritic cells (DC) within naïve DBA/2 and BALB/c kidneys before transplantation showed no differences between the number of DC within these organs. The majority of these cells in both strains were myeloid, $CD8^-$ (94%), with only a small proportion of lymphoid ($CD8^+$) and plasmacytoid DC. They were also predominantly negative for the activation markers CD40 and CD86 (98.6% and 91% respectively). Next, we examined the migration of donor passenger leukocytes out of the donor organs into the spleens of recipients by staining for donor class II MHC^+ cells at various time points. The number of donor passenger leukocytes within the spleen of BALB/c kidney allograft recipients was significantly higher than that within the spleen of DBA/2 kidney allograft recipients by day 4 after transplant (10.61 ± 2.79 cf 2.19 ± 0.57 per hpf ($p=0.0102$)). Further phenotypic analysis of these cells showed that the proportions of different subsets were altered compared with naïve organs. Lymphoid DC, which only amount to only 6% of the total DC population were now the dominant subset, with up to 80% of donor passenger leukocytes expressing CD8. The proportion of cells expressing the activation markers CD40 and CD86 increased in both strain combinations, to 40%.

Conclusions Dendritic cells in naïve organs are predominantly myeloid in origin. They can be detected easily in spleens of recipients after transplantation but dendritic cells with lymphoid phenotype become predominant. Both populations upregulate the expression of activation markers post transplantation. Lower numbers of donor passenger leukocytes in spleens of DBA/2 kidney recipients than BALB/c recipients may account for the difference in graft survival. Experiments are in progress to determine whether this is due to migration elsewhere or increased cell death.

P06

Infiltration of Renal Tubules by Foxp3$^+$ T cells Mimics Rejection

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Introduction The outcome of an allo-immune response depends on the balance between conventional donor specific T cells and regulatory T cells, with the balance usually tipped towards rejection. This is occasionally reversed, resulting in spontaneous acceptance. This has been observed in small animal models as well as humans, most notably in liver but sometimes even in renal recipients.

Results Kidneys from DBA/2 mice enjoy prolonged survival in BL/6 mice, with 80% surviving over 80 days (MST=101 days), compared with only 17% of BALB/c donor kidneys surviving long term (MST =8 days); despite both donor strains being MHC identical (H-2^d). Long term acceptance of DBA/2 kidney allografts resulted in prolonged survival of donor but not 3rd party skin graft. To determine if regulatory T cells are responsible for this phenomenon, we investigated the expression of foxp3, a transcription factor expressed by regulatory T cells, using immunohistochemistry. Higher numbers of foxp3$^+$, regulatory T cells were found in spleens of DBA/2 (tolerant) than BALB/c (rejecting) kidney recipients (27.6$\pm$1.54 cf 12.11$\pm$4.37 per high power field (hpf) 8 days post transplantation, p=0.0079). Infiltration of the tubules by monocytes is a cardinal feature of acute rejection. However this occurs in both rejecting and tolerant kidney grafts in our model. On close inspection, some of the monocytes infiltrating tubules are foxp3$^+$, thus "mimicking" rejection. Higher numbers of foxp3$^+$ cells were found within DBA/2 grafts than BALB/c grafts (15.25$\pm$5.18 cf 7.56$\pm$4.79/hpf 4 days post transplantation). The ratio of foxp3$^+$ cells to total CD4$^+$ T cells was also higher within DBA/2 kidney grafts (1:5 compared with 1:9 within BALB/c grafts). Long term acceptors of DBA/2 kidneys with normal blood urea nitrogen maintain a high level of foxp3 expression (32.12$\pm$12.32/hpf), while mice with poor renal function have fewer foxp3$^+$ cells (9.8$\pm$9.17/hpf).

Conclusions Spontaneous acceptance is associated with higher numbers of foxp3$^+$ regulatory T cells. Monocyte infiltration is seen in both tolerant and rejecting grafts. Since graft function in tolerant recipients is normal, infiltration by mononuclear cells, including foxp3$^+$ regulatory T cells should be regarded as mimicking rather than causing rejection. Foxp3$^+$ to CD4$^+$ cell ratio in immunohistochemistry may help to verify this.

P07

C3a-C3aR interaction regulates the allostimulatory function of dendritic cells

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Our previous studies have shown that the absence of C3 in donor graft had a significant effect on prolonging graft survival, and C3-/- donor antigen presenting cells (APCs) have a reduced ability to stimulate allospecific T cells *in vitro* and to induce immune response *in vivo* suggesting that local production of complement plays an important role in modulating APC functions. However, the underlying mechanism remains unclear. In the current study, we investigated the role of C3a-C3a receptor (C3aR) interaction in modulating dendritic cell (DC) activation and allostimulatory function. We first assessed if expression of C3aR and generation of its ligand C3a result in enhanced autologous DC activation. Using RT-PCR, mRNA arrays, flow cytometry and ELISA, we show that several complement components and co-factors needed to cleave C3 (e.g. C3, factor B, C1q, and properdin) as well as C3aR are expressed in murine bone marrow (BM) dendritic cells (DCs); activation of secreted C3 occurs locally to release C3a.
We next determined if C3a-C3aR interaction modulates DC effector functions in the alloreactive T cell response. We prepared DCs from C3aR-/- mice or DCs from WT mice that were subsequently treated with C3aR antagonist (C3aRa). We then analysed activation phenotype of the DC in response to LPS stimulation and assessed their capacity to stimulate the alloreactive T cell responses *in vitro* and *in vivo*. We show, *in vitro*, that compared with untreated WT DCs, C3aR-/- DCs or WT DCs treated with C3aRa exhibit a tolerogenic cytokine profile with a lower IL-12 and higher IL-10 production; when co-cultured with naïve allogeneic $CD4^+$ T cells, they elicit significantly lower T cell responses measured by IFN-γ production and thymidine uptake. Mice receiving C3aRa treated DCs developed a weaker alloreactive T cell response, compared with mice receiving untreated DCs, measured by re-stimulation with alloantigen *ex vivo*.
Finally, using DCs from mice deficient in key components (i.e. C3, FB, C4, C6) for each pathway, we demonstrate that the alternative pathway of complement activation primarily underlies the complement-dependent enhancement of DC function in allostimulation *in vitro*.
Our findings show that complement mediated enhancement of DC function is dependent on an action of C3a on DC, offering an explanation, at least in part, for the critical effect of donor cell production of complement on T cell priming in the alloimmune response. Blockade of this novel function of C3a may prove to be a valuable therapeutic target.

Wednesday 28 March

Moderated Poster Session

Donation

P08

An Oral History Of Organ Donation And Transplantation In The United Kingdom Across Three Ethnic Groups

Glenn Smith[1], Anthony Warrens[1], Josip Car[1], Sonia Saxena[1], Harvinder Dulku[2], Pauline Reece[2]

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Despite several high profile campaigns overall donation rates remain low in practice, and even lower amongst people from Indo-Asian and African-Caribbean ethnic backgrounds. Reasons for this lower rate of donation are understood to be multi-dimensional and complex.
To try and address the severe shortfall of organs for transplantation overall and in particular for patients from Indo-Asian and African-Caribbean ethnic backgrounds, this study aimed to improve our understanding of the relationship between organ donation, transplantation and ethnicity.
To understand this complex relationship, we considered that by using oral histories to explore in-depth how some people developed their positive or semi-positive view of organ donation and transplantation, we could help address some of the issues that prevent others from wishing to donate.
We are currently well into the process of acquiring the oral histories of 75 people from a White British/Irish, Indo-Asian and African Caribbean ethnic background. By exploring these histories we are able to understand better the relationship between individual and social experiences over a person's life and how these experiences in-turn have informed their positive or semi-positive view of organ donation and transplantation.
Initial results indicate that being able to integrate organ donation and transplantation successfully alongside people's cultural and religious beliefs is aided by a community-spirited family background, being exposed to different cultures and beliefs, bearing witness to the suffering of those in need of an organ and being exposed to the idea of organ donation and transplantation from an early age or a key moment in life.
These oral histories will help us to have a better understanding of what is and is not likely to be possible to improve organ donation and, therefore, how best to focus scarce public funds.

P09

Non-Heart Beating Renal Donors With Extended Criteria Have Excellent Graft And Patient Outcomes

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INTRODUCTION. Non-heart beating donor (NHBD) programmes and the use of marginal heart-beating donors have proved beneficial in tackling rising transplant waiting lists. The quality of renal grafts from marginal non-heart-beating donors is unknown.
METHODS. We performed a retrospective review of outcome in 76 recipients of kidneys from 40 non-heart beating donors. Recipients were divided into two groups (ECD- or ECD+) if the donor satisfied extended criteria of age over 60, cerebrovascular cause of death, uncontrolled hypertension or creatinine over 133μmol/L (Metzger et al. *Am J Transplant* 2003; 3supp4: 114). We also included primary CNS malignancy and cold ichaemia time over 22 hours as extended criteria. Outcome measures were creatinine levels, estimated GFR (4 variable MDRD), delayed graft function (defined by need for post-operative dialysis), graft survival and patient survival.
RESULTS. 44 patients received grafts from NHBD without extended criteria (ECD-) and 32 patients were ECD+. ECD+ donors were older (52 *vs.* 38 years, $p<0.0001$) with higher serum creatinine (93 *vs.* 70 μmol/L, $p=0.016$). There were no other donor baseline differences (gender, Maastrict category, time since insult, time to asystole, warm ischaemia time, renal anatomical variants). ECD+ recipients were older (54 *vs.* 46 years, $p=0.015$) but otherwise there were no differences between the recipient groups at baseline (gender, side of graft, cause of ESRF, time or mode of dialysis, waiting time, previous transplant, matchability score, HLA mismatches, pre-operative creatinine). There were no differences between ECD- and ECD+ in delayed graft function (36% *vs.* 41%, $p=0.812$, Fisher's exact), graft survival (95% *vs.* 96%, $p=0.744$, Logrank) or patient survival (93% *vs.* 79%, 0.598, Logrank). There were no differences in serum creatinine at any time point ($p=0.337$, ANOVA). Estimated GFR was 9 ml/min lower in ECD+ during the first year following transplantation ($p=0.003$, ANOVA) but there was no difference at two years.
DISCUSSION. Renal grafts from non-heart beating donors who meet conventional extended donor criteria have excellent function and survival over the first two years. If the performance of these grafts is maintained in the intermediate term, then kidneys from marginal NHBD may be a further source of transplant organs.

P10

Using pressure flow characteristics of the machine perfused kidneys in assessment from kidneys retrieved from hypertensive Non-Heart Beating donors

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Increasing disparity between supply and demand for kidney transplantation has prompted many centres to use marginal donors such as Non-Heart Beating (NHB) donors or donors with a history of hypertension or diabetes.
History of hypertension is part of the criteria used by the United Network for Organ Sharing (UNOS) to define Expanded Criteria Donors (ECD).
Studies on recipients receiving kidneys from hypertensive cadaveric donors show inferior function of the kidneys compared to the normotensive donor group.
Most centres use the duration of hypertension and pre-transplant biopsies as criteria to assess the degree of damage to the kidney from donor hypertension. All these are crude predictors of the injury implemented to the kidney.
In this study, we analyzed 82 kidneys retrieved from 41 NHB donors. Out of 82 kidneys, 28 were retrieved from hypertensive donors (HTD group). The rest were used as control group.
All kidneys underwent hypothermic machine perfusion prior to transplantation. Pressure flow characteristics of the kidneys such as peak flow per 100 gram of renal mass, peak perfusion flow index per 100 gram of renal mass (peak PFI, calculated by peak flow per 100 gram of renal mass divided by mean systolic pressure), peak glutathione-S-Transferase (GST) per 100 gram of renal mass and finally resistance after 4 hours of perfusion was analyzed and compared in both groups.
After 4 hours of perfusion, HTD group had a significantly lower peak PFI and flow/100g ($p<0.001$) and higher resistance ($p=0.04$) compared to the control group.
Peak GST/100g was not different between groups.
In conclusion, pressure flow characteristics using kidney machine perfusion can be a useful tool in assessment of kidneys recovered from hypertensive donors prior to transplantation.

P11

Living Kidney Donors Will Accept Extreme Risks Irrespective Of Pre-Op Education

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Introduction: This study investigates risk perception within the context of living kidney donation. It continues from a study conducted in 2005 which focussed on the risk to their own lives donors would retrospectively have tolerated. On this occasion the study was extended to incorporate the general public with the intention of investigating whether the donation process influenced the results initially obtained. The factors investigated were recipient prognosis, donor-recipient relationship and risk communication methods.
Method: In August 2006 a questionnaire was distributed to attendees at GP surgeries in South London. Participants were presented with different potential recipients and clinical scenarios and were asked to select from a list of options the risk they would accept when donating. Risk communication was investigated by randomly dividing the sample into two groups and presenting risk differently. Group A were presented with 'risk of death' (i.e. 1 in 3000) and group B were presented with 'chance of survival' (i.e. 99.99%). In the previous study living donors were asked identical questions.
Results: 90 questionnaires were obtained from the GP sample, 46 in group A and 44 B. 76 were prepared to donate with 27 accepting the highest risk (1 in 2). There was a significant difference between the two questionnaire types ($p < 0.01$), the modal risk accepted by group A being 1 in 3000 and group B being 1 in 2. For the previous living donor sample ($n=61$) a similar pattern was observed. In both sample groups the majority accepted the same risk for each scenario and of those whose answers changed, 70% ($n= 43$) accepted higher risks as prognosis worsened. There was no significant difference ($p>0.05$) when considering donation to different recipients (where the questions were identically phrased). There was also no significant difference between the GP and living donor groups ($p>0.05$).
Discussion: Kidney donors will accept a much higher risk than the 1 in 3000 risk of death currently quoted with a large proportion willing to accept a risk as high as 50%. This is equally true for those who have been counselled and have undergone donation and for the general public. Those presented with risk in terms of survival will accept higher risks, suggesting communication methods impact on the response. These findings have implications for procedures carrying higher donor risk, such as donation by marginal donors and living liver donation.

P12

Dual Ipsilateral Renal Transplants using Long Donor Ureters;
A Distinct Lack of Ischaemic Ureteric Complications?

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Introduction
Ischaemic ureteral necrosis occurs in 2-5% of renal transplants, and represents the most frequently documented cause of early ureteric fistulae. The allograft ureter receives its blood supply solely from the renal artery and renal transplant training therefore advocates the use of the shortest possible length of ureteric graft. Dual ipsilateral kidney transplantation necessitates a longer ureter for the cephalad kidney, as this ureter must exceed the length of the caudal kidney, and allow a tension-free ureteroneocystostomy. All our dual renal transplants therefore involve one 12-15cm ureter, the distal portion of which lies in the middle segment beyond the territory of the preserved donor renal artery. Current wisdom would therefore suggest an increased likelihood of distal ischaemia, necrosis, and ureteric fistulae.
Materials and Methods
We reviewed our series of 17 dual ipsilateral transplants using incidence of early (within 1 month post-transplantation) and late (occurring after the first post-operative month) ischaemic ureteric fistulae.
Results
From 2003 to date our group has performed 17 dual ipsilateral renal transplants. One dual graft resulted in PNF (5.9%) without evidence of urological complications. The mean follow-up is 1.41 years +/-0.83. In this series we have not seen any ureteric complications in the early post-operative period, or during later follow-up.
Discussion
Despite the ureteric length required for dual ipsilateral renal transplantation we have not seen clinical evidence of distal ischaemia. In life the middle ureter lies beyond the territory of the renal artery. However, anatomical studies have demonstrated that longitudinal anastamoses are in evidence between individual arterial territories for the full length of the ureter.
Surgical renal transplant training also stresses the importance of tension free bladder anastamosis, and the preservation of peripelvic and periureteral fat so as not to damage the adventitia of the ureter where arterial anastamosis occurs. This series would suggest that where such techniques are employed, longer ureters may be used without increasing the risk of ischaemic complications.

P13

Can we Retrospectively Tissue Type an Absent Kidney Donor?

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Increasingly patients travel abroad to receive a renal transplant. The unit providing long-term management for this patient often has limited information about the donor and, in the event that this kidney is lost, this may have implications for re-transplantation since it may not be clear to which HLA antigens the patient had been exposed. At present, donor HLA typing is performed using DNA extracted from intact donor cells. As it is clearly not possible to obtain fresh cells from all donors for retesting, we hypothesised that it would be possible to HLA type the donor from urine samples taken from the recipient. 50 ml urine samples were subjected to DNA extraction and purification by the QIAamp Viral Mini Kit and the DNA used in standard HLA class I (HLA-A, B and C) and class II (HLA-DR) PCR-SSP assays. Donor and recipient HLA types were determined from peripheral blood and compared with the data obtained from the urine of 37 stable renal transplant recipients. In 35 cases all mismatched donor HLA alleles were identified in the urine. Similarly, we were able to determine a complete HLA type in 12 of 13 normal controls. In conclusion, urine samples from transplant recipients can usually be used retrospectively to generate historical HLA typing on kidney donors who might no longer

P14

Developing a Non-Heart Beating Programme – A Valuable and Reliable Source of Kidney Transplants

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Introduction; The increasing shortage of donors despite growing waiting lists continues to be a major problem for all organs. Locally we have a daily average of 230 patients active on the kidney waiting list. Since July 2002 we have had a non-heart beating (NHB) programme, initially in the neurosurgical intensive care unit (ICU) then gradually expanding region wide.
Method; Following extensive preparation and education in all ICUs covered in the region, we have been able to gradually expand the programme. Using data collected from the Potential Donor Audit (PDA) we have been able to target our resources to the areas of greater donor potential in order to create a reliable and manageable programme.
Results; During the 52 months the NHB programme has been in place we have facilitated 46 donors, resulting in 80 kidney transplants. Figure 1 shows the expansion of the non heart beating programme over the past 4 full years from 6 donors in 2003 to 15 in 2006. This has made a significant contribution the total numbers of kidneys transplanted in this region (Fig 2).

Fig 1

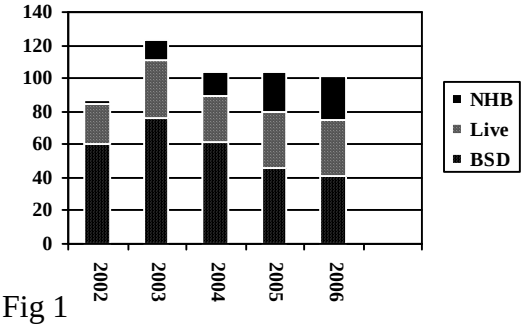

Fig 2

Conclusion; A NHB programme can contribute to a significant reduction in local waiting lists and offers additional hope to potential recipients. A reliable number of donors can be expected and data from the PDA supports further potential programme growth.

P15

Renal Transplantation from Elderly Non Heart Beating Donors: A Single Centre Experience.

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Kidney transplantation remains the treatment of choice in end stage renal disease providing long-term benefits in patient survival and quality of life. In an effort to meet the increasing demand for transplantation many centres are expanding their donor pool by using marginal donors or extended criteria donors (ECD). Use of elderly donors has been associated with poor graft outcome. Non-heart beating donors (NHBD) are generally regarded as marginal donors and most centres in the UK do not accept NHBD over the age of 60 years. We report our experience of renal transplantation from elderly NHBD over the age of 60 years.

From January 2004 to May 2006, 15 patients were transplanted at our centre from non-heart beating donors older than 60 years. Median donor age was 66 years (Mean 66.6yrs) and recipient age was 66 years (mean 66.4 yrs). Mean time on the waiting list for the recipient was 46 months. 80% of patients had delayed graft function, with median hospital stay of 21 days. With median follow up time of 13.5 months, one-year graft survival was 100% and one-year median serum creatinine level of 169 μmol/l (interquartile range 36).

We conclude that the use of carefully selected non-heart beating donor kidneys from elderly donors can have favourable outcome. In our centre, we have used such kidneys in age-matched recipient with long times on the transplant waiting list. These recipients are otherwise unlikely to receive a cadaveric kidney through the standard allocation scheme.

P16

Making the Donation Request

Olive mc gowan, rebecca smith

Leeds Teaching Hospitals NHS TRust, Leeds, -

Globally there is a critical shortage of donor organs to meet the demands for solid organ transplantation. The UK relative refusal rates are particularly of concern.
Collaborative Requesting has been discussed as a solution to alleviate high relative refusal rates. Some of the recent literature suggests that this approach is effective in reducing refusal rates. Therefore Collaborative Requesting was introduced in a unit with higher than average relative refusal rates.
It was decided to measure success or otherwise in terms of whether the quality of care families received was enhanced. The ultimate aim was to assess whether this change in practice made a difference to families been approached for organ donation, in terms of whether their informational and emotional needs were met at the time of the donation request.
This qualitative study employed a semi-structures interview schedule and both donor and non donor families were interviewed. Six families participated in this study. Overall the study results indicated both positive and negative experiences from the interviewees. A few important issues and areas for improvement are identified; in particular the need for relatives to understand that death has occurred before the donation discussion, the importance of utilising a planned approach for the donation conversation and finally importance of bereavement counselling irrespective of the families decision to donate. A key factor in the donation request is incorporating a “planned approach” between the consultant intensivist, nursing staff and the transplant co-ordinator.

P17

Comparison Of Hypothermic Machine Perfusion Versus Static Cold Storage For Kidneys From Controlled Non-Heart Beating Donors From Two Centres

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Introduction

Retrospective data from registry sources (UNOS) suggests a benefit for hypothermic machine preservation of kidneys from marginal donors. Controlled (Maastricht III & IV) non-heart beating donors (NHBD) provide kidneys with some ischaemic damage and because different units utilise different methods of preservation an opportunity for audit in this area exists.

Methods

Centre 1 routinely uses machine perfusion for assessment and preservation of kidneys from NHBD's. Centre 2 uses static storage and relies upon subjective assessment of viability. Data were collected retrospectively for outcomes over a similar time period (2002-06). Both units used tacrolimus based immunosuppression.

Results

	Machine perfusion Centre 1	**Static storage Centre 2**	**p value**
Donor (n)	33	40	-
Median Age yrs (range)	49 (10-67)	48 (12-69)	ns (MWU)
Median Agonal time (mins)	15 (0–248)	10 (0-92)	0.016(MWU)
1st WIT mean ± SD (mins)	19.2 ± 5.7	16.1 ± 4.9	0.014 (t-test)
Recipient (n)	60	75	-
Median Age yrs (range)	55 (20-76)	50 (23-71)	ns (MWU)
Cold ischaemic time (hrs)	22.5 ± 4.8	17.7 ± 4.7	<0.001(t-test)
%Primary non-function (n)	3.3 (2)	2.6 (2)	ns (X^2)
%Delayed graft function (n)	36.2 (21)	38.4 (28)	ns (X^2)
eGFR 3 months, mean ± SD	43.7 ± 11.8	49.4 ± 19.5	ns (t-test)
eGFR 1 year, mean ± SD	45.2 ± 15.4	49.8 ± 17.4	ns (t-test)

Discussion

Outcomes for kidneys from controlled NHBD's were similar for the two units utilising different storage methods. Machine perfusion added to viability assessment in centre 1 so that kidneys from 5 donors with acute renal failure and 4 donors with poor in situ perfusion were transplanted (data not shown). A randomised controlled trial is required to assess the potential benefits of machine perfusion over cold storage.

P18

Impact of Pulsatile Perfusion On Postoperative Outcome Of Kidneys From Controlled Non-Heart-Beating Donors

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INTRODUCTION: Non-heart-beating donors (NHBD) have higher incidence of delayed graft function (DGF) than HBD. Pulsatile perfusion (PP) has showed to be effective to diminish the rate of DGF. The aim of this study was to address whether PP should be obligatory to preserve kidneys from NHBD and also, whether NHBD preserved by PP could achieve similar rates of DGF than HBD.
PATIENTS AND METHODS: A retrospective analysis between recipients of organs from NHBD preserved by PP (NHBD PP) and NHBD preserved by static storage (NHBD SS) was performed. Results of NHBD PP were further compared with those obtained from HBD preserved by SS (HBD SS). End-points were incidence of immediate and delayed graft function (IGF and DGF), acute rejection (AR), 1 and 2-years serum creatinine, graft survival and patient survival.
RESULTS: From March 1st, 2002 to December 31st, 2005, Thirty transplants with organs from NHBD SS and 28 from NHBD PP were performed. Seventy HBD SS received induction therapy (IT) and were included as the control group. Donors were well matched, but, recipients were significantly younger in NHBD PP (54.1y +- 1.8 vs 45.1y +- 2-5) There was no difference in warm and cold ischemic times (20.40 +- 1.3 m vs 18.14 +- 0.2 m and 1152 h +- 52 vs 1161 h +- 59) and all patients received IT. IGF was significantly better (53.6% vs 13.3%) and DGF and AR lower in NHBD PP (42.8% vs 83.3% and 23% vs 14.2%). One year graft and patient survival were similar but, serum creatinine was lower in NHBD PP. We further compared NHBD PP and HBD SS. Donors and recipients were well matched. NHBD PP was poorly HLA-matched and both groups received IT with monoclonal antibodies (92% and 85.5%). IGF was still lower and DGF higher in the NHBD PP (53.6% vs 67.1% and 42.8% vs 30%) than HBD SS but, these differences did not reach statistically significance.
CONCLUSION: Outcome of NHBD PP is better than NHBD SS. Poorly HLA matched NHBD can achieve similar rates of IGF, DGF and graft survival as HBD SS when NHBD are preserved by pulsatile perfusion instead of static cold storage.

P19

Awareness and attitude to organ donation in young adults – a critical analysis

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Aims
Organ donation rates in the UK is inferior to Europe and could be improved. The current awareness and attitude of 'A' level students, where intervention may prove useful, is not known. The aim of our study was to systematically analyse this aspect.
Methods
We developed, validated and administered a questionnaire exploring the knowledge and attitude to organ donation of 16 to 18 year old students in a single city. A Clinical Organ Donation Attitude Scale (CODAS) was developed in association with clinical psychologists to test attitude. The questionnaire was distributed to all schools and administered by the teachers during class hours. Using the data, we developed a knowledge score (KS) and attitude score. We compared various demographic factors and the Deprivation Index of areas where schools are located, to assess the differences.
Results
Ten comprehensive (CS) and 4 independent schools (IS) were approached, of which 10 participated (7 (CS), 3 (IS)) in the study. There were 871 responses. The KS was significantly better in independent schools (P =0.0001), girls (P=0.04), better parents' occupation (P=0.006), Caucasians and Indians (P=0.035) and those who had a driving licence (P=0.03). Among the comprehensive schools KS was lower in schools with a higher deprivation index. The attitude score suggesting favourable attitude to organ donation was significantly better in children of parents with higher education (P=0.05), occupation (P=0.002), Caucasians (P=0.001), Christians (P=0.0001) and had a trend towards CS located in areas with low deprivation index and to independent schools. There was a significant correlation between KS and attitude scores (P=0.0001).
Conclusion
We conclude that deprivation is an important predictor of poor knowledge and attitude to organ donation. As there is a significant correlation between knowledge and attitude, targeted teaching of young adults could improve organ donation rates.

P20

Kidney Damage at Organ Retrieval

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Objective:
Aim of this study was to identify the frequency of kidney damage during retrieval and its effects on graft survival.
Methods:
Study was done at Royal London Hospital from 1st January 2005 to 1st April 2006. All Cadaveric kidneys transplanted during this period were included. The disparity between retrieval and transplant teams findings regarding kidney damage was noted. The effects of kidney damage on graft survival at one, three and six months was recorded in terms of Urea, Creatinine and eGFR.
Results:
During this period 40 cadaveric kidneys were transplanted. Out of these four were labelled as damaged by the retrieval team, whereas a total of 16 were found to be damaged by the transplant team. Arterial damage was found in eight, which included polar artery damage, damage to patch or a partial patch. Vein damage was present in eleven, which comprised of holes in vein, stretch damage and partial patch. Mesoureter was stripped in one case. Four kidneys were not well perfused. Two patients developed renal vein thrombosis, out of these one had a damaged vein (repaired by the transplant team) and the other patient had evidence of cuagulopathy. All of these kidneys were retrieved by liver teams. Thirty nine were multi-organ retrievals. Kidney damage was mostly found in patients of 40 to 55 years of age. There was no significant difference in Urea, Creatinine and eGFR at one, three and six months among patients who received damaged vs undamaged kidneys.
Conclusion:
The rate of kidney damage at Cadaveric retrieval is higher than reported, but there is no significant difference in graft survival.

P21

Clinical Assessment Of Donor Kidney Quality At The Moment Of Retrieval As A Tool To Predict Early Postoperative Outcome Of Non-Heart-Beating Donors

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INTRODUCTION: The deceased donor (DD) score (DDS) is a scoring system based on established clinical donor factors at the moment of retrieval, able to identify kidneys at highest risk of post-transplantation graft dysfunction and failure. However its ability to assess kidney quality and predict postoperative outcome in NHBD is unclear.
PATIENTS AND METHODS: A retrospective analysis of our cohort of DD was performed to validate the predictive ability of DDS. Organ donor quality was assessed using the DSS organ grade and a correlation with immediate graft function (IGF), primary non-function (PNF), delayed graft function (DGF), 1-year graft function and graft survival were investigated. In a further sub-analysis, the DDS was calculated in three different subsets of DD: Kidneys from HBD transplanted alone (HBD KA), transplanted simultaneously with a pancreatic graft (HBD SPK) and kidneys from NHBD transplanted alone (NHBD)
RESULTS: From March 1st, 2002 to December 31st, 2005, 278 kidney transplants with kidneys from DD were performed. Data from 269 transplants were retrospectively analysed. 168 kidneys from HBD and 58 from NHBD were transplanted alone and 46 kidneys from HBD transplanted simultaneously with a pancreatic graft. 68% of the kidneys from DD were classified as optimal organs (DSS grade A and B) and 32% as marginal organs (grades C and D). The NHBD group had the higher rate of optimal donors (88.9%) as opposed to HBD KA (58.3%). DSS organ grade correlated very well with immediate graft function, delayed graft function, and graft function in HBD. However, DSS was able to predict IGF and DGF but not 1-year graft function and graf survival in NHBD.
CONCLUSIONS: DDS provided a quantitative approach to assess organ quality, stratify DD into risk groups and predict post-transplant renal function in both subsets of HBD. However, a better score for NHBD may need to be implemented to mimic the success of DDS in HBD.

Wednesday 29 March

Moderated Poster Session

Immunosuppression

P22

Chronic Renal Allograft Salvage – Reducing or Eliminating Calcineurin Inhibitors. A Single Centre Prospective follow up of More than Three Years in Cohort of 50

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BACKGROUND: Long-term maintenance therapy with calcineurin inhibitors (CNI) results in a considerable incidence of chronic renal dysfunction. In this prospective study we assess the safety and efficacy of rescue therapy with mycophenolate mofetil (MMF) in patients with chronic allograft nephropathy (CAN) and their 3 years follow-ups. **METHODS:** 50 renal transplant recipients with chronic deterioration in graft function were enrolled. 27 of these patients had CNI monotherapy as their primary immunsuppression. In all patients the immunosuppression regime was changed to MMF and prednisolone with or without low dose CNI. The median period from transplantation to conversion was 21 months (range 2-173). The median follow-up was 42 months (7-91). The parameters included following conversion: systolic and diastolic blood pressure, antihypertensive medications, leucopoenia and anaemia and need for treatment, GI disturbances, weight loss, hyperlipidaemia, hyperglycaemia, changes and doses of immunossupressants and reasons for alteration/discontinuation, graft and patient survival. Renal function was measured by the glomerular filtration rate (GFR) obtained by creatinine clearance (Cockcroft-Gault). Patient data were recorded at baseline, 3, 6 and 9 months and at 1, 2 and 3 years post-conversion. All co-morbidity prior to conversion was recorded. CAN was featured on biopsy of 38 recipients. The other 12 were converted without biopsy. **RESULTS:** During the follow up period the serum creatinine concentration decreased from a median value of 316 mg/dl (169-586) to 187 mg/dl (75-412) [$p<0.05$]. GFR increased from a median value of 28.5 (15.0-91.8) to 46 (24-91) [$p<0.05$]. Overall >3 years patient and graft survival of: 86% and 60% respectively. No patient experienced episodes of acute rejection. In 32 patients (64%) CNI were discontinued. This did not confer any significant advantage in allograft function improvement when compared to those patients maintained on low dose CNI. During follow up 5 (28%) grafts were lost in CNI reduction group and 9 (28%) in CNI elimination group. There were however 6 deaths with functioning graft in CNI elimination group, with the median period for death from conversion of 32months (range 7-62). **CONCLUSIONS:** This study has shown that it is possible to safely and significantly improve renal function in CAN by reducing the dose of CIN and adding an alternative non-nephrotoxic immunosuppressant with a good long-term outcome.

P23

Low-dose Sirolimus In The First 8 Weeks Following Renal Transplantation Accompanied By Daclizumab Induction, MMF And Steroids: The Experience Of The SYMPHONY Study

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Introduction.
The randomized, open-label trial SYMPHONY compared standard immunosuppression (cyclosporine - CsA - , MMF 2g/day and steroids) to 3 regimens with daclizumab induction and low-doses of either ciclosporin (LD-CsA), tacrolimus (LD-TAC) or sirolimus (LD-SRL) in 1645 de-novo renal transplant patients over 1 year. Here we present further data on patients in the LD-SRL group.

Methods.
The SRL loading dose was 9 mg/day for the first 3 days post-transplant, followed by 3 mg/day and adjusted to maintain through levels of 4-8 ng/ml. In 389 evaluable patients we analyzed the time course of SRL trough levels at week 1-8 and correlated them with selected clinical outcomes.

Results.
At week 1 (first mandatory measurement), 16% of the patients were below, 53% within and 31% above target. Similar percentages were observed at the following measurements (week 8: 10%, 51% and 39%, respectively). Less than 4% of the patients were constantly above or below target, pointing to a correct reaction to off-target levels. The average SRL dosage was 2.93 mg at week 8. The rate of biopsy proven acute rejections (BPAR - excluding borderline rejections) in LD-SRL at 1 year (37%) was higher that in the other groups (12-26%). The increase in BPAR emerged mainly after week 8. Only a weak correlation of SRL levels with BPAR rate, total cholesterol, triglycerides and wound healing problems (more common than in the other groups) could be identified. Patients with initial levels below target did not seem to be at an undue risk of future rejections. In a separate pharmacokinetic sub-study of patients from all groups, MPA exposure in LD-SRL was similar to that observed for LD-TAC at week 4.

Discussion.
From previous studies we estimate that adding LD-SRL to a CNI-free regimen with daclizumab induction, MMF and steroids conferred a reduction in BPARs of about 15%. The protection over the first 8 weeks was comparable to that of LD-CsA, but thereafter it was inferior to all other tested regimens. The proposed initial dosing regimen was appropriate to reach the target range given the variability of levels in this clinical setting. The room for increasing SRL immunosuppression should be evaluated against its specific toxicity profile.

P24

Alemtuzumab Induction Therapy & Steroid-free Immunosuppression in Pancreas Transplantation.

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Introduction: Alemtuzumab (Campath-1H) is a humanised anti-CD52 antibody, which has a powerful lytic effect on T & B lymphocytes and is known to have clinical activity in a number of conditions mediated by lymphocytes. The impact of Alemtuzumab induction and steroid-free immunosuppression in pancreas transplantation was evaluated.

Materials and methods: 70 transplants were performed in 69 patients, who underwent a simultaneous pancreas kidney (SPK), pancreas after kidney (PAK) or a Pancreas transplant alone (PTA). They received 30 mg of Campath intravenously on day 0 and 1, with tacrolimus (trough levels of 8-12ng/ml) and mycophenolate mofetil 500mg BD for maintenance immunosuppression. Patient and graft survival, rejection rate and adverse events were obtained prospectively by review of charts and case notes.

Results: There were 45 males and 24 females in the group with a median age of 39.5 years (range 31-60 years). 2 patients had favourable matched organs while the mean HLA mismatch was 4. 58. The median length of follow-up was 5 months (range 1-26 months). Thirty-day mortality in the group was 0%; the overall patient survival is 96%. 93 % (n=54) of the patients are off dialysis while 87% (n=61) have a functioning pancreatic allograft. Two patients (2.8%) had BK nephropathy, but still have functioning renal grafts. 18 patients received steroid pulse therapy for 19 rejection episodes (27%), on the basis of graft dysfunction. 5 patients (7.1%) had positive CMV antigenemia. 18 patients (25.7%) had re-operations; the causes included abdominal wall dehiscence, bleeding, acalculous cholecystitis, renal vein thrombosis, donor duodenal leak, peri-pancreatic abscess and abdominal compartment syndrome. 10 patients (14%) remain on prednisolone at the time of assessment. None of the patients had fungal infections or post-transplant lymphoproliferative disorder.

Conclusion: **Our results suggest that Alemtuzumab is safe and efficacious, with low incidence of rejection despite a steroid free immunosuppression in 86% of patients.**

P25

Initial Immunosuppression For Deceased Donor Kidney Transplants – A Single Centre Audit Against NICE Guidance And Unit Policy

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Since 1981 this Unit used calcineurin inhibitor monotherapy as initial immunosuppression for adult recipients of heart beating, deceased donor, kidney alone transplants. In September 2004, NICE guidance recommended induction with basiliximab or daclizumab, in combination with tacrolimus or ciclosporin and that MMF be avoided with the exception of those deemed "high risk of nephrotoxicity". In May 2005 we revised our policy to incorporate NICE guidance, with a plan for steroid avoidance where possible, in-line with the growing evidence base. Our primary immunosuppressive regimen became basiliximab induction followed by tacrolimus monotherapy.

Methods

We report 202 transplants between January 2004 and October 2006. We assess adherence to NICE guidelines and compliance with unit policy. We define "high risk of nephrotoxicity" as those with a cold ischaemic time greater than 18 hours (median), the presence of delayed graft function, or second or subsequent grafts.

Results

	Induction basiliximab	Tacrolimus monotherapy at:		MMF	Prednisolone in first 3 months
		1 Mth	3 Mths		
Pre-NICE Jan04-Aug04	10/11 (91%)	0/11	0/11	8/11 0/8[b]	6/11 2/6[b]
Post-NICE Sep04-Apr05	7/57 (12%)	2/57 2/20[a]	4/57 2/20[a]	23/57 5/23[b]	38/57 24/38[b]
Post-Policy May05-Oct06	119/134 (89%)	25/134 15/38[a]	22/134 12/38[a]	34/134 13/34[b]	52/134 32/52[b]

*[a]Number of patients prescribed tacrolimus monotherapy in which it was indicated

*[b]Prescriptions outside NICE guidelines or agreed unit policy

Conclusions

Our unit complies with basiliximab induction. The use of tacrolimus monotherapy was not maximised or sustained and there was a notable proportion of MMF prescribed outside the agreed policy when correcting for high risk cases. Adjusting for rejection episodes, prednisolone is prescribed in a high proportion of cases within the first three months. These results will inform future practice on our Unit.

P26

A Putative "Target" Ciclosporin Level In Renal Transplant Patients With Delayed Graft Function

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Delayed graft function (DGF) following renal transplantation has an association with worse long term outcomes. It is well established that early acute rejection episodes have a detrimental effect on graft survival and that rejection superimposed on DGF is particularly deleterious. There is a historical practice to reduce calcineurin inhibitor dose in the presence of DGF and thus a potential risk of acute rejection. The aim of this study was to seek an association between 2 hour post dose ciclosporin (C2) levels and biopsy proven acute rejection (BPAR) episodes in patients with dialysis dependent DGF, as this has not previously been described.

We identified 75 patients with DGF from 217 consecutive deceased donor renal transplants treated with a ciclosporin based immunosuppressive regimen, performed between 2003 and 2006. Within this group 57 patients underwent renal biopsy for ongoing dialysis dependency at day 5 post transplantation. Of this group, 26% displayed BPAR (Banff 1A or greater).

The C2 levels taken at the time of biopsy were significantly lower in those patients with BPAR than in those without (851±494ng/ml vs 1279±485ng/ml; p=0.005). Multivariate analysis revealed that higher ciclosporin levels were associated with a reduced risk of rejection (OR per 100ng/ml: 0.80; 95%CI: 0.68-0.94; p=0.007), and that an increased number of HLA-DR mismatches was associated with an increased risk of rejection (OR: 1.91; 95%CI: 1.56-3.76; p=0.002). The use of Mycophenolate Mofetil and Basiliximab were associated with a trend to reduction in the risk of rejection, but failed to reach significance (p=0.22 and 0.18 respectively). No association was found between C2 levels and the duration of dialysis. ROC curve analysis revealed C2 levels to be of moderate predictive value for acute rejection, with a c-statistic of 0.75. A C2 level of 1110ng/ml discriminated patients with and without rejection (during the period of DGF). This is the first description of a putative "target" C2 level in patients experiencing DGF and suggests that levels should be optimised in this clinical scenario.

P27

CAMPATH-1H For The Treatment Of Acute Rejection In Kidney Transplant Recipients: 10 Year Follow-up

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Introduction: Campath-1H (Alemtuzumab) is a humanised CD52 monoclonal antibody that causes profound B and T lymphocyte depletion. It is an effective induction agent in renal transplantation which may permit a steroid-free maintenance regimen. A number of centres have also used Campath-1H for the treatment of acute humoral and cellular rejection, but there is no published data on long-term outcome in this patient group. We wished to ascertain 10 year follow-up data in a cohort of patients who received Campath-1H for the treatment of acute rejection.

Methods: 15 patients were identified who had received intravenous Campath-1H for biopsy-proven acute rejection between November 1991 and June 1994. Follow-up data including patient survival, graft survival, serum creatinine, lymphocyte counts, infection and malignancy rates were gathered from hospital notes, biochemistry and haematology laboratory databases, our in-house transplant database, UK Transplant and regional transplant co-ordinators.

Results:

Patient demographics: Mean patient age 41 years (range 20-63). Gender: 11 male, 4 female. **Previous transplants:** One n=13; Three n=1; Four n=1. ***Nature of rejection episodes:*** Acute cellular rejection n=12. Humoral rejection n=1. Mixed humoral and cellular rejection n=2. ***Efficacy:*** Rejection reversed in all. ***Total dose of Campath-1H:*** mean 55mg (24-70mg). Outcomes: see Table 1.

Table 1:

OUTCOME	1 Year	5 Year	10 Year	12 Year
Patient survival	80%	80%	60%	53%
Graft survival	73.3%	60%	53%	47%
Creatinine (□mol/l)	170(90-391)	190(134-370)	129(100-170)	-
Lymphocytes (x10^9/l)	0.8(0.2-1.4)	0.88(0.2-1.3)	1.1(0.7-1.5)	-

Adverse events: Malignancy n=2, polyarthritis n=2, severe infections n=7.

Discussion: Campath -1H is an effective treatment for acute rejection, but may increase the risk of infection, particularly in the short-term. The occurrence of polyarthritis in 2 patients (one of which became rheumatoid factor positive) within 2 years of treatment is of interest and adds to the autoimmune complications which have been described following Campath-1H treatment.

P28

Subcutaneous Administration Of Alemtuzumab Avoids First Dose Reaction But Maintains Efficacy In Combined Kidney-Pancreas Transplantation

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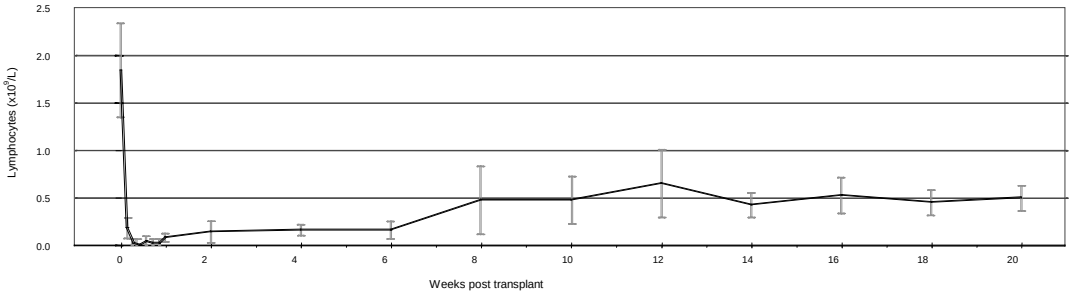
Introduction: Alemtuzumab is a humanised anti-CD52 monoclonal antibody that causes profound B and T lymphocyte depletion and is increasingly used as induction therapy in solid organ transplantation as well as in the treatment of haematological maliganancies and rheumatological disorders. Traditionally it has been given by intravenous (IV) injection, but this route of administration is associated with a first dose cytokine-release response in some individuals, characterised by hypotension, pyrexia, rash, and bronchoconstriction. In contrast, data from rheumatological and haematological patients suggests that subcutaneous (SC) administration of alemtuzumab prevents these first dose reactions.

Methods: Alemtuzumab induction therapy is effective and allows the use of a steroid-free maintenance regimen, prompting its use in simultaneous pancreas and kidney (SPK) transplantation. Avoidance of first dose side effects, such as hypotension, is particularly important in these patients where venous thrombosis is a serious concern. Therefore, we wished to determine the safety and efficacy of SC administration of alemtuzumab in SPK transplantation. Seventeen SPK recipients with type I diabetes mellitus were treated with 30mg of SC alemtuzumab intraoperatively and day 1 following transplantation. Both doses were preceded by an anti-histamine and the first dose by 1g of IV methyl prednisolone. Maintenance immunosuppression with tacrolimus (0.075mg/kg) was commenced on day 3.

Results: First dose cytokine response: 0/17 patients. Lymphocyte depletion occurred within 24 hours and was sustained beyond 4 months (Figure 1).

Figure 1: Lymphocyte count patients 1-5



Discussion: SC administration of alemtuzumab is effective in causing lymphocyte depletion but avoids first dose reactions.

P29

Role of Monoclonal Antibody Based-Induction Therapy On Postoperative Outcome Of Kidneys From Non-Heart-Beating Donors

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INTRODUCTION: Induction therapy (IT) has increased the incidence of immediate graft function (IGF) and diminished the rate of delayed graft function (DGF) in NHBD. However the role of monoclonal antibodies as IT in this subset of patients is still unclear.
PATIENTS AND METHODS: The objective of this study was to compare induction with anti-thymocyte globulin (ATG) versus induction therapy with monoclonal antibodies (MI) in NHBD. A retrospective analysis of clinical outcome of our cohort of NHBD was done and NHBD treated with MI were compared with NHBD who received ATG as IT. The role of each antibody was further investigated comparing the outcome of NHBD preserved with PP treated with Camp-1 versus those treated with Bsx.
RESULTS: Between March 1st, 2002 and December 31st, 2005, Fifty-eight kidney transplants with organs from NHBD were performed. We compared 30 recipients of kidneys from NHBD treated with ATG (NHBD ATG) and 28 NHBD treated with MI (NHBD MI). Donor and recipient data were well matched. Recipients in the NHBD MI group were younger (46.7 +- 3.8 vs 53.4 +- 1.0), best HLA-matched and received more second transplants (19.3% vs 0%) CIT was similar but, NHBD MI group was preserved by PP. IGF was statistically higher and DGF lower in the NHBD MI group (50% vs 14.3% and 46.1 vs 82.1%) whereas AR rate was smaller in the ATG group (0% vs 7.7%). There was no difference in 1 and 2-year graft and patient survival. In a sub/analysis of NHBD MI group, 15 received Cmp-1 and 11 Bsx. Donor and recipients data were well matched. IGF was higher and DGF and AR were lower in the Cmp-1. However, these differences did not reach significance: (60% vs 48.2%, 40% vs 54.5% and 6.2% vs 9.1% respectively) One and 2-year graft and patient survival were better in the Cap-1.
CONCLUSION: Induction therapy with monoclonal antibodies produced better clinical outcome than induction with ATG in NHBD and Campath-1 produced better IGF, lower incidence of DGF and superior graft and patient survival than Basiliximab.

Wednesday 29 March

Moderated Poster Session

Ischaemia – Reperfusion Injury

P30

FTY720 Reduces The Pro-inflammatory Cascade Initiated By Ischaemia-reperfusion Injury

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Background - Ischaemia-reperfusion injury (IRI) is an unavoidable process in renal transplantation, it has an important influence on early and late graft function. The pathophysioogical processes involved are complex but broadly consist of endothelial and tissue injury as a result of free radical production and lytic enzymes released from infiltrating neutrophils. This process, particularly the infiltration of inflammatory cells, is driven by a number of pro-inflammatory cytokines such as IL-1, IL-6 and TNF-α. Lymphocytes have not been considered a key cellular mediator in IRI but recent evidence has suggested they play a key role. We aim to investigate the effects of the new immunosuppressant FTY720 (which produces peripheral lymphopaenia by homing lymphocytes back to secondary lymphoid tissue) in a rat model of IRI. **Methods -** A rat model of IRI was used in which male Sprague-Dawley rats underwent bilateral flank incision with removal of the right kidney and clamping of the left renal hilum for 45mins. Five groups of animals were studied (n=4 per group). A control group (nephrectomy only), IRI only, IRI + FTY720 (1mg/kg/d),IRI + cyclosporine (CYA) (15mg/kg/d) and IRI + FTY720(1mg/kg/d) + CYA (15mg/kg/d). Animals were sacrificed at 1,6, 12 and 24 hours and 3, 5,7 and 10 days. **Results -** Serum creatinine (SCr) was markedly reduced in the FTY720 group in comparison to both IRI only and IRI + CYA treated animals; furthermore, the addition of FTY720 to CYA resulted in a reduction in SCr in comparison to CYA treatment only. Tubular diameter and tubular necrosis, other markers of injury severity, also showed a similar reduction in FTY720 treated animals. Assessment of myeloperoxidase activity (a marker of neutrophil infiltration) demonstrated a reduction in FTY720 treated animals (when compared to IRI + CYA and IRI only), either alone (3.7 ± 0.7 v 30 ± 1 and 26 ± 0.9, $P<0.05$) or in conjunction with CYA (4.1 ± 0.8 v 30 ± 1 and 26 ± 0.9, $P<0.05$). Measurement of inflammatory cytokines demonstrated a reduction in IL-1, IL-6 and TNF-α in the FTY720 treated animals. The improvement in both functional and morphological parameters, in addition to the reduction in pro-inflammatory cytokines was associated with a significant reduction in infiltrating lymphocytes. **Conclusion -** The early inflammatory events following ischaemia-reperfusion injury may be reduced by FTY720. This could translate to reduction in the incidence of delayed graft function and improvements in long term graft survival.

P31

FTY720 Reduces Extra-cellular Matrix Expansion Associated With Ischaemia-reperfusion Induced Injury

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Background - Ischaemia-reperfusion (IR) is a strong risk factor associated with the development of chronic allograft nephropathy (CAN). This effect is often exacerbated by immunosuppressive medications. Traditionally the macrophage was thought to stimulate fibroblast activity in CAN, recent evidence supports a role for lymphocytes. FTY 720 is a new immunosupressant that promotes lymphocyte sequestration into lymph nodes. This study investigated the effect of FTY 720 on renal fibrosis in the rat following IR injury.

Methods - A rat model of IRI was used in which male Sprague-Dawley rats underwent bilateral flank incision with removal of the right kidney and clamping of the left renal hilum for 45mins. 5 groups of animals were studied (n=4), nephrectomy only, IRI only, IRI + FTY720 (1mg/kg/d, IRI + cyclosporine (CYA) (15mg/kg/d) and IRI + FTY 720 (1mg/kg/d) and CYA (15mg/kg/d). Animals were sacrificed at 30 days.

Results - Serum creatinine (SCr) was significantly reduced in the FTY720 treated animals. IRI alone produced a significant increase in SCr compared with neprectomised animals (138μmol/l v 55μmol/l, $P<0.05$). This effect was potentiated by treatment with CYA (173μmol/l v 55μmol/l, $P<0.05$). Treatment with FTY 720 significantly reduced SCr in rats following IRI alone (81μmol/l v 138μmol/l, $P<0.01$) and in rats following IRI + CYA (98μmol/l v 173μmol/l, $P< 0.014$). Parallel changes were seen in the levels of proteinuria. IRI alone produced a significant increase in MT staining compared with nephrectomised animals (16.08% v 0.29%, $P<0.05$). This effect was potentiated by treatment with CYA (20.62% v 16.08%, $P = 0.022$). Treatment with FTY 720 reduced the level of MT staining in rats following IRI alone (7.45% v 16.08%, $P<0.05$) and in rats following IRI + CYA (7.45% v 20.62%, $P<0.05$). TGF-β was considerably reduced in FTY720 treated animals (compared with CYA + IRI and IRI only), either alone (196 ± 31pg/ml v 1105 ± 59pg/ml and 611 ± 38, $P< 0.05$) or in conjunction with CYA (423 ± 26pg/ml v 1105 ± 59pg/ml and 611 ± 38, $P< 0.05$).

Conclusion - Our study shows that treatment with FTY720 can reduce renal fibrosis as a result of ischaemia-reperfusion induced injury, both alone and in conjunction with cyclosporine. This provides promising evidence for using FTY720 in a calcineurin free or reduced dose immunosuppression protocol in an effort to reduce the incidence of CAN.

P32

The Effect Of Body Temperature In A Rat Model Of Renal Ischaemia-reperfusion Injury

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Background - Renal ischaemia-rperfusion (IRI) is an unavoidable event in renal transplantation, the effects of IRI can be seen in both the acute and long-term function of the transplanted organ. As such research into the pathophysiology of ischaemia-reperfusion is at the forefront of transplantation research. Animal models, particularly in the rat, provide a useful research tool in studying the intricacies of IRI and in evaluating new treatments. We describe a model of right nephrectomy and left renal clamping for 45mins and demonstrate the effects of temperature variation during the ischaemic period.

Methods - Male Sprague-Dawley rats (under isoflurane anaesthesia) underwent bilateral flank incision with removal of the right kidney and clamping of the left renal hilum for 45mins. The animal were divided into 3 groups (n=6), group 1 had the procedure performed on a heating mat with no temperature control facilities, group 2 used no heating mat and group 3 used a rectal temperature controlled homeothermic blanket system (Harvard medical, UK). Temperature was taken every 5mins throughout the procedure and blood samples were taken on a daily basis post-op via tail vein venepuncture.

Results - The average temperature at the end of the procedure in group 1 was 39.67°C and the creatinine at day 3 was 574 $\pm$ 17.84, in group 2 the temperature was 32.6°C and the creatinine was 115 $\pm$ 4.06 and in group 3 the temperature was maintained between 36.5 -37°C and the serum creatinine was 329 $\pm$ 19.18. The temperature of the animal during the ischaemia phase of IRI significantly affects the severity of injury. Relative hyperthtermia resulted in more severe renal injury and unrecoverable acute renal failure, no source of heat led to a relative hypothermia and reduction on renal injury. Use of the homeothermic heating blanket led to a rise in creatinine by day 3, indicating a significant ischaemic stimulus; however, by day 10 the creatinine had returned to normal.

Conclusion - This illustrates the importance of temperature as a variable in animal models of IRI and thus should be clearly stated in all experimental methods to ensure an appropriate ischaemic stimulus and for adequate comparisons between various therapeutic interventions.

P33

Control of Sulfate Metabolism in Endothelial Cells Can be Targeted to Inhibit Ischaemia Reperfusion Dependent Leukocyte Recruitment.

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Sulfur plays many vital roles in maintaining cellular function. It is derived from sulfate and sulfur rich amino acids in the diet and is important in the recruitment of inflammatory cells through sulfation of endothelial and leukocyte ligands and receptors. Therefore we tested whether controlling sulfur metabolism could be exploited in a model of ischeamia reperfusion injury. Using isolated endothelial cells and a physiological shear stress leukocyte adhesion assay we show enhanced leukocyte recruitment dependent on sulfate following hypoxia reoxygenation (H/R). Kidney sulfate uptake is controlled by a sodium sulfate co-transporter which is sensitive to heavy metals. Indeed, the addition of tungstate or molybdate inhibited not only the H/R sulfate enhanced recruitment but also H/R only recruitment suggesting both rapid and de-novo sulfation events occurring from cellular sulfate stores. In the absence of H/R, sulfate slowed leukocyte rolling events but did not stimulate adhesion at physiological sulfate concentrations (~300 □mol / L). In contrast, the sulfur containing cysteine precursor N-acetyl cysteine (NAC) caused a decrease in rolling velocity and an increase in adhesion at concentrations used clinically in the absence of H/R. This suggests differential metabolism or uptake for each compound with sulfate requiring H/R dependent changes. Depletion of stored sulfate (Phospho-adenosine phospho-sulphate, PAPS) should also reduce sulfate dependent processes. Phenolic compounds are detoxified by sulfation and have the potential to deplete stores of PAPS via the phenol sulfur transferase (PST) enzymes. We therefore used acetylated salicylic acid (ASA), acetaminophen and apocynin, simple phenolics in H/R and H/R sulfate dependent recruitment. Both H/R sulfate and H/R alone recruitment was inhibited by the phenolics. These compounds also increased rolling velocity back to control levels. In comparison, tungstate or molybdate inhibited adhesion but had no effect on rolling velocity. Therefore, the control of sulfate metabolism represents a novel therapeutic target to reduce ischaemia reperfusion dependent inflammation in transplanted organs

P34

Relaxin, The Pregnancy Hormone, As A Therapy To Improve Kidneys Damaged By Ischaemia Reperfusion

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Introduction. Relaxin (RLX) is a polypeptide hormone secreted by the corpus luteum and responsible for the massive increase in renal blood flow and glomerular filtration rate associated with early pregnancy in both humans and rats; further anti-fibrotic effects have also been characterised. The vasorelaxation is mediated by augmented endothelial nitric oxide synthase (*e*NOS) activity and the signal transduced by endothelin type B (ET-B) receptors on endothelial cells. We hypothesised that RLX treatment could successfully oppose the renal vasoconstriction associated with severe ischaemia reperfusion injury.

Methods. After 30 minutes of post-mortem warm ischaemia rodent kidneys (n=6 per group) were *in situ* perfused with UW solution ± 1 nmol recombinant human relaxin (rhRLX; BAS medical, Inc.) for one hour and then stored for 24 hours at 4°C (UW ± rhRLX) before reperfusion with a warmed oxygenated balanced salt solution (Krebs ± rhRLX). Control kidneys were reperfused directly after animal death (Krebs). The functional presence of ET-B receptors was then elicited by adding agonists (acetylcholine, phenylephrine, endothelin-1, endothelin-3) to the reperfusion circuit and measuring the change in vascular resistance.

Results. *e*NOS activity (acetylcholine) and vascular smooth muscle contractile function (phenylephrine) were significantly degraded by the combination of warm and cold ischaemia; independent of treatment with rhRLX (ANOVA $p<0.05$ and $p<0.001$). Surprisingly, the contractile response to endothelin was significantly greater in UW + rhRLX treated kidneys than both the control ($p<0.01$) and UW – rhRLX ($p<0.001$) groups. Blocking experiments confirmed that this was due to vascular smooth muscle expression of ET-B receptors.

Discussion. In the absence of viable functional vascular endothelium rhRLX promotes renal vasoconstriction, rather than dilatation, by up regulating ET-B receptors on vascular smooth muscle cells. These results offer a mechanistic explanation for the divergent responses of kidney grafts to pregnancy [1]. Further investigations should concentrate on the anti-fibrotic potential of RLX to prevent the development of chronic allograft nephropathy, prior to the onset of vascular dysfunction.

Reference. Davison JM. “The effect of pregnancy on kidney function in renal allograft recipients.” Kidney Int 1985; 27 (1): 74-9.

P35

Effects Of High Dose Erythropoietin (EPO) On Ischemia/Reperfusion (I/R) Injury In A Porcine Kidney Model

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Introduction:
Erythropoietin (EPO) has been shown to have anti-apoptotic action mediated via various mechanisms hence protecting against I/R (Ischaemia/Reperfusion) injury. This study investigated the effect of high dose of EPO (5000 units), administered in blood at the time of warm perfusion in a model of controlled NHBD kidneys.

Methods:
Porcine kidneys (n=6) were subjected to 10min warm ischaemia and preserved after as follows:
Group 1: 16hr Cold storage (CS)+2hr Warm resuscitation preservation (WRP)
Group 2: 16hr CS+ 2 hr WRP (EPO)
Group 3: 18hr CS
Various haemodynamic and functional parameters were then assessed during 3hr reperfusion with autologous blood.

Results:
Renal blood flow improved in Groups 1& 2 vs Group 3 (563±119 vs 491±95 vs 325±70; $P<0.01$). The total urine output showed no difference between Groups (271±172 vs 359±184 vs 302±211; Group1, 2& 3 respectively). Percentage of serum creatinine fall was significantly better in Groups1 & 2 vs Group 3 (64±17 vs 60±11 vs 44±13; $p= 0.04$). The fractional excretion of sodium was significantly lower for Group1 & 2 vs Group 3 (17±14 vs 18±9.vs 49±21 respectively; $p=0.01$). There was a marginal improvement in oxygen consumption in Groups 1 & 2 vs Group3 (39±10 vs 46±10.vs 24±12 respectively). All these parameters showed no difference between Group 1 and 2.

Discussion:
EPO did not seem to add any further benefits when used as a manipulating agent during two hours of WRP in a controlled NHBD Kidney.

P36

Elevated Preoperative Recipient Neutrophil-Lymphocyte Ratio (NLR) Increases The Risk of Delayed Graft Function.

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Introduction The incidence of delayed graft function (DGF) in renal transplants from cadaveric heart-beating donors (HBD) is 20–30% in the UK. DGF has substantive economic effects and may adversely affect overall outcome. The development of DGF is influenced mainly by donor and recipient factors, including donor age, type, cause of death, graft quality as well as durations of cold and warm ischaemia times. The neutrophil-lymphocte ratio (NLR) provides an indictor of inflammatory status. The inflammatory response can result in leukocyte sequestration in the renal vascular bed and vasoconstriction leading a 'low flow' or 'no reflow' state resulting in ATN. We have studied the effect of preoperative elevated NLR in the recipient on the risk of developing delayed graft function.
Methods Retrospective analysis of the preoperative white cell and differential counts of 455 renal transplant recipients between 2003 and 2005. Recipients were excluded if preoperative WCC were not available or if they developed surgical complications that lead to DGF. An elevated NLR was regarded as a ratio >3.5:1.
Results 398 kidney transplants were included in this study. 249 patients received kidneys from HBDs, 61 from NHBDs and 88 from living donors (LD). 103 recipients (26%) developed DGF, and of these, 67 (65%) had NLR >3.5. Of the 295 recipients with primary graft function, 44 (15%) had elevated NLR. Therefore, 61% (67/113) of recipients with elevated NLR had delayed graft function. When looking solely at the LD group, 5/7(71%) recipients with DGF had elevated NLR. A total of 17 recipients were found to have high NLR, 5 of which had DGF (29%), compared to 2 of 61 recipients with low NLR (3%). Univariate analysis revealed four factors that significantly influenced graft function; NLR, CIT, donor type and recipient gender. On multivariate analysis, both donor type ($p=0.014$ HR=2.421 CI=1.195-4.905 (NHBD) and $p=0.024$ HR=0.289 CI=0.099-0.846 (LD)) and NLR ($p<0.0001$ HR=10.673 CI=6.151-18.518) remained significant.
Conclusions Our data suggests that recipient preoperative NLR affects the immediate post operative graft function. This is most pertinent the live donor setting where a recipient with a high preoperative NLR is ten times more likely to develop DGF.

P37

Complement activation associated to ischaemia and reperfusion in clinical renal transplantation.

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The complement system is an important mediator of ischaemia-reperfusion (I/R) injury. The formation of membrane attack complex and the generation of anaphylatoxins such as C3a, C4a, C5a can potentially mediate I/R injury.
Objective: To demonstrate and characterise the pattern of complement activation in renal transplant recipients.
Methods: Twenty four patients were divided into 3 groups according to the source of the graft: live donors (n=6), heart beating donors (n=14) and non-heart beating donors (n=4). Peripheral blood samples were taken at induction, just before reperfusion, 1 hr after reperfusion and 24 hrs post transplantation. Serum Complement Haemolytic Activity (CH50) for classic and alternative pathways was measured by serial dilutions of conventional haemolytic assay. Serum C3 and C4 fractions were measured by nephelometry.
Results: There was statistically significant complement consumption in recipients of kidneys from heart beating and non-heart beating cadaveric donors in contrast with recipients of live related donor kidneys, indicated by reduced complement haemolytic activity and reduced levels of C3 and C4 at 1 hr post reperfusion in both cadaveric groups. There were minimal changes of complement parameters in samples from patients that received live donor kidneys.
Complement activation 1 hour post reperfusion: Live Donor recipient Vs Heart beating cadaveric donor recipient C3 (P=0.002), C4 (P=0.006), CH50 Classical (P=0.009), CH50 Alternative (P=0.001). Live Donor recipient Vs Non Heart beating cadaveric donor recipient: C3 (P=0.001), C4 (P=0.002), CH50 Classical (P=0.001), CH50 Alternative (P=0.003). Heart beating Vs Non heart beating C3 (P=0.154), C4 (P=0.493), CH50 Classical (P=0.172), CH50 Alternative (P=0.026).
Conclusion: There is significant complement activation in the first hour after reperfusion of the graft in the groups subjected to more severe ischaemic injury. This is highly suggestive of the involvement of the complement system in clinical kidney transplantation, associated to ischaemia and reperfusion.
These results indicate that downregulation of the complement system remains a potential therapeutic target for the management of ischaemia and reperfusion injury in transplantation.

Wednesday 28 March

Moderated Poster Session

Living Donation

P38

Mini-open Versus Standard Open And Laparoscopic Live Donor Nephrectomy: A Meta-analytical Comparison

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Aim: Mini-open donor nephrectomy (MODN) is a technique that potentially combines the advantages of the standard open (SODN) and the laparoscopic (LDN) techniques. This study is a meta-analytical comparison of these techniques.
Methods: A literature search was performed for studies comparing MODN to either SODN or LDN. Thirteen studies published between 1998 and 2006 met our selection criteria. Of a total 1652 patients, 584 (35.3%) underwent MODN, 532 (32.2%) SODN and 536 (32.4%) LDN. The following outcomes were evaluated: operative and warm ischaemia times, estimated blood loss, length of hospital stay, in-patient analgesia requirement, total donor complications and recipient ureteric complications.
Results*:* *MODN vs. SODN:* Operative time was significantly shorter for SODN by 13 mins ($p=0.04$) while hospital stay was shorter for MODN by 1.33 days ($p<0.001$). No significant differences were found for warm ischaemia time ($p=0.98$), blood loss ($p=0.06$), analgesia requirement ($p=0.12$), donor complications ($p=0.25$) or ureteric complications ($p=0.21$). *MODN vs. LDN:* Operative and warm ischemia times were significantly shorter for the MODN by 63.2mins ($p<0.001$) and 175.3secs ($p<0.001$) respectively. No significant differences were found for blood loss ($p=0.53$), analgesia requirement ($p=0.93$), hospital stay ($p=0.17$), donor complications ($p=0.30$) or ureteric complications ($p=0.79$).
Conclusion: The MODN technique is associated with longer operative time (but only by 13 mins which is probably not clinically significant) but shorter hospital stay compared to SODN as well as with shorter operative and warm ischaemia times compared to LDN. This data indicate that MODN combines the advantages of the SODN and LDN techniques and could be considered as a valuable alternative for live donor nephrectomies.

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Reasons For Declining Live Kidney Donors-A Single Centre Experience

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Introduction: Many potential donors are referred for live kidney donation, but only small percentage actually become donors. The aim of this study was to determine the reasons for non-donation and to examine the factors which could be modified to increase the number of live kidney donation.
Methods: A review of departmental database and case notes of all potential live kidney donors (PLKD) referred between January 1996 and November 2006 was carried out and data was analysed to establish the reasons for non-donation.
Results: Of the 262 PLKDs evaluated, 78 (30%) proceeded to actual kidney donation. The reasons for non-donation are shown in table below.

Donor health-related reasons	56 (30.4%)
Recipient-related reasons	54 (29.4%)
ABO-incompatible	26 (14%)
Positive cross-match	19 (10.3%)
Declined by donor	13 (7%)
Less preferred match (>1 donor from the same family)	16 (8.7%)
Total	184

The donor-related reasons for non-donation were renal vascular abnormalities (n=16, 28.5 %), low glomerular filtration rate (n=11, 19.6%), medical causes (n=9, 16%), urological abnormalities (n=9, 16%), hypertension (n=6, 10.7%), neuropsychiatric problems (n=3, 5.3%), and high body mass index (n=2, 3.6%). Although the PLKDs were suitable, donation was declined for recipient-related reasons such as existing cardiovascular co-morbidities (n= 26, 48%), a kidney transplant from a deceased donor (n=19, 35%) or other live donor source (n= 2, 3.7%), patients transferred to other centres (n=2, 3.7%), and improved renal function (n=1, 1.9%).
Discussion: Nearly a quarter of the donors (n=45) could not proceed to kidney donation from ABO incompatibility and positive cross match, which is a potential future source of donors to utilise, as increasing number of transplant centres are adopting desensitisation and paired organ donation programmes. Importantly, thorough evaluation of the recipients is mandatory to exclude unsuitable recipients at a very early stage of live donor work-up in order to avoid disappointments.

P40

Hand-Assisted Retroperitoneascopic Living-Donor Nephrectomy: 45 cases

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BACKGROUND: Hand assisted retroperitoneoscopic live donor nephrectomy (HARLDN) is a well established technique in Scandinavian countries. Since 2005 we have started using HARLDN in our living donor transplant programme. We report here our first 45 donors nephrectomized with HARLDN.
METHODS: All living-donor nephrectomies performed at our centre from February 2005 to November 2006 using the HARLDN are included. The operation is performed in the manner described by Wadström[1] with minor modifications.
RESULTS: The median age of the donors was 45 years; 24 were women and 21 men. Their median BMI was 26 (20-35). 19 donors had complex anatomy, including one donor with double vena cava and one with a retroaortic left renal vein. In 3 cases, the right kidney was retrieved. None of the operations was converted to open nephrectomy. Median operating time was 95 min (65-175). Median warm ischaemic time was 90 sec. (40-300). Median estimated blood loss was 40 ml (0-440). The median serum creatinine on admission was 82 (57-130); and at the time of discharge from hospital 118 (83-170). All of the donors demonstrated rapid recovery. Median hospital stay was 2 post-op days (1-3). All transplanted kidneys had immediate function except two. There were 2 cases with complications (4.4%) – 1 minor wound infection and 1 incisional hernia. In 2004, before the advent of HARLDN we performed 11 living donor transplants. This year (2006) we are on target to do 35 HARLDN living donor transplants.
DISCUSSION: We have found HARLDN to be a safe and efficient way to perform living-donor nephrectomy and it is popular among living kidney donors, more than doubling the number of living donor transplants.
1. Wadstrom J. Hand assisted retroperitoneoscopic living donor nephrectomy: experience from the first 75 consecutive cases. Transplantation, 2005; 80: 1060 -1066.

P41

Attempting to Increase Live Organ Donation in the Indo-Asian and Black Communities in West London

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The Hammersmith Hospital serves a population with a high proportion of end-stage renal failure patients drawn from the Indo-Asian (IA) and black (B) communities. Since 2000, we have attempted to increase live donation to our patients by employing 1.5 whole-time equivalent (WTE) transplant coordinators to work with these communities. From 2003, we employed another WTE coordinator to work with the Caucasian (C) community. This report summarises our experience in encouraging live donation in these three communities in West London. Of 523 potential recipients reviewed, 143 (27%) were C, 139 (27%) were B and 241 (46%) were IA. 156 (30%) of these patients did not wish to consider live donation. This was a less common issue in the C community (16; 11%) than in the B group (38; 30%) but was common in the IA group (102; 42%), although inability to identify potential donors showed a very different distribution (C: 45=31%; B: 47=34%; IA: 41=17%). Considering the donors who came forward for work-up, there were more females in the C and IA groups, but more males in the B group (male:female ratios C: 0.83; B: 1.16; IA: 0.73). In all groups, the majority were related (C=73%; B=73%; IA=57%). Amongst the unrelated group of potential donors, the percentages of husbands, wives and friends were evenly split in the C community: 31%/28%/31%; however, husbands represented the largest group of unrelated donors in the B community: 45%/27%/27%; and wives were the commonest in the IA community: 28%/53%/8%. Of the 238 potential donors, 29 (12%) withdrew their consent during the assessment process, 49 (21%) were the wrong blood group and 6 (3%) had a positive direct crossmatch. 43 (18%) were found to be medically unsuitable: this proved to be a bigger problem in the two minority communities: C 10%; B 22%; IA 28%. The commonest causes for medical exclusion were hypertension, diabetes and low donor GFR. 4% (all B and IA) were unable to be assessed properly because of visa problems. While a significant number are still in the process of being worked up, to date, 15% of donors considered have actually given their kidneys. However, there is a great imbalance between the three groups in terms of this “conversion rate”: C=24%; B=10%; IA=6%. This is in large measure due to the unexpected discovery of medical unsuitability and the fact that many potetnal donors live abroad in the B and IA groups.

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Quality Of Life Following Live Donor Renal Transplantation-A Single Centre Experience

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Introduction: The aim of this study was to assess the QoL of renal transplant recipients following live donor transplantation (LDRTx), and to compare this with their pre-transplant levels and with that of healthy controls.
Methods: Over a period of 16 years, 75 LDRTx were performed. Short Form-36 (SF-36) Health Survey and Kidney Transplant Questionnaires (KTQ) were used as assessment tools. Pre-transplant scores were estimated by participants in retrospect.
Results: Of 58/67 (86.5%) recipients approached participated in the study and 38/120 (31.67%) of the control group responded to the postal questionnaires. The results of SF-36 analysis are shown in table below.

SF-36	Pre-Tx (a)	Post-Tx (b)	Control (c)	P Value (a vs. b)	P Value (b vs. c)
PF	48.02 ± 27.45	70.6 ± 34.09	83.68 ± 23	0.00015	0.027
RP	17.24 ± 29.69	65.09 ± 41.61	92.11 ± 21.83	<0.005	<0.005
BP	58.91 ± 29.42	71.84 ± 29.06	84.47 ± 25.61	0.017	0.028
GH	21.84 ± 17.16	53.53 ± 26.1	73.34 ± 28.09	<0.005	0.00085
V	29.66 ± 18.44	63.19 ± 21.47	69.21 ± 22.04	<0.005	0.19
SF	42.67 ± 27	77.16 ± 28.11	80.92 ± 35.68	<0.005	0.59
RE	43.68 ± 42.9	75.86 ± 38.38	90.35 ± 36.27	<0.005	0.065
MH	59.17 ± 21.71	78.83 ± 16.72	76.74 ± 22.78	<0.005	0.98
PCS	35.13 ± 17.36	64.85 ± 25.2	80.56 ± 16.77	<0.005	0.00041
MCS	39.4 ± 19.15	69.31 ± 21.89	78.11 ± 24.74	<0.005	0.079
Total	40.15 ± 18.82	69.26 ± 23.72	81.35 ± 19.09	<0.005	0.0071

PF, Physical Function; RP, Role Physical; BP, Bodily Pain; GH, General Health; V, Vitality; SF, Social Functioning; RE, Role Emotional; MH, Mental Health; PCS, Physical Component Summary; MCS, Mental Component Summary)
All of the post-transplant scores for KTQ dimensions such as Physical Symptoms, Fatigue, Uncertainty/fear and Emotional, were statistically and clinically significantly higher compared to the pre-transplant values.
Discussion: There was significant improvement in QoL as evidenced by an increase in all SF-36 and KTQ dimensions, except in the Appearance dimension of the latter, in renal transplant recipients following LDRTx.

P43

Keyhole Mini-Open Donor Nephrectomy A Single Institution Experience

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INTRODUCTION: The critical factors in donor nephrectomy are absolute donor safety and provision of a high quality allograft. Minimising donor morbidity is also important; particularly decreasing wound pain and achieving a small cosmetic scar. Mini-open (MODN) and laparoscopic donor nephrectomy aim to achieve these goals. We have modified our technique of MODN in order to further minimise donor incisions and morbidity whilst ensuring an excellent recipient graft.
METHODS: We have prospectively audited our MODN series. We have previously described our incorporation of laparoscopic surgical instruments in MODN; such as linear articulated stapling devices for artery, vein and ureter. Briefly it consists in performing an open small loin incision with no rib resection and a retroperitoneal approach. New modifications include surgeons' use of headlights with 2.5x magnification loupes and use of two or three 2.5cm hand-held wound retractors rather than the previously used Omni-Tract.
RESULTS: In the last year 2 surgeons have performed 76 MODN (46 female) with the modified technique. The left kidney was harvested in 67 cases. Average patient body mass index (BMI) was 27 (17.5 to 44). The average skin incision length was 6.6cm (4.5-10cm); kidney out time 82 minutes (30-180); operative time 124 minutes (50-220); warm ischaemia time 4 minutes (1.5-10); estimated blood loss 115mls (20-450); and length of post operative hospital stay 5.2 days (3-8). 9 donors had multiple renal arteries on the harvested kidney as predicted on preoperative MRA. 2 arterial vascular anastomosis were required in 18 recipients and 3 in one recipient.
Six donors had minor post operative complications: one respiratory tract infection; one episode of fast atrial fibrillation; one ileus despite the retroperitoneal approach; one urinary tract infection; one urinary retention. All recipients had primary graft function except one recipient who had a graft nephrectomy on day 4-post operation for renal vein thrombosis.
CONCLUSIONS: MODN can be performed safely through an extraperitoneal incision that is as small as used to retrieve a donor kidney harvested laparoscopically. This technique is applicable to almost all-potential donors regardless of BMI. MODN provides excellent grafts for transplantation and has allowed us to expand our living donor program such that now over 70% of renal transplantation in our unit are living donation.

P44

Both Sided Retroperitoneoscopic Living-Donor Programme: First Year Experience

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BACKGROUND: Since 11/2005 we have adopted hand assisted retroperitoneoscopic live donor nephrectomy (HARLDN) for left and right sided living-donor nephrectomies our programme.
METHODS: All living-donor nephrectomies performed at our centre from 11/2005 to 11/2006 were included and followed prospectively.
RESULTS: Left sided nephrectomies: 27 donors, one donor had retroaortic left renal vein, 11 donors (40.74 %) had complex anatomy. Non of the operations was converted to open. Median operating time was 100 min (65-140). Median warm ischaemic time was 83 sec (40-158). Median estimated blood loss was 20 ml (0-100). Median admission serum creatinine was 79 (59-111), discharge 121 (88-170). Righ sided nephrectomies: 3 donors, one donor had simple anatomy, one donor had two veins and one had two arteries and two veins. Non of the operations was converted to open. Operating time was 125, 145 and 175 minutes. Warm ischaemic times were 105, 112 and 145 sec. Estimated blood loss was 20, 45 and 440 ml. The serum creatinine on admission was 57, 83 and 84, at the time of discharge from hospital 87, 90 and 117. Mean hospital stay was in both groups 2 postop days (1-3); 3.5 days from admission (Tuesday evening) to discharge (Friday morning). All of the donors demostrated rapid recovery and had no complications. All donors will have long term follow up. All transplanted kidneys had immediate function. We haven’t seen any complications, so the complication rate is 0 %.
DISCUSSION: Switch to HARLDN technique for right sided nephrectomies including donors with complex anatomy can be done just by decision, no criteria is needed. To offer the pure endoscopic programme seems to be one of the ways how to increase the number of living donor kidney transplants.

P45

Preservation of Renal Integrity and Function in a New Laparoscopic Donor Nephrectomy Programme

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Introduction: The changing practice of open donor nephrectomy (ODN) to laparoscopic donor nephrectomy (LDN) has been accompanied by concerns regarding the integrity and preservation of function in the donor kidney particularly when more marginal recipients are undergoing transplantation. Although more than 50% of all donor nephrectomies in USA are performed by LDN there are relatively few centres offering this technique in the UK. Centres not performing the LDN may need to be persuaded that the renal anatomy of the donor kidneys and subsequent recipient graft function are not compromised by a switch to a minimally invasive technique. We describe our experience of the first 39 cases performed in our centre.
Methods: We performed a retrospective study of prospectively collected data on the first 39 laparoscopic donor nephrectomies between December 2004 and November 2006.The following dataset was collected for the donor: side of donor kidney, primary warm ischaemia time, renal artery length, renal vein length, kidney weight and length of operation. For the recipient, the following data was recorded: creatinine at 2 weeks, 3 months and 12 months and incidence of delayed graft function. Vascular and urological complications were also documented.
Results: Out of 39 operations, all kidneys were procured and transplanted successfully with only 2 (5.1%) open conversions. 29 (74 %) kidneys were retrieved from the left side and 10 (26%) were from the right side. The primary warm ischaemia time was 3.57 ± 1.34 mins (mean ± SD). The length of the renal artery was 2.9. ± 0.6 cm and the renal vein was 2.7 ± 0.85 cm. The kidney weight was 174.2 ± 48.13 grammes. The duration of the operation was 164.3 ± 30 minutes. Recipient creatinine at 2 weeks, 24 weeks and 52 weeks post transplant were 138.1 ± 77.9µmol/l, 134.5 ± 33.8 µmol/l and 131 ± 39.8 µmol/l respectively. There were no cases of delayed graft function. There were no vascular complications but one ureteric stenosis detected at 3 months which needed ureteric reimplantation.
Discussion: As more centres adopt a LDN approach from traditional methods of procurement there will be concerns that the new technique may have a detrimental effect on graft function. We have demonstrated that despite the inevitable learning curve experience a LDN approach can be incorporated into a renal transplant programme without compromise of the renal integrity and function.

P46

Is There A Detrimental Effect Of Pneumoperitoneum In Laparoscopic Donor Nephrectomy?

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Laparoscopic donor nephrectomy is rapidly becoming the gold standard for live donor nephrectomy. However, a potential detrimental effect of pneumoperitoneum on the function of the graft has been a reason for concern in the literature.
OBJECTIVES: To investigate potential unfavourable effect of laparoscopic donor nephrectomy on early graft function.
METHODS: Between June 2003 and Oct 2006, 81 live donor renal transplants were performed at our institution. Demographic, operative, follow up data on patients and graft function were collected and analysed.
RESULTS: Hand-assisted laparoscopic nephrectomy (LDN) was carried out in 43 patients, of whom 5 were converted to open. The rest (38) underwent conventional open nephrectomy (ODN). There was no difference in donor and recipient age, gender or in the operative and anastomotic times between the LDN versus ODN. The donors of LDN had no significant complications, while 2 of the ODN required blood transfusion due to operative blood loss. The possible association between the length of the donor operation and the early post operative drop in creatinine was explored, with no significant correlation found in either group (LDN R=0.15, ODN R=0.03). There was unexplained delayed graft function (DGF) in 3 cases in the LDN group (7 %) versus 1 case (2.6%) in the ODN. Other two cases of DGF in the LDN group were related to anastomotic complications (1) and prolonged warm ischaemia (1). The DGF incidence was not influenced by the length of the operation. Post operative recipient creatinine levels at day 1, 7, 6 months and 1 year did not show significant differences between the laparoscopic and the open nephrectomies.
CONCLUSIONS: There is no evidence in this series that pneumoperitoneum during laparoscopic donor nephrectomy has a harmful effect on the outcome of the graft.

P47

The Outcome of Liver Donor Kidney Transplant with Multiple Arteries

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Introduction: The renal allografts with multiple renal arteries have been considered a relative contraindication for transplant due to increased risk of associated complications. This present study describes our long term experience with multiple artery renal allografts from live donors.
Methods: In this multicentric study among 923, live donor transplants 201 (21%) live renal allografts with multiple arteries were performed, between January 1985 to December 2004. We recorded and analyzed the number of arteries, techniques of arterial anastomosis, allograft outcome in terms of post transplant hypertension, acute tubular necrosis, and rejection, vascular and urological complications.
Results: There were no graft losses due to vascular or surgical complications. Acute tubular necrosis was reported in 1.5% of the allografts. Post-operative hypertension was seen in 4% recipients. Other complications as postoperative vascular complications and urological complications were encountered in 3.5% and 5.5% allografts respectively. The mean serum Cr levels at 1, 6, 12, 60 and 120 months post transplant were 147umol/L, 127umol/L, 138umol/L, 163umol/L and 240umol/L respectively.

male: female	6:1
mean age (in years)	37.4
mean follow-up (in months)	98 months (min 3m; max 144)
mean serum Cr umol/L at 12 months	138
mean serum Cr umol/L at 60 months	163
mean serum Cr umol/L at 120 months	240
mean systolic blood pressure mmHg at 12 months	132.2+/- 30.3
mean systolic blood pressure mmHg at 60 months	138.8+/- 18.4
mean systolic blood pressure mmHg at 120 months	142.2+/- 21.5
acute tubular necrosis %	1.49
vascular complications %	3.48
urological complications %	5.47

Conclusion: Although the use of live donor kidney grafts with multiple arteries presumed to increase risk of complication, in this large cohort study of twenty years, it appears that: the number of renal arteries did not have any adverse impact on the outcome of transplant. This study demonstrates that live donor allografts with multiple renal arteries are safe to be utilized for renal transplantation. It will not also helps to increase the availability of organs for donation but also relieves any disappointment of the donor and patients family.

Wednesday 29 March

Moderated Poster Session

Paediatric Transplantation

P48

Transition Of Care Between Paediatric and Adult Nephrology in Renal Transplant

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Introduction:
Between 01/1995 and 06/2006 73 children (below 16 years old) received a renal transplant. 32 of those patients with the functioning renal graft within an age of 15-18 years were transferred to four different adult nephrology units. This transition between paediatric and adult nephrology clinics could interrupt the continuity of care and affect transplant function. We aimed to review their progress after the transfer to the adult's clinic. We investigated the changes in renal functions after the transfer and evaluated the graft survival.
Methods:
29 patients, transplanted on average when 12.5 and referred to adult clinic at the mean age of 17, had their GFRs (Cockroft-Gault formula) measured at 3 subsequent times during the transition period from paediatrics to adult nephrology clinic: on transfer, 2 and 4 years after the transfer. We retrospectively collected and analysed these data according to subsequent outcome.
Results:
The incidence of transplant failure was high. Of the 29 patients 10 patients (35%) ($p<0.01$) lost their graft within 4 years of the follow up in the adult clinic and required dialysis. The mean GFR on the transfer to adult clinics was 78.8, and fell to 65.6 and 54.1 after 2 and 4 years respectively. If this group was subdivided into those whose transplant survived and those whose did not, the data could be presented in the following table:

	GFR transfer	**GFR 2 years**	**GFR 4 years**
Graft survival	75.5 ml/s	71.12 ml/s	68.05 ml/s
Graft failure	85 ml/s	55.95 ml/s	21.1 ml/s

Tacrolimus levels were significantly lower ($p<0.04$) in the patients whose graft failed compared to those whose graft survived throughout the transition period what may be related to non-compliance.
Discussion:
We concluded that adolescents and young adult renal transplant recipients are a high-risk group for the renal graft loss what is probably due to non-compliance. However, the scale of this problem is even larger because in 72% of cases GFRs were declining throughout the transition period.

P49

Survey Of The Use Of Non-Heart Beating Organs In Paediatric Practice

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Introduction
With the global shortage of donated kidneys for transplantation UK Transplant invested in programmes to retrieve organs from non-heart beating (NHB) donors. Whilst this has increased the numbers of organs available for transplant into adult recipients it does not appear to have had a significant effect on paediatric practice. The aim of this survey was to look at current paediatric practice.
Method
In June 2006 an online questionnaire was sent to research leads at all 13 paediatric nephrology units in the UK. Non-responders were sent a further reminder.
Results
Replies were received from 12 units giving a 92% response rate. 10 units were aware of local NHB programmes. Since the establishment of UKT funded NHB programmes only one unit had actually transplanted a NHB organ into a paediatric recipient. Another unit was offering them to paediatric patients and had three children on the waiting list for them. Both these units had local programmes that retrieved organs of Maastricht category 3 and 4. None of the units whose local programmes involved retrieval of category 2 organs were offering organs to paediatric recipients.
Of the units not using these organs the main reason given was insufficient data regarding the use of these organs in children. In units where a local programme had been running for more than three years lack of data in adults to extrapolate to the paediatric population and poorer outcome compared to organs from other sources were also quoted.
Conclusions
This survey demonstrates that although most paediatric nephrology units have local NHB retrieval programmes these organs are not being transplanted into the paediatric population. Whilst there is a lack of data regarding the use of organs from NHB donors into paediatric recipients there is good evidence that, in adults, organs from NHB donors have equivalent survival to those from heart beating donors. Therefore, they should be strongly considered as an option for paediatric patients, but this will require better communication between surgeons and paediatric nephrologists.

P50

Outcomes After Bladder Augmentation

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Introduction: Lower urinary tract dysfunction (LUTD) is an important aetiology of end-stage renal disease in children, which usually requires renal transplantation and bladder intervention. The aim of this study is to assess whether the timing of the LUTD intervention has any effect on graft outcome or complication rates.
Methods: We retrospectively studied 56 paediatric patients with lower urinary tract dysfunction and a renal transplantation between August 1990 and December 2004 at 2 major teaching hospitals in London. The mean follow-up was 6.2 years.
Results: 49 patients were male (88%) and 7 were female (12%). Mean transplantation age was 6.6 years.
The cause of LUTD was posterior urethral valves (PUV), with or without dysplastic kidneys in 36 (64%); hostile bladders with or without dysplastic kidneys in 16 (29%). Miscellaneous causes in 7%. There were no significant differences in the aetiology of LUTD between the pre-, post- or non intervention groups.
18 augmentation cystoplasties with Mitrofanoff, 9 Mitrofanoffs alone and 1 vesicostomy were performed. Of these, 14 patients (25%) had their intervention pre-transplant, 12 (21%) had post-transplant, 19 (34%) had no intervention, 1 (2%) had intra-transplant and 1 (2%) had both pre- and post-transplant.
Acute graft rejection occurred in 24 (43%) patients, post-transplant urinary tract infections in 18 patients (32%), lymphocoele in 3 patients (5%), slow graft function in 2 (4%), haemorrhage in 2 patients (4%) and bladder calculus formation in 1 patient (2%). No anastomotic leaks were seen.
11/14 (79%) of the pre-transplant group's grafts were functioning at the time of study, compared with 9/12 (75%) of the post-transplant group. 16/19 (84%) of the non-intervention group were functioning at the time of the study.
There was no significant difference in outcome between the different intervention groups.
Conclusions: Renal transplantation in children with LUTD is associated with an excellent outcome in terms of graft and patient survival. The timing of the LUTD intervention has no significant effect on the outcome of the renal transplant or complication rate. Urinary tract infections were very frequent complications in all groups studied. Further research is indicated to corroborate the findings of this study and to ascertain the optimal time for LUTD intervention.

P51

The Use Of Porcine Dermal Collagen Implants In Assisting Abdominal Wall Closure Of Paediatric Renal Transplant Recipients With Donor Size Discrepancy

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Introduction
Children may be offered kidneys from donors considerably larger than themselves. In such cases the kidneys are often transplanted intra-abdominally onto the aorta and vena cava. Abdominal wall closure may be difficult due to the size discrepancy and intra-operative swelling of the abdominal contents exacerbates this. There is a risk of abdominal compartment syndrome leading to graft compromise. The use of meshes to facilitate abdominal wall closure may result in dense intra-abdominal adhesions, which may make further surgery or peritoneal dialysis difficult.
Methods
We present a series of 5 such cases in which abdominal wall closure was facilitated by the use of porcine dermal collagen implant (PDCI). Five children (ages 2, 9, 9, 9 & 15 years) received transplanted kidneys from adult donors of significantly greater weight. In 4 recipients the kidney was transplanted onto the aorta and vena cava intra-abdominally using a midline incision. In the fifth the kidney was anatomised onto the iliac vessels. In each case PDCI was used to assist closure of the deeper layers of the abdominal wall. The overlying skin was closed normally. Maximum follow up was 3 years.
Results
In all cases primary closure was achieved. One child received a 2nd intra-abdominal transplant as an emergency, which later failed. All the other kidneys are functioning well. One recipient developed a small incisional hernia 3 years post transplant. Another recipient developed a skin dehiscence over the implant 23 days post-operatively. The implant was removed and the skin closed. He and the other 2 recipients recovered well and had no wound complications.
Discussion
PDCI is a permanent, non-absorbable implant available as sheets. It is acellular, non-immunogenic and causes minimal adhesions to bowel. Alternative closure methods do not have these advantages. PDCI facilitated abdominal wall closure in these patients with donor-recipient size discrepancy. In one case the PDCI was removed but had allowed closure at the time of operation. With incomplete abdominal wall closure rates of graft complication, multiple organ failure and systemic infection may be higher. The lack of adhesions facilitates future surgery.

P52

The Manchester Transition Pathway for young adults: A five year evaluation

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It is well recognised that renal transplantation is the most successful and cost effective treatment for children and adolescents with renal failure and approximately 76% of all paediatric recipients with end stage renal failure in the UK will have a functioning transplant (Renal Association 2005).
Due to significant advances in medical science, the majority of these children and adolescents will survive into adulthood and this has resulted in increasing numbers of young people requiring transition from paediatric to adult units. This growing problem has attracted interest from several professional bodies and has prompted the Government to address transition in some detail (Department of Health 2004 & Department of Health 2006).
Working in collaboration with the paediatric and adult regional transplant centres, the Manchester Transition Pathway was designed to support adolescents and young people with functioning transplants through the process of transition. The pathway begins at the paediatric centre at 14 years of age and moves with the young adult on transfer between the ages of 17 – 19 years to the adult services offering support up to the age of 22 years.
Evaluation of the process is by monitoring compliance with medication regimes, attendance at clinic and by canvassing the views of the service users by the use of satisfaction questionnaires.
Outcomes: The pathway has been utilized for a total of 85 adolescents and young adults over the last 5 years. 75 are at various stages throughout the pathway both within the children's clinic and adult clinic and 10 young adults have completed the pathway to date.
The pathway has been well received and there has been positive feedback from the service users.
There have been a total of 4 graft losses between 2001 and 2003, 3 of which were expected and no graft losses in the subsequent 3 years.
Attendance at clinic has been variable however there have been no young adults lost to follow up to date.

Wednesday 28 March

Moderated Poster Session

Preservation

P53

Does Cold Ischemia Impair Renal Function in Kidneys transplanted from non-heart beating Donors?

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Background: Due to greater than ever need for kidney donors, transplantation from non-heart-beating donors (NHBD) has significantly increased over the last years. However, ischemic injury at the time of cardiac arrest in NHBD is more pronounced, and these kidneys are often considered marginal. A compounding factor is cold ischemia, and its impact on graft function creates time, regional and logistical constraints. To determine whether prolonged cold ischemia causes delayed graft function and whether this has an impact on longer term graft function, we retrospectively studied renal function in pairs of kidneys derived from NHBD consecutively transplanted into unrelated recipients.

Patient Selection and Methods: Twenty-five pairs of kidneys from NHBD were transplanted at the North Bristol NHS Trust between 2002 and 2005. The kidneys were implanted sequentially into two different recipients. The first kidney graft was received by the patient with the best HLA match, whereas the second graft went to the longest waiter. Frequent postoperative measurement of renal profile parameters [Urea and electrolytes, Creatinine, estimated Glomerular Filtration Rate (eGFR)] were carried out in the recipients between postoperative days 1 and 180.

Results: The mean cold ischemia time for the transplantation into the first recipient was 943 ± 198 minutes. The mean cold ischemia time for transplantation into the second recipient was 1252 ± 311 minutes. We report that, despite prolonged ischemia time in the second graft, postoperative renal function was not significantly different from renal function in the first graft. The eGFR and Creatinine levels on days 1 to 180 did not differ significantly between the recipients of the first and second kidney from one NHBD. Moreover, these renal function parameters did not correlate to the prolongation of cold ischemia incurred between the first and the second transplant.

Conclusions: These findings demonstrate that in kidneys derived from NHBD, a moderate increase in cold ischemia alone would not hamper renal function. Therefore, it appears to be safe and acceptable to endeavor sequential rather than parallel transplants in renal grafts from NHBD.

P54

Warm Resuscitation Preservation (WRP) In An Isolated Haemoperfused Porcine Kidney Model

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Abstract

Intoduction:

Normothermic preservation has been shown to improve the metabolic support and maintain the viability of ischaemically-damaged organs retrieved from non-heart beating donors (NHBD) prior to transplantation. This study investigated the effects of Warm resuscitation preservation (WRP) with blood in a model of controlled NHBD kidneys.

Methods:

Porcine kidneys (n=6) were subjected to 10min warm ischaemia and preserved as follows:
Group 1: 2hr cold storage(CS),
Group 2: 18hr CS,
Group 3: 18hr Cold preservation (CP),
Group 4: 16hr CS + 2hr WRP.
Renal haemodynamics and function were then measured during 3hr reperfusion with autologous blood.

Results:

Increasing CS from 2hr to 18hr reduced renal blood flow (AUC 444±57 vs 325±70; P<0.01), but this was restored by WRP (563±119; P=0.035 vs 18hr CS) with no difference seen compared to CP (600±319). Renal function was also better in Groups 1, 3 and 4 vs Group 2 (% serum creatinine fall 92± 6, 79±9 and 64±17 vs 44±13% respectively, P=0.001).
AUC serum creatinine was significantly lower in Group1 compared to Group2 (1102±260 vs 2156±401; P = 0.002) and to Group4 (1756±280; P = 0.009), while Group 4 was similar to Group3 (1354±300). Tubular function was also improved in Groups 1, 3 and 4 vs Group 2 (P=0.001). Renal ADP: ATP ratio was significantly lower following WRP compared to pre-perfusion levels in all Groups (P= <0.05).

Discussion:

Warm Resuscitation Preservation was able to reverse some of the deleterious effects of cold storage in this model of controlled NHBD kidneys, as well as adequately resuscitate kidneys compared to 18 hours of cold preservation.

P55

Effects Of Carbon Monoxide Releasing Molecule (CORM-3) 0n Reperfusion In A Controlled Non Heart Beating Donor (NHBD) Haemoperfused Porcine Kidney Model

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Introduction:
CORM-3 a transitional metal carbonyl possesses the ability to liberate CO under appropriate conditions and function as CO-releasing molecule in biological systems and thereby have a direct ability to influence intracellular pathways that involve apoptosis and inflammation, hence I/R (Ischaemia/Reperfusion) injury. This study investigated the effects of CORM-3 administered in blood at the time of reperfusion in a model of controlled NHBD kidneys.
Methods:
Porcine kidneys (n=6) were subjected to 10min warm ischaemia and reperfused after 18hr Cold storage (CS) as follows:
Group 1: CORM-3 (tricarbonylchloro(glycinato)ruthenium(II)
Group 2: iCORM-3 (Inactive CO-releasing molecule)
Group 3: Control
Renal haemodynamics and function were then measured during 3hr reperfusion with autologous blood.
Results:
The total urine output was significantly better in Group1 (793±212) vs Group2 (368±72) and Group3 (302±211)[P=0.01]. Renal blood flow improved from Group1 vs Group2 & 3 (774±19 vs 448±88 vs 325±70; P=0.002). AUC of creatinine clearance was significantly better in Group1 vs Group2 & 3 (14±6 vs 3.3±0.1 vs 2.2±2; p= 0.006). While the fractional excretion of sodium was significantly lower for Group1 vs Group2 & 3 (50.7±27 vs105±6 vs 117±38; p=0.04).
Discussion:
CORM-3 as a manipulating agent significantly ameliorates the effects of reperfusion in a controlled NHBD Kidney.

P56

The Influence On Energy Kinetics And Histology Of Different Preservation Solutions Seen During Cold Ischaemia In The Liver

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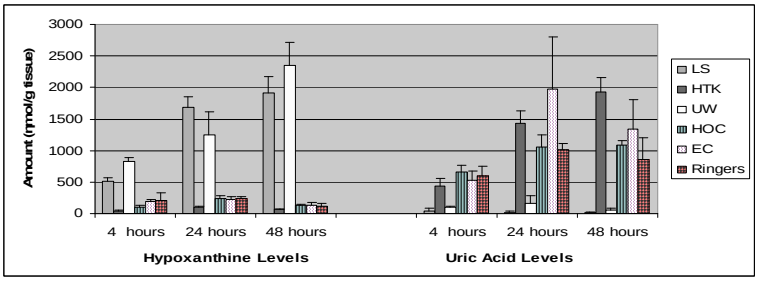
Cold ischaemia in rat liver was studied to compare energy kinetics and histological changes over time, when perfused with different preservation solutions.
Livers were perfused with a phosphate buffered sucrose based solution (LS: under development at our institute), and compared against: Ringers, Hyperosmolar citrate (HOC), University of Wisconsin (UW), Euro-Collins (EC) and Histidine-Tryptophan-Ketoglutarate (HTK). At various time points, samples were analysed for ATP and metabolites by HPLC and histological changes by PAS/Gordon & Sweet's Reticulin stain (n=4 at each point).
Fig.1: Hypoxanthine and Uric Acid in Perfused Tissue During Cold Ischaemia



In all livers ATP, ADP, AMP and Adenosine degraded over 4 hours. In UW and LS flushed livers degradation was halted beyond hypoxanthine, but continued in the other groups (Fig.1). This led to a significant reduction in the accumulation of xanthine and uric acid during cold ischaemia in the UW/LS groups compared to the other solutions ($p<0.05$). Histological analysis showed protected architecture with reticulin scaffold maintained in the UW/LS groups, whilst tissue degeneration was seen from early time points in the other groups. HTK lost all glycogen after 10 minutes. However, throughout ischaemia, signs of pathological injury were more pronounced in UW than LS preserved tissue.
In conclusion, cold ischaemia in the liver is characterized by dynamic biochemical changes coincident to often rapid pathological injury, influenced by the choice of perfusion fluid. The addition of allopurinol in UW/LS appears critical and may also affect the degree of subsequent reperfusion injury. The data support the notion that LS offers improved preservation over UW and the impetus to shorten ischaemic times in clinical transplantation, as pathological changes occur in even short periods of ischaemia

P57

The Evaluation Of Carbon Monoxide Concentrations In An Isolated Porcine Kidney Model

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Introduction
The toxic gas carbon monoxide (CO) has been shown to exert cytoprotective actions against ischaemia reperfusion injury. The aim of this study was to evaluate different concentrations of a CO releasing molecule CORM-3 in an isolated porcine kidney model during reperfusion.
Methods
An isolated organ preservation system (IOPS) was used to perfuse porcine kidney with normothermic autologous blood for 3 hours under physiological conditions after a period of 18 hours cold storage. Different concentrations of CORM-3 were infused during the first hour.
Group1: 400µm
Group2: 200µm
Group3: 100µm
Group4: 50µm
Results
Renal blood flow (RBF) was significantly better in groups 2, 3 and 4 [Area under curve (AUC) 141±51, 481±182, 643±139, 774±19; P=0.012; groups 1-4 respectively]. Renal function was also significantly improved in groups 3 and 4 compared to group 1 (AUC creatinine fall; 2398±416, 1789±59, 1256±143, 1450±335; P=0.006 groups 1-4 respectively) and (AUC creatinine clearance; 0.4±0.2, 2.8±1.1, 13.1±1.6, 14±5.8; P=0.003 groups 1-4). Tubular function was also improved in groups 3 and 4 compared to group 1 with less sodium excretion (P=0.004). Groups 3 and 4 had a higher total urine output compared to group 1 (778±292, 793±212 v 75±67ml; P=0.003 respectively). In each of the groups there was less than a 1% detection of carboxyhaemoglobin after 1 and 3 hours of reperfusion.
Discussion
The lower concentrations of CORM-3 demonstrated significantly improved renal function compared to the higher concentrations. Renal function was severely impaired in 400µm group despite no increased carboxyhaemoglobin levels in the blood.

P58

The Effects of Nitric Oxide and Carbon Monoxide in Renal Preservation

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Introduction

Nitric oxide (NO) and carbon monoxide (CO) have been reported to exert vasodilatory effects minimising ischaemia reperfusion injury. This study used an isolated porcine kidney model to assess the effects of administering the NO donor sodium nitroprusside (SNP) and the CO releasing molecule (CORM-3) during a period of warm preservation (WP) followed by reperfusion.

Methods

Kidneys were perfused under WP conditions after 10 minutes of warm ischaemia and 16 hours of cold storage as follows

Group1: SNP
Group2: Control
Group3: CORM-3
Group4: iCORM-3 (inactive)

Renal function and viability were then assessed during reperfusion.

Results

SNP and CORM-3 increased renal blood flow (RBF) during WP [Area under the curve (AUC):SNP 457±144, CORM-3 476±171, control 296±119, iCORM-3 247±89;P=0.014]. After reperfusion RBF was significantly improved in CORM-3 group compared to the control group (AUC 751± 222, 435±94.9; P=0.02) and comparative to other groups. Creatinine clearance and creatinine fall was significantly improved in CORM-3 group compared to iCORM-3 (AUC; 7.4±7.4 vs 1.3±0.6;P=0.02 and AUC 1662±538 vs 2255±169;P=0.03, respectively). Creatinine fall and clearance were numerically lower in SNP and control groups but did not reach statistical significance compared to CORM-3 group. There was a negative correlation between RBF during WP and functional parameters during reperfusion (Creatinine, r = -0.7217;P=<0.0001, sodium excretion, r = -0.9121;P=<0.0001).

Discussion

The beneficial vasodilatory effects of CORM-3 during WP improved renal function during reperfusion. Although the effects of SNP were comparable to CORM-3 they were less pronounced. This model also demonstrated the benefit of WP in predicting post transplant renal function.

P59

Rate Of Cooling In Organ Preservation

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Introduction

The importance of slowing metabolism by reducing the temperature through adequate perfusion is a fundamental paradigm of organ preservation. This study aimed to measure the efficiency of cooling using different preservation solutions and to determine whether flushing an organ at a normothermic temperature prior to hypothermia had any beneficial effects on the rate of cooling.

Methods

Porcine kidneys (n = 4) were retrieved and temperature probes placed at two depths within the kidney, 20mm and 5mm. Kidneys were infused at a hydrostatic pressure of 100 cmH_2O with either 500ml UW 4°C, 500ml Soltran 4°C or 250ml AQIX® RS-I 30°C immediately followed by 250ml AQIX® RS-I 4°C. The temperature and rate of flow were recorded throughout.

Results

The rate of perfusion with UW solution was significantly lower than both Soltran and AQIX® RS-I, 5 ± 1.3 vs 12 ± 3.9 vs 13.4 ± 3.2 ml/min/100g respectively (P = 0.018). Kidneys flushed with Soltran reached 10°C at a significantly faster rate than AQIX® RS-I at depth of both 20mm and 5mm (Table 1). Overall there was no significant difference between the rate of temperature fall in the groups during the hypothermic flush at either depth (P = 0.115, 0.118, respectively).

Group	20mm	5mm
UW	16.8 ± 2.2	16 ± 3.7
AQIX	21.5 ± 4.0*	21.8 ± 4.4*
SOLTRAN	11.5 ± 4.9*	10.8 ± 3.6*
P value	0.029	0.026

Table1. Duration for the kidney to reach 10°C (minutes)

Discussion

Flushing the kidney normothermically before a hypothermic flush did not increase the rate of cooling compared to traditional hypothermic solutions. Despite the viscosity of UW and slower perfusion the rate, temperature fall was equivalent to both that of Soltran and AQIX® RS-I.

P60

Primary renal function following prolonged cold Ischaemia: IMPACT OF Re-flush with UW solution prior to implantation

Niaz Ahmad, Ahmed Al-Mukhtar, Glen Bonney, Karim Halazun, Sonal Asthana, Krishna Menon.

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OBJECTIVES
Prolonged cold ischaemia is associated with an increased incidence of delayed graft function (DGF) and primary non function (PNF). The relationship is linear with increasing risk after every hour of cold ischaemia. Most centres in the United Kingdom do not accept or transplant kidneys from cadaveric heart beating donors with a projected cold ischaemia time of 24 hours or more at the time of implantation. Most of these kidneys are flushed with and stored in Hyperosmolar citrate solution (Marshall's HOC solution).
METHODS
In our centre a DGF rate of 50% is seen following cold ischaemia time of 18 hours or more. We present the results of eleven consecutive kidney transplants with cold ischaemia time ranging from 23 hours to 43 hours. The kidneys upon arrival were flushed by gravity with 500-750 ml of cold University of Wisconsin solution (Viaspan, DuPont) and stored in this solution prior to re-implantation.
RESULTS
All kidneys had primary function though rate of fall in serum creatinine was slow. The mean serum creatinine was 149 $mM.L^{-1}$ at one month and 137 $mM.L^{-1}$ at six months. No acute rejection was observed in the first month after transplantation.
CONCLUSIONS
Re-flush with UW confers a beneficial effect in kidneys with prolonged cold ischaemia with resultant primary graft function. This may have impact on utilisation and long term outcome of cadaveric kidneys with prolonged cold ischaemia.

P61

Use of a Nomogram to Predict Delayed Graft Function in Renal Transplant

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Objectives: The incidence of delayed graft function (DGF) is 20 – 30% in renal transplant from cadaveric heart-beating donors (HBD) in the UK. DGF has substantive economic effect in managing renal transplant and may adversely affect the outcome. Irish et al (2003) developed a nomogram to predict the likelihood of DGF based on 19,706 renal transplants1. In the present study, we have validated the nomogram in 127 consecutive cadaveric renal transplants in our centre.
Methods: Delayed graft function (DGF) was defined as the need for dialysis in the first week after transplantation. We analysed prospectively collected data from 127 consecutive adult (age >16 years) cadaveric renal transplant in 2004. Primary non function (n=1) was excluded. Potential risk factors for DGF were enumerated, scored and percentage prediction of likelihood of developing DGF was estimated using the nomogram. This was validated against the true incidence of DGF in the recipients.
Results: Out of 127 recipients, 38 (29.9%) developed DGF. Median percentage prediction risk for developing DGF was found to be 55 % i.e. half of the recipients who developed DGF had a predictive value of >55%. ROC curve analysis (concordance C index) of % prediction of DGF showed a 'c' statistic of 0.688. This was the same as in the quoted study.
Conclusion: Reported accuracy ('c' statistic of 0.69) is significant and matches well with the accuracy ('c' statistic of 0.70) reported by the authors nomogram. Hence our study validates the nomogram for its prospective use to predict the likelihood of DGF. This can impact transplant outcome by making tailored changes to transplant protocol and allocation of such kidneys that are likely to suffer DGF.
Irish WD et al. Nomogram for predicting the likelihood of delayed graft function in adult cadaveric renal transplant recipients. J Am Soc Nephrol. 2003 Nov; 14(11):2967-74

P62

Viability Testing using Machine Perfusion and Perfusate Enzyme Analysis: The Effect of Warm Ischaemia in an Animal Model

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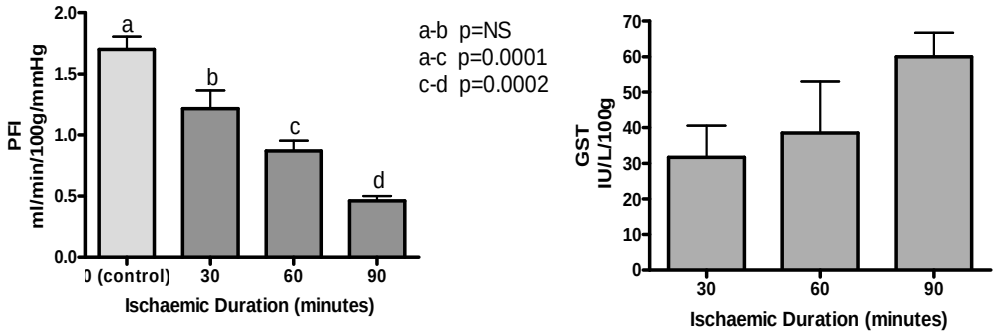
Introduction. Hypothermic machine perfusion allows assessment of non heart beating donor (NHBD) organ viability. The Perfusion Flow Index (PFI) and perfusate glutathione-S-transferase (GST) levels constitute primary and secondary viability criteria at our centre. PFI is calculated by flow per 100g renal mass divided by mean systolic pressure, with a threshold of viability of >0.4 ml/min/100g/mmHg. The GST viability threshold is 100 IU/L/100g. Intra-renal resistance has been shown to rise with duration of warm ischaemia in a porcine model but to date PFI and GST viability tests have yet to be validated in a prospective animal study.
Methods. Juvenile landrace pigs were subjected to periods of warm renal ischaemia of 30, 60 and 90 mins. Two kidneys were used as controls, with normal perfusion prior to retrieval. After rapid laparotomy the kidneys were placed on ice and prepared for machine perfusion. PFI and peak GST levels were then calculated during 4 hours of machine perfusion using local NHBD protocols.
Results. PFI decreased significantly with increasing ischaemic time, demonstrating a linear relationship. Peak GST levels during machine perfusion also showed a clear rising trend with increasing ischaemic duration.



Discussion. The PFI and GST levels during machine perfusion accurately reflect in-situ ischaemic duration and thus allow reliable assessment of injury. This study provides further support for the use of combined PFI and GST enzyme viability assessment in NHBD renal transplantation.

P63

Effects of Erythropoietin on Apoptosis and Inflammation in Ischaemic Porcine Kidneys Preserved by Normothermic Machine Haemoperfusion

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Background: Ischaemia/reperfusion (I/R) injury is an important process in kidney transplantation. The loss of graft cells may be due to tubular cell apoptosis and interstitial inflammation. Caspase-3 plays a central role in both apoptosis and inflammation. However, the mechanisms of I/R injury are far from clear and effective treatments still need to be defined. Clinically, erythropoietin (EPO) has been widely used and its receptors are expressed in many tissues including kidneys. EPO, therefore, may have specific renoprotective effects.
Methods: In this study, we evaluated the effects of EPO on apoptosis (*in situ* end labelling fragmented DNA) and caspase-3 activation (enzyme cleavage assay) in ischaemic porcine kidneys using an *ex vivo* isolated organ perfusion system. Porcine kidneys (n=6) were subjected to 10 minutes warm ischaemia and 16-hour (16h) static cold storage (CS). Normothermic perfusion (NP) was performed for 2-hour (2h) with oxygenated autologous blood with and without 5000 units/L of EPO.
Results: 2h NP with EPO significantly decreased the number of apoptosis in tubules of 16h CS kidneys (0.03 ± 0.02 per 400× field) compared to those without EPO (0.15 ± 0.04, $p<0.05$). The number of apoptotic cells in the tubular lumen was numerically increased (2.35 ± 0.23 vs. 1.65 ± 0.33), but did not reach statistical significance, with no change in the interstitial area. However, NP did not affect tubular apoptosis compared with pre (0.12 ± 0.03) and post CS (0.07 ± 0.03), while NP only increased interstitial apoptosis compared with that in both pre (0.18 ± 0.12) and post CS (0.20 ± 0.09) kidney tissues. Caspase-3 activity was significantly increased by 2h NP with EPO in 16h CS kidneys (0.114 ± 0.021 pmol AMC liberated/minute/μg protein) in contrast to that in the kidneys without EPO (0.048 ± 0.017), which may reflect the increase of apoptosis in the tubular lumen. In addition, 2h NP with or without EPO significantly increased the level of caspase-3 activity compared to that in the pre (0.011 ± 0.003) and post CS (0.009 ± 0.001) kidney tissues.
Conclusion: NP restores metabolism and may favour infiltrated inflammatory cells to apoptosis through caspase-3 activation. EPO applied during 2h NP may have a renoprotective action with lower apoptosis in tubules, but higher apoptosis in the tubular lumen and increased caspase-3 activity. EPO may not only induced the apoptosis of inflammatory cells but also drive them into the tubular lumen. This phenomenon might link to a clearance mechanism of inflammation in ischaemic kidneys.

P64

Leukocyte depletion enhances liver perfusion during extended isolated normothermic preservation

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Introduction

Liver ischaemia/reperfusion injury is a multifactorial process in which leukocytes have an important role. Normothermic haemoperfused liver preservation is an experimental technique affording extended preservation times. This pilot study aimed to establish whether leukocyte depletion would enhance normothermic preservation.

Methods

Porcine livers were retrieved from heart-beating donors and perfused with blood group identical porcine blood for 20 hours. The normothermic perfusion circuit utilises standard cardiopulmonary bypass technology and allows detailed monitoring of perfusion haemodynamics and sampling of perfusate for biochemical analysis. The experimental group (n=3) was perfused with blood that had been partially leukocyte-depleted prior to priming and the circuit included an in-line leukocyte filter. In 2 of 3 experiments this filter was used for 20 hours and in the third for just 6 hours by which point leukocyte depletion was felt to be complete. The blood used for the control group (n=4) was not filtered at any point. By means of a gate-clamp the arterial perfusion pressure was controlled (target 85-95mmHg) and the pump speed adjusted to obtain a low IVC pressure (target 0-5mmHg).

Results

Leukocyte depletion resulted in significantly higher total blood flow through the liver ($p=0.01$) with significantly higher portal flow ($p=0.01$). Arterial, portal and IVC perfusion pressures between groups were not significantly different ($p=0.13$, 0.30 & 0.23 respectively) indicating that the vascular resistance within the liver is reduced. Despite the enhanced perfusion characteristics function does not appear to be improved with similar ALT and AST rises, bile production and correction of perfusate base excess observed.

Conclusion

Leukocyte-depletion of blood prior to and during normothermic preservation perfusion of porcine livers results in enhanced perfusion of the liver. This is indicated by greater portal flow at similar portal perfusion pressures. Leukocyte adherence is known to occur during ischaemia/reperfusion and this may be the underlying mechanism retarding perfusion when whole blood is used.

Thursday 29 March

Moderated Poster Session

Cardiothoracic Organ Transplantation

P65

Induction Immunosupression using Rabbit Antithymocyte Globulin in Heart Transplantation: is the Timing Important?

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Background
The timing of induction of immunosuppressive treatment following heart transplantation with rabbit antithymocyte globulin (RATG) is not well established. RATG can be given intra-operatively or in the early post-operative period. The aim of this study was to evaluate timing of RATG administration on the incidence of rejection and survival in heart transplant patients.
Methods
One hundred and sixty one *de novo* heart transplant recipients were included in the study. Fifty eight recipients were given the first dose of RATG before the removal of cross clamp (group 1), while 103 patients were given the first dose of RATG in the intensive care unit (group 2). Both groups received two further doses of RATG and maintenance Immunosuppression as per standard protocol.
Results
The study groups displayed similar preoperative and demographic variables. We could not demonstrate a statistically significant difference between group 1 and group 2 in the incidence of acute rejection episodes (0.98 ± 1.5 in group 1 versus 1.4 ±1.9 in group 2, $p=0.15$). Furthermore, there were no significant differences between groups in the time to first rejection episode and survival ($p=0.26$).
Conclusions
There were no statistically significant differences between intra-operative and post operative RATG administration on the incidence of rejection or survival. This is a novel finding yet to be described in the literature with relevance to future clinical practice.

P66

Post-transplantation Malignancy In Heart And Lung Transplant Patients; A Single Centre Experience.

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Introduction:
An increased risk of malignant disease is well recognised following cardiothoracic transplantation. However, a comparison of the frequencies of common post-transplant malignancies (skin cancers, lymphomas, lung cancers) following heart and lung transplantation is not well described. In this study we assessed and compared the frequency of various malignancies following heart or lung transplantation in our centre.

Methods:
Between April 1987 and March 2006, a total of 592 patients underwent cardiothoracic transplantation at our centre (372 heart transplants, 220 lung transplants). All the case records were reviewed retrospectively to assess the occurrence of any malignancy.

Results:
We detected a total of 154 malignancies in 128 cardiothoracic transplant recipients, (106 hearts, 22 lungs), representing an overall cancer frequency of 21.6% (28.5% in heart recipients and 10.0% in lung recipients, $p<0.001$). The most common malignancies were skin carcinomas, with a frequency of 17.06%. 97% (98/101) of all the skin cancers occurred in heart recipients, showing a direct correlation with their long post-transplant survival compared to lung recipients ($p<0.001$). Comparing heart and lung recipient groups, we found no statistically significant difference in the frequency of lymphomas (2.2% vs 1.3%, $p=0.563$) or de novo lung cancer (2.2% vs 2.7%, $p=0.563$). Multiple malignancies occurred in 26 patients.

Discussion:
The risk of carcinoma occurrence following cardiothoracic transplantation is very high, with an overall frequency of 21.6%, which is much higher than the previously reported multicentre data (6-11%). While the overall frequency of malignancy was higher in heart transplant recipients compared to lung recipients, we found no significant difference in the frequency of lymphomas and lung cancers between the two groups.

P67

CYP3A5 Polymorphism, Cyclosporine Pharmacokinetics and Freedom from Rejection in Cardiac Transplant Patients.

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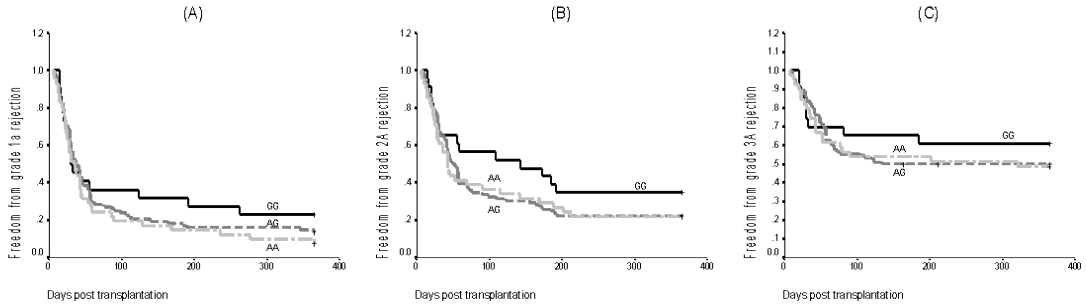
Introduction: CYP3A5 is part of the cytochrome P450 (CYP) enzyme family responsible for the phase 1 metabolism of immunosuppressive drugs. CYP3A5 gene single nucleotide polymorphisms (SNPs) have been shown to correlate with the absence of the the CYP3A5 gene in some individuals where the CYP3A5* (2283A→G) allele in intron 3 results in a truncated protein with partial loss of CYP3A5 activity. In renal transplant patients CYP3A5 SNPs have been correlated with high and low Tacrolimus and Cyclosporine (CyA) levels with CYP3A5 GG having been correlated with higher Tacrolimus and CyA levels. The objective of our study was to asses the impact of this SNP on cardiac transplant patient's drug levels, pharmacokinetics and freedom from rejection. **Methods**: We genotyped 170 cardiac transplant patients who were transplanted over an 18 year period. Patients received a standard immunosuppressive regime and were biopsied at standard intervals post transplantation. **Results**: 44 patients were genotyped AA, 100 patients AG and 25 patients GG. 1 patient could not be genotyped. There were no significant differences between groups in terms of donor or recipeint age, HLA mismatch, CMV mismatch or ischaemic time. We found no significant differences between patients at 3 or 12 months in terms of CyA dosage, trough plasma levels, or Prednisolone dosage. In addition we found no statistically significant impact of CYP3A5 on freedom from endomyocardial biopsy proven rejection, although freedom from grade 1A, 2A and 3A rejection was improved in the GG group [Figure 1]. **Conclusions**: In contrast to renal transplant patients we found that the CYP3A5 gene had no influence on drug levels in cardiac transplant patients. We were also not able to show any impact of the gene on freedom from rejection.

Figure 1 Actuarial (Kaplan Meier) freedom from endomyocardial biopsy proven rejection according to CYP 3A5 genotype.



CYP3A5 genotype actuarial (Kaplan Meier) freedom from grade ≥1A rejection (A), grade ≥ 2A rejection (B) and grade ≥ 3A rejection (C). There was no overall difference between actuarial freedom from grade ≥1A, 2A or 3A rejection by the log rank test for the CYP3A5 genotypes.

Thursday 29 March

Moderated Poster Session

Infection

P68

CD8+ T cell responses against cytomegalovirus (CMV) in kidney transplant recipients matched or mismatched for CMV status

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Introduction: CMV infection frequently occurs after renal transplantation owing to the need for immunosuppression. CMV negative recipients of CMV positive kidneys are at greater risk owing to the lack of pre-existing immunity to CMV. Despite this, some of these patients do not suffer from post-transplant CMV viraemia. The aims of this study were to investigate T cell responses to CMV in CMV+ and CMV- recipients of kidneys from CMV+ donors.
Methods: Peripheral blood mononuclear cells were obtained from HLA-A2+ renal transplant patients, labelled with anti-CD8 and an HLA-A2 'pentamer' bound to the immunodominant CMV p65 peptide NLVPMVATV, and analysed by 2-colour flow cytometry. Results were expressed as pentamer+ cells as a % of total bright CD8+ cells. Patient CMV status was monitored by PCR.
Results: As shown below, most CMV- recipients of CMV- kidneys showed no CMV-specific T cell responses, while most CMV+ recipients had a significant proportion of CMV-specific CD8+ T cells.

Donor	Recipient	CMV infection	n	Mean % pentamer+ CD8+ cells ± sem
CMV -	CMV -	n/a	37	0.035 ± 0.02
CMV +	CMV +	n/a	56	2.78 ± 0.89
CMV -	CMV +	n/a	37	1.14 ± 0.37
CMV +	CMV -	Yes	13	1.91 ± 1.02 *
CMV +	CMV -	No	16	0.03 ± 0.18 *

CMV- recipients of CMV+ kidneys who subsequently had an episode of CMV viraemia had high numbers of CMV-specific T cells, while those without detected episodes of viraemia had very low numbers (* $p < 0.01$, Wilcoxon). Patients followed sequentially showed high levels of CMV-specific T cells soon after an episode of CMV viraemia, which decreased when the infection was cleared.
Discussion: The results suggest that CMV- recipients of CMV+ kidneys in whom CMV is subsequently reactivated make a CD8+ T cell response to CMV despite being immunosuppressed. Those in whom CMV is not reactivated do not respond, suggesting either that infective CMV may not always be transferred with the transplant or that latent CMV present in the donor kidney is not always reactivated in the recipient.

P69

Bacterial Infection And Its Role In Ureteric Contractility And Signalling

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Urinary tract infection is a common cause of morbidity pre and post-transplantation. Over 80% of urinary tract infections are caused by *E. coli*, which initiate release of cytokines such as interleukins (IL) from urothelial cells. However, little is known about the normal characteristics of ureteric physiology or how bacterial infection modulates smooth muscle contraction. We aimed to characterise the primary mediators controlling ureteric physiology using pharmacological tools and biochemical methods. Previous studies have shown that instillation of *E. coli* lipopolysaccharide (LPS), a major component of the cell wall of gram-negative bacteria, into rat bladder can initiate an inflammatory response similar to urinary tract infections[1]. Therefore, we studied the effect of LPS on contraction of human and rat ureter and the role of PKC in ureteric signalling using established methods[2].

Phasic contractions and calcium transients of human ureters were studied during exposure to pharmacological agents which modulate L-type calcium channels (1μM BayK8644 and 10μM Nifedipine), SERCA pump (20μM CPA) and BK channels (1mM TEA). Phasic contractions were also studied in the presence of LPS 10-100μg/ml. Further to this we studied PKC isoform expression and translocation of PKCα between the cytosol and membrane in response to LPS.

These studies show for the first time that it is possible to measure force stimulated by electrical field stimulation (EFS) while simultaneously recording emitted signals from the dual emission calcium indicator Indo-1 AM in cross-sectional rings of human ureter. Studies also show that contraction of the human ureter is regulated in part by L-type calcium channels and BK channels and to a lesser extent by the sarcoplasmic reticulum (SR).

Exposure of human and rat ureters to bacterial LPS caused a dose-dependent and reversible decrease in the force of EFS stimulated contractions and in the human caused translocation of PKCα from the cytosol to the membrane. Of the four PKC isoforms studied, 2 calcium dependent (α & β) and 2 calcium independent (ε & δ), 2 out of 4 isoforms were detected in the guinea pig and human ureter and only one in the rat ureter.

Our studies highlight that bacterial infection initiates a signalling cascade mediated by PKC-α which may play an important role in modulating ureteric contractility.

P70

Low Incidence of Polyoma Virus (BKV) Nephopathy

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Introduction: Polyoma virus is increasingly recognised as a cause of interstitial nephritis in renal transplants. The incidence ranges from 1-9% in different countries and it is an important cause of graft dysfunction. Polyoma interstitial nephritis can cause difficulties in biopsy interpretation especially in the differentiation from acute rejection. We have knowingly seen three cases in biopsies in the last three years, one of which was subtle. All were associated with inflammation and tubulitis and were positive for BKV(SV40) immunohistochemically. Our incidence seems low (<1%)and we needed to consider whether we are missing cases.
Aims:To determine the background incidence of BKV in renal transplant biopsies performed for graft dysfunction using immunohistochemistry for BKV detection, and to assesss whether we are likely to be missing cases
Materials, Methods and Results: Phase 1:-Pilot study-Initially as a pilot study all transplant biopsies showing interstitial inflammation between January and June 2005 were selected for the study. A total of 100 transplant biopsies were performed for graft dysfunction in the first six months of 2005, of which 29 cases had evidence of tubulointerstitial inflammation.All 29 cases (plus 4 day 0 -ve controls) were stained for BKV. All the cases were negative. Phase 2:-In the next part of the study, cases were selected based on the time of biopsy irrespective of their histological findings. In the pilot study most of the 29 biopsies were done in the first month post transplant. A literature search showed that the peak time range from transplantation to detection of the virus was between 3 and 18 months.We therefore selected cases with biopsies performed between 2 to 24 months post transplant from all the renal transplant biopsies performed in 2004. Out of a total of 191 biopsies performed for graft dysfunction 35 fulfilled this criteria.The 35 cases were stained as before for BKV. 34 of the cases were negative for BKV and 1 was positive. This case had however been diagnosed with polyoma interstitial nephritis on light microscopy and confirmed by immunohistochemistry at the time of biopsy. Discussion: The results of the study confirmed our thoughts that the incidence of BKV in our centre is low (<1%) compared to other centres within this country and elsewhere. The study reassured us that we have not been missing cases of BKV nephropathy on histology.The main reason why the incidence is low is most probably related to differences in immunosuppression.

P71

Positive Virology in a Non Heart Beating Organ Donor

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This study outlines the case of a 55year old man who was referred to the transplant co-ordinator as a potential non heart beating kidney donor, who was later found to be hepatitis B and hepatitis C positive. The intention is to discuss the series of events which led to the implementation of the positive virology policy issued by UKT and the donor family follow up. This scenario had not been encountered by the team involved and so represents the first time the policy was to be tested.
The donor was admitted to the A&E department having sustained a head injury; a CT scan showed he had a severe unsurvivable head injury. After being informed of the prognosis, the family approached the staff about the possibility of organ donation. He was referred as a suitable non heart beating donor and was therefore transferred to ICU for palliative care and to facilitate donation. Whilst carrying out the patient assessment the family noted a history of illegal drug use, namely cannabis, but denied any IV drugs. Consent was obtained to proceed with kidney donation and to take a blood sample for virology testing. No contraindications to solid organ donation were noted and following withdrawal of treatment the patient was transferred to theatre and the retrieval operation commenced. During the operation, the virology results were reported; the patient was hepatitis B core antibody positive and hepatitis C positive. The transplant surgeon decided to abandon the operation due to suitability.
The positive virology policy was consulted. The family were informed that the kidneys had not been removed due to a blood result received in theatre and that further follow up would be offered to them in the near future. The circumstances of the donor referral made some aspects the policy implementation problematic. Advice was sought from the Clinical Director for Nephrology and Transplant, as the positive result has implications for the health of surviving family members. The consultant for infectious diseases was also contacted for further advice about disease transmission. The intention is to set up a meeting with the significant family, the Transplant Co-ordinator and the clinicians involved.
The policy was only recently published and this is the first experience of the team involved. Experiences shared could benefit others in similar circumstances and is of significance because of responsibility of the transplant community to donor families who are only aware of the virology result as they offered the gift of life.

P72

Septicaemia and Urinary Tract Infections During CMV Activation in Kidney Transplant Recipients

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Background: CMV infection, septicaemia and urinary tract infection (UTI) have significant outcomes in the post-transplant outcomes. Not much is known about the possible secondary induction of bacterial infection secondary to CMV activation.
Objectives: To compare the septicaemia and UTI rates between active CMV disease and CMV negative groups, and effect of anti-viral prophylaxis in influencing this outcome.
Methods: A retrospective study of consecutive non-diabetic kidney transplant patients in a single unit from May 1995 to April 2005 to compare a cohort of active CMV disease patients with negative CMV cohort for septicaemia and urinary tract infection rates, and the impact of anti-viral prophylaxis in rates of infection.
Results: 297 patients received a kidney transplant.180 M, 117 F; mean age at transplant 43.1 years; 60 from living donors and 237 from deceased; Follow-up period was 1 year; Active CMV disease was seen in 61(19.4%); negative CMV were 110(37%); and remaining were carriers or asymptomatic seroconverters. Within 3 months after transplantation, CMV activation was seen in 22(78.5%), and sepsis in 41(67.2%). Median duration of activation of CMV disease was 2.8 months, compared 5 months for occurrence of septicaemia. Patients with septicaemia were significantly higher in the active CMV group as compared to the negative CMV group (p=0.001). Episodes of multiple septicaemias were also higher in this group (p=0.004). In active CMV group, episode of septicaemia were seen to cluster within 3 months of CMV activation in 16(76.1%). Opportunistic infections like pneumocystis, legionella and herpes were also seen to cluster with CMV within 2 weeks during its activation in 6(85.1%) cases. Episodes of UTI were also significantly higher in the active CMV group (p=0.001). Although gram-negative bacterial infections were higher in the active CMV group [17(62.1%) versus 10(40%)], this was not statistically significant. There was a trend for lower bacterial infection rates in the CMV anti-viral prophylacted group as compared to those without prophylaxis. There were no significant differences in episodes or profile of bacteraemia on comparing the IgM positive versus IgM negative sub-groups of active CMV disease.
Conclusion: CMV disease carry significant risks of bacterial and opportunistic infections that have a tendency to flock together. Role of anti-bacterial prophylaxis maybe considered during CMV activation. Effects of immunosuppressive medications may be a possible root cause, and they should be carefully tailored to avoid risks of bacteraemia.

P73

Impact of Adult Polycystic Kidney Disease on Kidney Transplant Outcomes. A Single Centre Experience over 10 years

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INTRODUCTION: Is there a significant increase in the cyst related complications in APKD patients in the post-transplant period? Do they have different outcomes compared to the non-APKD group?
PATIENTS AND METHODS: Retrospective observational study of consecutive non-diabetic adult patients who had a first kidney transplant during 01/05/1995 to 31/04/2005.Comparison of 1 year pre-transplant status was made with the post-transplant period of 1 year to see any difference in outcomes; Comparison of cohort of APKD patients with matched control arm of non-APKD recipients during 1 year follow-up.
RESULTS: 307 adult patients receiving a first kidney transplant; 187 M, 120 F. APKD seen in 41 (13.3%) patients. Of these, 47 pre-transplant diabetics were excluded. No significant difference in the incidence of haemorrhage in the kidney cysts, liver cysts, and episodes of haematuria between the pre-transplant and post-transplant periods of 1 year. Bacteraemic episodes and UTI were significantly higher in the post-transplant period [9(23.6%) versus 2(5.2%), p=0.04] and [20(52.6%) versus 6(5.2%), P=0.01]. A tendency towards greater haematuria [18.4% versus 7.8%] and haemorrhage into the kidney cysts [13.1% versus 2.6%]; native nephrectomy required in 2(4.5%) cases; Gross haematuria seen in 3(7.8%); nephrostomy required in 2(4.5%). No significant differences in the episodes of bacteraemia, urinary tract infections and CMV activation; graft survival and patient survival, mean MDRD GFR and calculated creatinine between the study arm of APKD patients (n=38) and matched control (n=131) at 1 year follow-up. A higher trend for NODAT was seen in non- APKD group. A significant lesser proportion of APKD population was seen to have episodes of kidney allograft rejection [10(22.7%) versus 125(41.3%), p<0.018]. Vascular rejections were significantly lower in the APKD group.
CONCLUSION: There is a significant increase in bacteraemic and urinary tract infections in the post-transplant period in APKD population, but this increase was not seen in a matched cohort of non-APKD in the post-transplant period. APKD patients receiving a kidney transplant do not necessarily need a pre-transplant native nephrectomy.

P74

Immunosuppression dose reduction (ISDR) in Kaposi's sarcoma: the use of sequential lymphocyte activation antigen expression.

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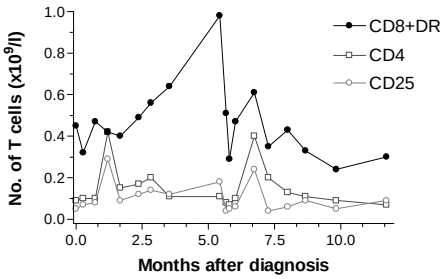
HHV-8 infected individuals who develop KS are thought not to mount a cytotoxic T-lymphocyte (CTL) response against the virally transformed tumour. In renal transplant recipients who develop KS, remission is known to occur if immunosuppression is stopped, with subsequent loss of the graft. Our centre successfully manages Epstein-Barr virus positive (EBV^+) post-transplant lymphoproliferative disease (PTLD) by titrating down immunosuppression until an anti-viral response is elicited. Based on this experience we adopted a similar protocol in managing renal transplant patients with KS by ISDR while monitoring the degree of CTL activation. This study aims to discover whether: ISDR leads to a rise in activated CTL; lymphocyte activation in KS differs from that seen in EBV^+ PTLD; the rise in activated CTLs correlates with a clinical response; and monitoring of activation facilitates ISDR and maintain graft function.

We retrospectively reviewed the case notes and immunology of the 323 renal transplant recipients seen at our centre from 1999-2006. Three of the seven who developed KS had sufficient data for the study: they underwent ISDR and had T-cell activation assays every two weeks for at least one year and two of these maintained graft function.

On ISDR patients produced a rise in the number of activated CTLs (CD8+DR), consistent with an effective anti-viral response, and the rise correlated with a clinical response. One case is illustrated below:



The CTL rise is slower in KS than that seen in PTLD and KS generates a greater level of CD4+ activation than is seen in PTLD. We recommend monitoring CTL activation status to aid safe ISDR while attempting to preserve graft function.

P75

Incidence Of Polyoma Viruria After Renal Transplantation In A Steroid Avoidance Regime

Cheralathan Arunachalam[1], Baljit Saundh[2], David Border[1], Helen Campbell[1], Stephen Tibble[1], Chas Newstead[1], Andrew Lewington[2], Antony Hale[1], Richard Baker[1]

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Introduction: Since January 1st 2004 we have been using tacrolimus based immunosuppression with steroid avoidance in our renal transplant programme. We were concerned by increased reports of polyoma infection under tacrolimus and MMF based immunosuppression but on the other hand the BK virus contains a glucocorticoid response element which may favour steroid avoidance. We studied the incidence of BK and JC viruria in the first 12 months after transplantation.

Methods: Urine samples were collected at 5 days, 1 month, 3 months, 6 months and 12 months after transplantation in 60 patients. Samples were analysed by real time PCR for BK and JC viruria (Stratagene MX3000P).
Results: Twelve patients (20%) had positive samples for BK virus and eight patients (13%) were positive for JC virus. None were positive for both.

	BK Positive	JC Positive	Neg for BK& JC
No. of Patients	12	8	40
M: F	6:6	5:3	29:11
Age	48.2 ± 9.7	41.1 ± 10.7	49.4 ± 12.9
Transplant Type LD:Cad	2:10	0:8	7:33
Rejection Episodes	1	0	6
BK Nephropathy	1	0	0
CMV Disease	1	0	2

Different patterns of BK and JC reactivation were observed, BK viruria was detected after 3 months in 10/12 patients whereas JC viruria was usually detected immediately after transplantation (6/8). One patient had biopsy proven BK nephropathy (in BK Pos group). Interestingly rejection episodes occurred almost exclusively (6/7) in those without viruria.
Discussion: In this group of patients BK viruria was detected in 20% of patients in the first year which is less than other series (c. 35-50%). Only one case of BK nephropathy resulted. Further reduction in BK viruria (and BK nephropathy) may be possible with screening and pre-emptive reduction of immunosuppression.

Thursday 30 March

Moderated Poster Session

Kidney

P76

Level Of Renal Function And Serum Erythropoietin Levels Independently Predict Anaemia Post-Renal Transplantation

Kim Sinnamon[1], Aisling Courtney[1], Peter Maxwell[1], Peter McNamee[1], Geraldine Savage[2], Damian Fogarty[1]

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Background
Post-renal transplant anaemia is a potentially reversible cardiovascular risk factor. Graft function, immunosuppressive agents and inhibition of the renin-angiotensin system have been implicated in its aetiology. The evaluation of erythropoietin levels may contribute to understanding the relative contributions of these factors.
Methods
207 renal transplant recipients attending the Belfast City Hospital were studied. Clinical and laboratory data were extracted from the medical records and laboratory systems.
Results
Of the 207 patients (126 male), 47 (22.7%) were found to be anaemic according to K/DOQI criteria. The anaemic group had a significantly higher mean serum creatinine level (162.8 µmol/L vs. 131.0 µmol/L, $p<0.001$) and lower mean estimated glomerular filtration rate (41.5 ml/min vs. 54.9 ml/min, $p<0.001$) than the non-anaemic group. Individual immunosuppressive regimens were comparable between those with and those without anaemia. Angiotensin converting enzyme inhibitor (ACE-I) or angiotensin receptor blocker (ARB) administration was not more prevalent in those with anaemia compared to those without (36.2% vs. 38.8%, $p=0.88$).
There was a significant inverse correlation between haemoglobin levels and serum erythropoietin (EPO) levels ($R=-0.29$, $p<0.001$), but not between EPO levels and eGFR ($R=0.02$, $p=0.74$). Higher EPO levels were predictive of anaemia, independent of renal function in multivariate analysis.
Conclusion
Anaemia is common in post-renal transplant patients. The levels of renal function and serum erythropoietin, and not immunosuppressive regimens or ACE-I/ARB use, are strong and independent predictors of anaemia.

P77

Discontinuing Treatment Of Secondary Hyperparathyroidism With The Calcimimetic Cinacalcet at Renal Transplantation Predisposes to Early Hypercalcaemia

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INTRODUCTION: The calcimimetic Cinacalcet is now an established treatment for the secondary hyperparathyroidism of renal failure, and an increasing number of patients with severe parathyroid hyperplasia are on this agent at the time of transplantation. Successful *de novo* treatment with Cinacalcet in patients with persisting hyperparathyroidism and Hypercalcaemia after renal transplantation has also been described. However, it is unknown whether this agent should be continued at the time of transplantation in patients already established on this therapy. We describe three cases where Cinacalcet was discontinued at transplantation.
METHODS: Three patients received Cinacalcet for at least 3 months before renal transplantation. At the time of transplantation, Cinacalcet therapy was discontinued in all three patients. Calcium, Phosphate and PTH levels were monitored for 6 months post transplantation. Cinacalcet was reintroduced after 3 months in two patients.
RESULTS: All patients demonstrated significant increases in serum calcium within 7 days of transplantation, despite primary allograft function. Serum calcium reached a zenith at 21 days, and remained elevated thereafter. The degree of hypercalcaemia was related to the severity of hyperparathyroidism pre transplantation. Serum calcium and serum phosphate levels were inversely related. In all patients, hyperparathyroidism persisted post transplantation. In two patients, hypercalcaemia post transplantation was successfully treated by reintroduction of Cinacalcet
DISCUSSION: Cinacalcet therapy is reserved for patients with the most severe parathyroid disease in many centres. Dialysis patients with severe parathyroid disease treated with Cinacalcet are at risk of early, severe hypercalcaemia post transplantation if Cinacalcet is discontinued. As post transplant hypercalcaemia could be detrimental to allograft function, these results suggest a need for continued titration of Cinacalcet to serum calcium after transplantation.

P78

Soluble CD30 In Patients With Antibody-Mediated Rejection Of The Kidney Allograft

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IKEM, Prague, Czech Republic

The aim of our study was to evaluate the clinical significance of measurement of the soluble CD30 (sCD30) molecule for the diagnosis of antibody-mediated (humoral) rejection. Sixty-four kidney transplant recipients (thirty-one C4d-positive and thirty-three control patients) were included into the study. Soluble CD30 levels were evaluated before transplant and during periods of graft function deterioration. The median concentrations of the sCD30 molecule were identical in C4d-positive and C4d-negative patients before and after transplantation (65.5 vs. 65.0 and 28.2 vs. 36.0 U/ml respectively). C4d+ patients who developed DSA de novo after transplant had a tendency to have higher sCD30 levels before transplantation (80.7 U/ml, n=8) in comparison with C4d-negative patients (65.0 U/ml, n=15), however, this difference did not reach statistical significance. Diffuse C4d-positivity in graft biopsies and the incidence of donor-specific antibodies were significantly associated with long-term worsening of graft function. Our study suggests that evaluation of soluble CD30 levels before transplantation and during episodes of antibody-mediated rejection might not be helpful for the differential diagnosis of this severe immunological complication.

P79

Impact of the Revised UK Transplant Scheme for Allocation of Kidneys from Heart-beating, Deceased Donors in the North of England and Scotland

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Introduction: On 3 April 2006 the revised UK T scheme for allocation of kidneys from heart-beating deceased donors commenced. The scheme uses regional allocation to minimise cold ischaemia time and our 6 transplant centres ("Alliance"), comprising almost 40% of total transplant activity in the UK (2005 data), collaborated to review activity totalling 330 transplants in the six months before and six months after the implementation of the new scheme. **Results:** For the whole 12m period transplant activity varied between centres from 13.8 to 24.3 transplants per million of centre retrieval population. The median CIT ranged from 14.2 to 20.9h in a 6 month period.

Centre with:	**transplants 6/12 pre-revision**	**transplants 6/12 post-revision**	**% change**
Greatest activity reduction	32	16	-100
Greatest activity increase	39	57	+46
Local kidneys used locally increased	5	10	+100
Local kidneys used locally decreased	6	1	-83
Alliance donor kidneys increased	10	24	+140
Alliance donor kidneys decreased	15	6	-60
UK donor kidneys increased	6	9	+50
UK donor kidneys decreased	6	2	-67
Median wait time greatest change	314d	1906d	
HLA spec defaulted greatest increase	20%	74%	
ABO-B recipient greatest increase	6.3%	31.3%	
Recipient non-white greatest increase	4.0%	27.6%	

None of the centres reached the activity level predicted by UK T simulations. No median CIT changed significantly. **Discussion**: The period studied may not reflect long-term effects of the revised national allocation policy but major changes in unit activity were observed. These were mainly in the direction intended by the revision. The implications of changes in unit activity and the resulting concerns must be addressed in the UK T monitoring process.

P80

Long term graft function of transplanted kidneys from hypertensive Non-Heart Beating donors

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Most transplant centres consider hypertensive donors as marginal donors.
Although current data suggest that cadaveric donor hypertension is associated with decreased graft survival[i]-[ii], there are no studies to date to assess the impact of donor hypertension on recipient graft survival from NHB donors.
Prevalence of hypertension (Blood Pressure more than 140/90 mm Hg) in people aged 35-64 years, has been estimated to be 44.2 % in Europe.
In this study, we analyzed short and long term graft function of 115 single Non-Heart beating recipients transplanted between 1998 and 2005 in our centre.
18 recipients received kidneys from hypertensive donors (HTD group). The rest were used as control group.
All kidneys underwent viability assessment using pressure flow characteristics using hypothermic machine perfusion and perfusate enzyme level prior to transplantation.
Mean donor age was 52.50 ± 9.87 and 40.38 ± 15.42 in HTD and control group ($p<0.001$). There was no difference between groups in other confounding factors such as warm and cold ischaemic times, HLA mismatch and number of controlled and uncontrolled donors.
There was no significant statistical difference between the groups in delayed graft function, primary non function and rejection rate.
Mean GFR using MDRD formula after 12 months was 23.81±13.01 and 44.63±15.51 ml/min/1.73m^2 in HTD and control groups respectively ($p=0.019$). After 24 months, the GFR was 34.97±13.17 and 45.92±16.97 ml/min/1.73m^2 in HTD and control groups respectively ($p=0.05$).
In conclusion, using viability testing, kidneys retrieved from hypertensive NHB donors can be transplanted. Inferior long term function of these grafts compared to kidneys from normotensive donors prompts careful recipient selection.

P81

Does Nephrectomy Influence Graft Survival in Kidney Re-Transplantation

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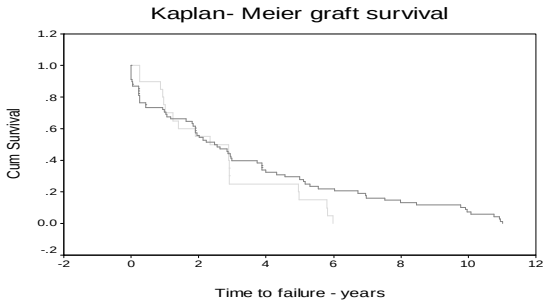
Introduction: Re- transplantation is being increasingly performed worldwide. Graft outcome varies from that of primary grafts depending on multitude of factors.
We analyzed data of our patients with re-transplantation to see whether graft survival is affected by removal of previous failed graft
Methods: Patients undergoing re-transplantation in our unit from January 1993 to April 2005 were included. Data was collected about patients' demographics, HLA, PRA, donor type and number of re-transplants. Graft survival was calculated by Kaplan-Meier and compared by log-rank test. Multivariate analysis was done by Cox regression
Results: Number of patients was 89 with 60% males (53) and mean age 38 years. Whites were 76(85.4%), blacks 8 (9%) and Asians 5%(5.6%). HLA mismatches were 2.28 (mean). PRA was 34.72 (mean). 74 (83%) had second transplant, 9 (10%) had third, 5 (6%) had fourth and 1(1%) had fifth transplant. 68 (76%) had nephrectomy and 21(24%) did not undergo nephrectomy. Heart beating deceased donor transplants were 74 (83%), non-heart beating 4 (4.5%), living related 10 (11.2%) and living un-related 1 (1.1%). 24 (27%) grafts failed. One, 2 and 3 years actuarial graft survival with nephrectomy was 70%, 60% and 40%, and 70%, 55%, and 25% without it respectively. The difference between the two was not statistically significant (P= .19). Number of retransplants, HLA mismatches and PRA did not affect the outcome
Conclusion: Graft survival after re-transplantation seems to be inferior to primary grafting and is little influenced by nephrectomy



P82

Gastric Banding For The Treatment Of Morbid Obesity In ESRF Prior To Renal Transplantation: The Business Case

Anusha Edwards, Sally Norton, Justin Morgan

Southmead Hospital, Bristol, United Kingdom

Introduction
Morbidly obese patients are poor candidates for transplantation as they pose anaesthetic and surgical difficulties, with the associated co-morbidities, of hypertension and type II diabetes, adversely effecting outcome. Bariatric surgery is more effective than other weight loss strategies and has been supported by NICE. We report on the financial case for gastric banding in morbidly obese patients with ESRF prior to transplantation in our unit.

Patients
In July 2006, there were 275 patients on the active waiting list for renal transplantation with 53 being worked up, 44 currently suspended and 130 being considered. Of these 502 patients, 303 had a record of body mass index (BMI) with 5 patients having a BMI greater than 40. 4 further patients had a BMI greater than 35 and type II diabetes mellitus. All potentially eligible 9 patients were receiving haemodialysis and only 2 were on the active waiting list.

Costs
Haemodialysis and erythropoietin cost £30,608p.a. The average transplantation costs £20,861 rising to £24,774 if using a live donor. Immunosuppression costs on average £6,000p.a. Outpatient attendances cost £5,580 in the first year and then drop to about £744. 50-80% of obese patients with type II diabetes and/or hypertension can be cured of their disease and medication costs significantly reduced by the use of gastric banding at a cost of around £6,500.

Discussion
Successful gastric banding and subsequent transplantation could save at least £24,000/patient p.a. This represents a considerable cost benefit, as the average “lifespan” of a transplanted kidney in our unit is 10 years. This may be a conservative estimate. Due to the gross discrepancy between the numbers of organs available and those required it makes both medical and financial sense to optimise the health of recipients in order to improve long-term graft and patient outcomes.

Conclusion
We believe that teamwork between bariatric and transplant surgeons could lead to vastly improved patient and graft survival in morbidly obese patients with ESRF and provide considerable cost savings.

P83

Changes in the Prescription of Non-immunosuppressive Agents for Renal Allograft Recipients in the Last Decade

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Introduction. Since 1996 we have offered all our renal allograft recipients a comprehensive 'Annual Review' (AR) which has enabled (a) detailed medical assessment, (b) risk identification, (c) health promotion and education and (d) data collection and analysis to be undertaken. From 1996 to 2005 inclusive, 1296 patients (816 male and 480 female) have undergone a total of 5479 ARs. Currently, over 700 patients attend the out-patient clinic in any one year. A recent analysis of this prospective study has identified a number of trends in the prescription of non-immunosuppressive drugs. In this report we describe the changes in use of hypolipidaemic agents, vitamin D analogues, erythropoietin, aspirin, allopurinol, oral hypoglycaemic medication and insulin over the years 1996, 2000 and 2005.

Method. Every patient has all their medication reviewed and documented in detail at each visit. The information has been abstracted from the study database and is expressed below as the percentage of patients taking the particular drug at the time of their AR in that year.

Results.

	1996	**2000**	**2005**
Hypolipidaemics	4.0	19.3	43.9
Vitamin D	3.2	10.8	19.4
Erythropoeitin	1.5	1.8	5.8
Aspirin	17.8	28.7	47.1
Allopurinol	8.7	9.9	13.6
Oral hypoglycaemics	3.7	2.5	6.2
Insulin	6.2	10.8	6.6

Discussion. The use of insulin and oral hypoglycaemics does not appear to have changed significantly during this period despite a more aggressive approach to the diagnosis of glucose intolerance. Similarly, there is relatively little change in the use of allopurinol. However, the relative change in the use of aspirin, erythropoietin, vitamin D analogues and hypolipidaemic agents has increased very significantly (between 2.6 and nearly 11 fold for these agents) with the absolute use of both aspirin and hypolipidaemic drugs being greater than 40% in 2005. These data suggest that the (risk of) co-morbidity following renal transplantation, particularly in respect of cardiovascular disease, is now better recognised and is more appropriately treated.

P84

The Utility Of A Care Bundle Approach To The Long Term Management Of Renal Transplant Recipients

M Bairy, I Ahmed, C Burton, L Milnes, H Akbani, R Roberts, R Jeffrey, J Stoves

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Introduction: Hypercholesterolemia is highly prevalent in renal transplant recipients (RTRs) and treatment is recommended. Review of total serum cholesterol (SC) is one of several clinical reminders within a RTR care bundle that has been used consistently in our transplant follow-up clinic since 3/05. The reviewing clinician is prompted to make appropriate changes to lipid-lowering therapy according to the SC value (> 4.5 mmol/L) and other factors including concordance with the previous prescription.
Method: Outcome data were recorded for a cohort of RTRs (n = 148) from the time of introducing the care bundle through to 9/06. The Proton database was used to review patient prescription records and obtain SC values closest to 3/05 (t0), 3/06 (t12) and 9/06 (t18). Pre- and post-intervention SC values were compared using the paired t-test.
Results: 17 of the cohort of RTRs were commenced on statin therapy and a further 25 who were already on a statin had a dose increase (67 remained on the same dose of statin and 18 were consistently statin-free). 127 out of 148 RTRs received follow-up throughout the 18 months study period. The mean +/- SD values of SC for these patients were 4.59 +/- 0.87, 4.32 +/- 0.74 ($p<0.001$) and 4.22 +/- 0.69 mmol/L ($p<0.001$) at t0, t12 and t18 respectively. For RTRs in whom the statin prescription was changed (n = 42), SC was 5.06 +/-1.18, 4.55 +/- 0.81 ($p< 0.001$) and 4.33 +/- 1.04 ($p< 0.01$) at t0, t12 and t18 respectively.
Conclusion: This study suggests that the introduction of a care bundle containing a number of clinical reminders can be effective in supporting the long-term management of RTRs.

P85

Pre-Operative Clopidogrel Usage In Renal Transplantation – Is It Safe To Operate?

Aditya Kanwar, Colin Wilson, Dorota Overbeck, Derek Manas, Torpey Nick, Rix Dave, Jacques Brian, Soomro Naeem, White Steve, Kestevan Patrick, Talbot David

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Introduction: The advent of cardiac stenting has necessitated routine treatment with clopidogrel and aspirin. Our hospital has an "unofficial" policy of cancelling elective surgery with this combination. Many patients awaiting renal transplant have cardiovascular co-morbidities necessitating angioplasties. In general these patients have to be switched to a single agent before listing. In an urgent setting of renal transplantation, the risks and benefits involved in patients on Clopidogrel pre-operatively, have not been evaluated and are still debatable.
Methods: From a retrospective analysis of 571 patients from January 2001 to August 2006, we present 3 patients where clopidogrel and aspirin was present at the time of transplant.
Case 1 - 69 years female, with renovascular disease and hypertension. On clopidogrel and aspirin for left renal artery angioplasty. Transplanted in 2002. No transfusions required peri-operatively.
Case 2 – 51 years female, with obstructive uropathy secondary to renal calculi. On clopidogrel and aspirin for coronary angioplasty performed 6 months prior. Transplanted in 2003. No haemorrhagic complications requiring intervention.
Case 3 – 69 years female, with polycystic kidney disease. On clopidogrel due to ischemic heart disease with gastric intolerance to aspirin. Transplanted in 2006 with no peri-operative bleeding complications.
Results: In our limited experience, excessive blood loss has not been an issue with clopidogrel treatment with renal transplantation.
Discussion: Large sample studies are required, unequivocally demonstrating effects of clopidogrel administered pre-operatively in renal transplantation.

P86

Clinical Variables Poorly Predict Early Graft Function Following Renal Transplantation

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Delayed graft function (DGF) following renal transplantation remains a significant clinical challenge. It is associated with a prolonged post operative course leading to greater patient morbidity and ultimately reduced long term graft survival. This study aimed to test the ability of clinical variables (both independently and when incorporated into published scoring systems) to predict suboptimal early graft function in a multi-ethnic urban population, through a multivariate statistical model.

The scoring systems investigated were the USRDS score (Irish et al, JASN, 2003), deceased donor score (Nyberg et al, Transplant., 2005) and expanded criteria donor kidneys (Metzger et al, AJT, 2003). We prospectively collected the variables from 217 consecutive deceased donor renal transplants treated with a predominantly ciclosporin and azathioprine based immunosuppressive regimen, performed between 2003 and 2006. Their relationship with three parameters of suboptimal function: DGF (dialysis dependency), slow graft function (SGF, creatinine greater than 266umol/l at day 5 post transplantation) and the creatinine reduction ratio at day 2 (CRR2), was then determined.

Suboptimal early graft function was associated with the following individual clinical variables: donor age, donor body mass index, donor hypertension, donation following cardiac death, black recipient ethnicity and cold ischemic time ($p=<0.01$ for all; sum r^2: 0.20). All scoring systems showed associations with early graft function, although only the USRDS score remained in the multivariate model ($p=<0.01$; r^2 value: 0.12). Despite these associations, the predictive ability of the continuous individual clinical variables was poor and the USRDS scoring system was moderate at best (ROC curve analysis c-statistic ≤ 0.71).

This suggests that clinical variables, even when incorporated into established scoring systems, have a limited predictive ability for early graft function and caution should be exercised before altering patient management based solely on them.

P87

The Influence Of A Functional Heme Oxygenase-1 Gene Promoter Polymorphism On Outcomes In Renal Transplantation

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Heme oxygenase-1 (HO-1) is a cytoprotective molecule that is up-regulated in response to multiple noxious stimuli. It has anti-oxidant, anti-inflammatory, immunomodulatory and anti-apoptotic properties. In experimental transplant models increased HO-1 expression correlated with reduced acute and chronic injury. A functional promoter polymorphism (dinucleotide repeat $(GT)_n$) regulates HO-1 gene expression. The promoter variant with a short number of tandem GT repeats, (S allele), increases the rate of HO-1 gene transcription. We assessed the role of this HO-1 gene promoter polymorphism on renal transplant outcomes in a large single center study.
HO-1 genotypes, (short (S) allele <25 repeats, long (L) allele $\geq$ 25 repeats) were determined by PCR and capillary electrophoresis. DNA samples (n=1414) from a total of 707 donor/recipient pairs of first deceased donor renal transplants (99% Caucasian) were genotyped. The median duration of follow-up was 8.2 years.
Graft survival was not significantly different between kidneys from donors with and without an S-allele (p=0.28, hazard ratio 0.89, 95% CI 0.71-1.11). Recipient genotype did not impact graft survival (p=0.13, hazard ratio 1.19, 95% CI 0.95-1.48). Similarly neither donor nor recipient genotype influenced recipient survival (p=0.41, hazard ratio 0.89, 95% CI 0.67-1.18, and p=0.16, hazard ratio 1.22, 95% CI 0.93-1.62 respectively). The hazard ratios changed only minimally when the factors that significantly impacted survival were considered in multivariate analysis. The incidence of acute rejection or chronic allograft nephropathy was not affected by genotype.
Although HO-1 gene expression modifies outcomes in experimental transplant models, it does not appear to impact graft or recipient survival in clinical renal transplantation. There is no evidence of a differential protective effect of the S allele of the HO-1 gene promoter polymorphism.

P88

Renal pathologies accelerate biological ageing.

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Introduction:
Accelerated biological ageing, characterised by changes in telomere biology has been noted in an increasing number of pathologies. These include cardio vascular disease, neurodegeneration, a predisposition to transplant dysfunction and psychological disorders . The impact of telomere biology on renal pathologies remains poorly understood. Consequently, we have investigated whether having a renal pathology accelerates biological ageing and if this is reflected in accelerated telomere erosion and shorter telomeres in renal patients.
Aim: To determine if accelerated biological ageing as measured by telomere attrition is manifest in a renal population as a consequence of pathology.
Methods:
PBL telomere lengths were determined by Q- PCR, and validated by Southern blotting, in haemodialysis patients, renal transplant recipients and a healthy age and sex matched control population.
Results:
PBL telomere lengths were determined for haemodialysis patients (n=24; mean age 57.9) and renal transplant recipients (n=62 mean age 48.9) and compared to a normogram derived from healthy volunteers in the Glasgow population (n=159; mean age 52.7). No significant associations were found with age and sex between the groups. Telomere analyses, however, indicated that renal haemodialysis patients had shorter telomeres than controls and an accelerated rate of biological ageing ($p=0.03$). Similarly, Transplant recipients exhibited significantly shorter telomeres than the control population ($p=0.032$), though their rate of telomere attrition appears to be ameliorated by their allograft.
Conclusion:
Renal pathologies accelerate biological ageing and this is reflected in both shorter telomeres and an accelerated rate of telomere erosion.

P89

Blood Pressure (BP) Control In Renal Transplant Recipients: Are There Independent Predictors For Achieving Target BP ?

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Introduction: Post-transplant hypertension is a major risk factor for longterm graft and patient survival. Controlling hypertension reduces cardiovascular risk and improves long-term patient and graft outcome. The ERA/EDTA European Best Practice Guidelines 2002: Section IV.5.2 define target BP in this population.
Methods: Most recent office BP readings were collected for 513 renal transplant recipients at least 12 month post transplantation. In addition demographic data (sex, ethnicity, age), comorbidity (ischaemic heart disease (IHD), diabetes), medication (aspirin, ACE inhibitors, statins, immunosuppressants), biochemical variables (cholesterol, serum creatinine) and e-GFR were obtained.
Logistic regression analysis was then used to determine whether any co-variables were significant ($p<0.05$) independent predictors of achieving target BP (<130/85 mmHg).
Results: BP was to target in 49.5% of all patients. Sex, Diabetes, IHD and e-GFR all significantly predicted whether or not BP was to target. More women than men achieved target BP (55% vs 45%). 16.6% of the total population were diabetic, of whom a higher proportion (61.2% vs 47.2%) met the BP target. 12.9% of all patients had IHD and in this subgroup 36.4% met the BP target compared to 51.5% in the non-IHD population. Mean e-GFR in the to target group was significantly higher than in the not to target group (48.8 vs 45.6).
There was no statistically significant association between any of the other predictor variables and achieving target BP. 22.2% of all patients received prednisolone + tacrolimus + mycophenolate, 56.4% of whom had BP to target. 18.3% received prednisolone + cyclosporine, 44.7% of whom had BP to target. These two drug combinations were not however significantly different in predicting BP to target.
Discussion: Approximately 50% of renal transplant recipients had BP to target which is in line with previously published data. Being diabetic, female and a higher e-GFR increased the likelihood of achieving target BP. This may be a reflection of different care pathways in primary and secondary care for diabetics, elements of which may be transferable to the renal transplant population. Known IHD and lower e-GFR were independent negative predictors of achieving target BP. These groups of high risk patients need particular attention as their overall cardiovascular risk profile is worse and transplant follow up needs to be tailored accordingly.

P90

Can a USA Based Algorithm be Used to Predict Delayed Renal Graft Function in a UK Transplant Centre?

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Introduction
Delayed graft function (DGF) is a major problem in renal transplantation resulting in prolonged hospital stay, dialysis, increased risk of rejection and poor long-term outcome. Identifying at risk recipients would therefore be important in the choice and dosage of induction therapy to prevent DGF as well as enrollment in clinical trials. Scoring systems to predict the likelihood of DGF have been developed in the USA but not in the UK. We applied a USA scoring system to a single UK centre to see if it could identify transplant recipients at risk from DGF.
Methods
An algorithm developed in the USA by *Irish et al* was applied retrospectively to the last 101 consecutive cadaveric renal transplants to the end of June 2006 at single UK centre. DGF was defined as those patients requiring dialysis during the first ten days. A score of 144 would indicate a greater than 50% likelihood of developing DGF.
Results
A cohort of 55 males and 46 females were analysed during the study period. There was one technical failure and one primary non-function which were excluded from the analysis. Altogether 41 patients (41%) developed DGF. There were 65 patients with a score less than 144 (ie. less than 50% chance of developing DGF based on the USA algorithm). Of these 17 (26%) developed DGF. Of the 35 patients with a score of more than 144, 24 (69%) developed DGF. The positive predictive value for the algorithm in his study was 69% and the negative predictive value was 73%.
Conclusions
The USA algorithm when used to predict DGF in 101 consecutive renal transplant patients in a UK centre showed poor specificity and sensitivity. We therefore recommend that it undergoes modifications to make it applicable for a UK-based population.

P91

Early Outcomes of Renal Transplantation under the new UK Allocation Rules in a Single Centre.

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Introduction: A new system for allocating kidneys from deceased organs had come in effect from April 2006 in the UK in order to address the issue of long waiters. **Aim**: Examine the effect of the new allocation system on the early outcomes of cadaveric renal transplants in a single unit. **Method**: The characteristics of cadaveric renal transplants in the first 6 months of the new allocation system (NA) were compared to the respective six months in the year 2005 when the old allocation system (OA) was in effect. **Results**: 29 transplants were preformed under the NA, while 21 were performed in same period under OA. As per design of the NA the mean waiting time (WIT) for these transplants was longer than that of OA (4 years compared to 2 years, p=0.006). There were no statistical differences in the donor age, recipient age, and number of re-transplants.

	New System	Old System	p
Mean Donor Age in yrs	48.76 (median 56)	46.48 (51)	0.516
Recipient Age in yrs	50.83 (median54.46)	49.25 (49.41)	0.616
Retransplants	17.2%	14.3%	0.775
Mean WIT (median)	1444.41 days (1602)	751.95 (576)	0.006
% waiting on the list over 3 yrs	65.5%	19%	0.001

However there were more total HLA mismatches under the NA, (2.86 vs. 1.95), half patients with 0 DR MM (34.5 vs. 66.7 %) and half 000 MM (6.9 vs. 14.3%) compared to OA. There was a small reduction in the mean cold ischemic time under NA (24 min). The median first hospital stay was 10.73 vs. 8.78 days (NS) but more patients (3 vs.0) lost their graft. There was no difference in creatinine levels at 30 (196μmol/l in NA vs. 145μmol/l in OA).

Conclusion:

The new allocation system has allowed transplantation of patients waiting longer on the waiting list. There was also a slight reduction in the CIT under the new system. However there was an increase in the number of HLA mismatches and halving of 0 DR mismatches under the new system. The impact of those differences on the long term survival and particularly in sensitisation remains to be seen.

P92

The Penta-Nucleotide Repeat In The Promoter Of The LPA Gene Is Linked To Survival After Renal Transplantation And Not Renal Impairment

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Introduction: Serum Lipoprotein(a) [Lp(a)] is an independent risk factor for atherothrombotic disease. Variation in Lp(a) levels is controlled by polymorphisms within the Lp(a) subunit apolipoprotein(a) encoded by *LPA.* An inverse relationship exists between the number of penta-nucleotide repeats (PNR) in *LPA* and Lp(a) concentration. High levels of Lp(a) are a feature of impaired renal function.
Methods: We developed a fluorescence based fragment analysis assay to genotype rapidly the *LPA* PNR using an ABI genetic analyser 3130. 156 cadaveric primary renal transplant recipients (RTP), transplanted in 1995 and 1996, and 252 individuals with renal impairment (CRISIS study) recruited from 2002-2006 were compared to 96 controls; all were Caucasian. Allele distribution in controls was identical to published frequency data. Ten year outcome data were analysed for all the specific genotypes and the contribution of individual PNR alleles analysed.
Results: Genotypes from the CRISIS cohort reflected the distribution of the control population. The 8 PNR allele was decreased in the RTP compared to the controls and the CRISIS cohort (55%; 72%; 71%, p=0.0016). In the RTP the 10 PNR allele was increased compared to the CRISIS cohort and controls (19%; 14%; 12%), but did not reach significance (p=0.132). To assess the impact of PNR on survival after renal transplantation, frequencies were compared between recipients who had died within 10 years post-transplantation (33%) and those still living (67%). The 8 PNR allele was increased in deceased patients compared with those surviving at 10 years (p=0.0001). A compensatory decrease in the incidence of the 10 PNR allele was also associated with an increased mortality (p=0.0007).
Discussion: Shorter (7-9) PNR repeats carry a higher risk of atherothrombotic events which may contribute to this poorer prognosis. A higher potential incidence of atherothrombosis could be a contraindication to transplantation, and would suggest that the increase in longer repeats seen in the transplant population reflects clinical selection at the time of transplant assessment (pre1995). This analysis, however, cannot take into account changes in clinical practice over the intervening ten year period. Nevertheless, the strong statistical relationship seen with the skewed distribution towards longer alleles in those surviving 10 years post-transplant suggests a link with a reduced incidence of atherothrombotic events post-transplantation. Clinical data analysis is in progress to assess this association.

P93

Hyperglycaemia and Post Transplant Diabetes Mellitus After Kidney Transplantation with Different Immunosuppression Agents – A Single Centre Experience.

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Introduction. Hyperglycaemia (HG) and Post-Transplant Diabetes Mellitus (PTDM) are common after renal transplantation. The incidence varies with the definition of PTDM and the type of immunosuppression used. This study evaluates the effect of different immunosuppressive agents on the development of HG and PTDM in a group of kidney transplant (KTx) recipients.
Methods. 136 adults receiving allografts between Sep 2004 and Dec 2005 (mean follow-up, 10.8 ± 4 months; range 3.6 - 19.7) were initially included in the study. Subsequently, 22 patients were excluded: 8 missing data; 3 early graft failure and 11 diabetic prior to transplantation. The 114 adult recipients were split into three groups, based on the major immunosuppressive agent used: tacrolimus (TAC) (n=87), cyclosporine (CSA) (n=24) and sirolimus (SIR) (n=3). Blood glucose (BG) values and data on the incidence of PTDM and the immunosuppressive regimen employed were obtained from the transplant flow charts. The patients were compared for age at transplantion, gender, primary disease, BMI, ethnicity, use of steroids immediately pre- and post-transplantion, and incidence, onset and duration of HG / PTDM. HG was defined as 2 consecutive BG levels of ≥ 7mmol/l. PTDM was defined as the need for on-going hypoglycaemic medication.
Results. Elevated BG levels were present in 47/114 recipients (41%) and 6 were treated for PTDM. Raised BG was present in 44 (50%) in the TAC group and 3 (12.5%) of the CSA group (4 and 2 of whom, respectively, were treated for PTDM,). All 3 patients in the SIR group had normal BG values. Age, gender, ethnicity and BMI were similar in all groups. However, the incidence of HG between the TAC and the CSA group was different (p=0.016). The time of onset of PTDM was significantly shorter among TAC (57.7 ± 68 days) versus CSA (84.8 ± 144.6 days) (p=0.03). The mean prednisolone dose for those treated with TAC was 11.26 mg versus 12.83 mg for those treated with CSA. HG resolved in 6 of 47 patients (12.8%); range 6 -175days.
Discussion. The incidence of hyperglycaemia overall was high, 41%, in this series, although we took consecutive BG values (random or fasting) above 7mmol/l to be of significance. Nevertheless, this study does suggest a significant difference between TAC and CSA-treated KTx. In addition, it highlights the need for a tighter definition of PTDM, possibly including the use of HbA1c as a diagnostic marker

P94

Donor Factors Affecting Graft Survival In Cadaveric Renal Transplantation

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Introduction: Transplantation remains the best treatment option for end stage renal disease. The main limiting factor in renal transplant is a critical shortage of donor organs. Efforts to meet the increasing demands have included the expansion of live and non-heart beating donor programs and the use of suboptimal grafts. The main concern from using 'suboptimal' grafts remains inferior graft and patient outcome. We retrospectively analysed all cadaveric kidney transplants in our centre from 1995 to 2005 to identify the donor factors that influence graft survival.
Methods: The data used for analysis was retrieved from the UK transplant database and our unit's computerised database. We analysed donor age, sex, ethnicity, cause of death, duration of hospital stay, inotropic support, donor type, previous history of diabetes, hypertension, ischemic heart disease, cardiac arrest, retrieval creatinine and graft anatomy. Recipient age, sex, ethnicity, cold and warm ischemic time were also analysed.
Results: Over 10 years there were 1053 cadaveric renal transplants in our centre. Median ages of the donor and recipients were 45 years (Donor: 46% female, 54% male. Recipient: 38% female, 62 % male). Overall 5 year graft survival was 73%. Univariate regression analysis revealed that a donor history of hypertension, ischaemic heart disease and moderate to severe atheroma in the vessels of the graft were significant. On multivariate analysis, donor history of hypertension ($p=0.007$, HR 1.5 CI 1.122-2.040) and ischaemic heart disease ($p<0.001$, HR 2.479, CI 1.489-4.129) remained significant. Donor age, type and retrieval creatinine were not significant in terms of graft outcome.
Conclusions: Donor history of hypertension and ischaemic heart disease were the most important independent predictors of poor graft outcome in our analysis.
Acknowledgement: UK Transplant for providing data

P95

Heme Oxygenase Genotype In Kidney Donors

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Introduction

Heme oxygenase [HO-1], produced during periods of oxidative stress, catalyses the oxidation of anti-inflammatory heme generating end products. The length of a functional GT repeat polymorphism in the proximal promoter may influence transcription. Alleles with short GT repeats correlate with high HO-1 production and improved renal graft survival in animal and human studies. We report the distribution of allele length and 12 month graft outcomes in a UK donor population.

Methods

Cadaveric donor DNA (n=209) was amplified by PCR and Fragment Analysis was performed. Based on the frequency distribution ≤25 repeats was selected as a cut-off for short (S) allele size and >25 was selected for long (L) allele size. Outcome measures for each genotype (SS, SL, LL) were assessed according to creatinine levels, incidence of delayed graft function and numbers of rejection episodes.

Results

The number of GT repeats ranged from 12 to 38. After 12 months there were no statistically significant differences in graft outcome between the allele groups, including after HLA subgroup analysis, although surprisingly there is a trend towards more rejection episodes in the SS group.

Discussion

Consistent with the findings reported in earlier studies a bimodal allele distribution was observed in the study cohort. Genotype frequencies also approximated those previously reported. The presence of a short GT repeat allele however did not appear to be associated with lower post-transplant creatinine levels, less delayed graft function and less rejection episodes in our patient cohort.

P96

Social Deprivation Affects Rejection Rates but Not Graft Survival in Renal Transplantation

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Introduction

Social deprivation is known to have a negative impact on many aspects of health. The aim of this study was to examine if social deprivation impacted on outcomes of renal transplantation.

Methods

Data on all patients undergoing renal transplantation in a single centre, between 1997 and 2005, was analysed. Overall deprivation scores for the area of residence of all patients were obtained from the national statistics office. The overall score is a summary of different deprivation variables (income, health, employment, education etc.). Patients were divided into 4 groups (1= least deprived, 4 = most deprived) and rejection rates and graft survival were compared between groups.

Results

Social deprivation group	1 year graft survival	5 year graft survival
1	92%	79%
2	93%	78%
3	90%	69%
4	92%	76%

log-rank p=ns

The overall deprivation score was higher (more deprived) in those who experienced acute rejection compared to those who did not. (median 18.1 vs 23.0, mean 22.7 vs 25.3, p = 0.021). People that did have rejection were also more likely to come from a lower income (p=0.003), lower education (p=0.04) and less employment (p=0.02) area but not from lower health status (p=0.87) and less accessible areas (p=0.5).

Conclusion

Social deprivation has no impact on early and medium term graft survival following renal transplantation, but the risk of acute rejection episodes is higher in more socially deprived patients.

P97

Efficacy of early biopsy to detect acute rejection in kidney allograft recipients with delayed graft function

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Introduction

It is accepted that kidney transplant with delayed graft function (DGF) has poorer survival and function. This is more so when acute rejection (AR) occurs.
A diagnostic biopsy to establish the reason for the DGF, or the acknowledgement of AR, even if border line could improve the short and long term graft survival.

Methods

We retrospectively evaluated 358 kidney transplant recipients from January 2002 to September 2006. All patients who had dialysis, their serum creatinine levels increased, remained unchanged, or decreased less than 10% per day in three consecutive days in the first week after transplantation underwent a biopsy to evaluate the DGF.

Results

101 patients (28%) developed DGF and had an ultrasound guided kidney biopsy on 7th post operative day.
In all the cases the core biopsies were adequate (>20 glomeruli) for histological diagnosis. In 18,8% (n=19) of the biopsies AR was found, and following the Banff classification there were: three cases type 1a, three cases 1b, 10 cases type 2a and three cases type 2b. All the rejections were initially treated with methylprednisolone (500 mg/IV for three days). In two cases antithymocyte globulin was employed (2,5 mg/kg for 5 days) due to steroids resistance rejections. Two patients had post-biopsy bleeding that required surgical exploration.

Conclusions

Early biopsy in patients with DGF is a safe method that allows uncovering of AR that would be otherwise unknown. The immediate recognition and treatment of rejection episodes can certainly increase the long term survival and function of the renal transplants.

P98

Utility Of 24 Hour Ambulatory Blood Pressure Monitoring (ABPM) In The Renal Transplant Outpatient Setting

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Introduction: Control of blood pressure (BP) is perhaps the most import variable impacting the progression of chronic renal disease and has been shown to affect renal transplant survival. We were disappointed with our performance in the Renal Registry Report 2004 with less than 30% of patients achieving a BP less than 130/80. In the setting of a new chronic transplant care clinic we investigated this further using 24 hour ambulatory blood pressure monitoring (ABPM).
Methods: Clinic blood pressure data from patients undergoing regular follow up in the renal transplant clinic at St. James's University Hospital who were at least three months after transplantation were eligible for 24 hour ambulatory monitoring (APBM) (n=459). The mean of the BP at the last five clinic visits was calculated and those patients with the poorest control were invited to undergo ABPM (SpaceLabs 90207)
Results: 63 patients underwent ABPM. The mean age was 48.2 years, 15/63 were diabetic, 6/63 were current smokers and 47/63 had hypercholesterolaemia. The mean eGFR was 45.4 ± 14.3 mls/min/1.73m^2 and patients were taking 2.2 antihypertensive medications on average. The BP readings are shown below:

	Clinic	ABPM	P Value
Mean Systolic	156.7 ± 21.0	128.7 ± 14.6	P<0.0001
Mean Diastolic	85.0 ± 9.5	78.5 ± 8.3	P<0.0001
Systolic < 130	4.8%	60.3%	
Diastolic < 80	27.0%	66.7%	
BP < 130/80	3.2%	44.4%	

Conclusion: White coat hypertension is common in the outpatient setting. At our centre BP readings are not as poor as suggested in registry data as nearly half of all patients with apparently poor BP control actually have satisfactory pressures by ABPM. We must look at our method of ascertainment to see whether it can be improved in the busy clinic setting.

P99

Donation after Cardiac Death Kidney Transplantation in Leeds

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Introduction
We have established a donation after cardiac death (DCD) kidney transplantation programme in Leeds in an attempt to expand the available pool of donor kidneys. Here we report for the first time the results of controlled DCD kidney transplantation in Leeds.
Methods
"Proton" computer database and patient records were reviewed to obtain information about all DCD transplants performed between April 2002 and March 2006. Data was recorded and analysed using a computer spreadsheet.
Results
86 controlled DCD kidney transplants took place during this period with a progressive increase in the number of transplants performed from 6 in 2002 to 33 in 2005. 66% of patients were male and 34% female (age range 22- 78 years (mean 50.7)). 65% of patients were on haemodialysis at the time of transplantation and 35% on peritoneal dialysis. The minimum waitlist time range was 3- 204 months (mean 49.2). 5 patients were receiving their second transplant, 1 their third. There were 2 deaths perioperatively from myocardial infarction. The delayed graft function (DGF) rate was 63%, with 3 grafts failing to function adequately to prevent dialysis on discharge (4%). The patients with DGF were older, had spent longer on dialysis and had higher numbers of HLA mismatches than the non-DGF group. Mean creatinine values were 157, 158, 169 and 149 umol/l at years 1- 4 post transplant respectively. Biopsy proven acute cellular rejection occurred in only 9% of cases, vascular rejection in 3% and acute tubular necrosis in 28%. Graft loss occurred in 3 patients and 4 patients died over the study period, 3 with a functioning kidney, following discharge.
Discussion
Donation after cardiac death kidney transplantation has been used successfully to expand the potential kidney donor pool in Leeds. Delayed graft function rates are high but acute rejection rates are low with good medium term graft function.

Thursday 29 March

Moderated Poster Session

Liver

P100

Parenchymal CD8 Expression in "Normal" Liver Allografts

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Background and aims
One previous study suggested that low numbers of CD8+ T-cells in the hepatic parenchyma identified patients in whom withdrawal of immune suppression might be successful. The pattern of parenchymal CD8+ T-cell expression in long-established liver graft recipients with normal liver function tests was studied.
Methods
Parenchymal CD8+ cells were visualized by immunohistochemistry in liver tissue from 33 patients with normal liver tests more than 3 years from transplantation and compared with tissue from 6 normal controls and 1 healthy liver transplant recipient withdrawn from immune suppression. Biopsy images were analysed by "ImageJ" software for the number of CD8+ cells/cm^2 of parenchymal liver.
Results
The original indications for liver transplantation were PBC (8), PSC (6), acute liver failure after paracetamol (4), ALD (4), HCV (3), cryptogenic liver disease (2) and autoimmune hepatitis (AIH) (2), plus α1-anti-trypsin deficiency, APUDoma, fulminant HBV and cystic fibrosis (1 each).
The mean number of CD8+ cells/cm^2 in the study group was 105.4 +/- 66.2 (range 24.9 - 377.7) compared with 93 +/- 44.3 cells/cm^2 in controls (range 34.4 - 156.4), p = NS. Within the healthy transplant group, those with autoimmune disorders (PBC, PSC & AIH) had higher numbers of CD8+ cells compared with those transplanted for other conditions (means 132.7 vs 81.8, p = 0.013).
Conclusions
The number of parenchymal CD8+ cells was similar in established liver recipients with normal liver function tests and healthy controls; however, the original indication for transplantation influenced parenchymal CD8+ cell number. A low number of CD8+ parenchymal cells may identify a 'tolerant' group in whom immune suppression could be withdrawn, particularly those transplanted for conditions other than autoimmune disorders.

P101

Morbity and Mortality in 316 Consecutive Liver Grafts

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Background and Aims
Liver transplantation is an effective well-established therapy for end stage liver disease. Although mortality rates have improved, the long term morbidity may be considerable.
Methods
The case notes of 245 recipients of 316 consecutive liver grafts between January 1994 and January 1998 were censored systematically in 2006. Noteworthy clinical events and their timing from engraftment were recorded.
Results
A staggering 2623 complications were documented. Significant complications occurred in 95% recipients in year 1, 64% years 1 to 3, 57% years 3 to 5, 63% years 5 to 10 and 21% after year 10. Death occurred in 19% recipients in year 1, 4% years 1 to 3, 4% years 3 to 5, 7% years 5 to 10 and 1% after year 10. For each period, causes of death were similar: graft-related (21%), infection (41%), cancer-related (17%), other (14%) and cardiovascular (8%) respectively.
The most common causes of morbidity were graft-related, infection, hypertension and renal. The most common complications in year 1 were graft-related and infection (66% and 56% respectively). The incidence of common complications were similar for each period thereafter: 16% years 1 to 3, 13% years 3 to 5, 19% years 5 to 10 and 2% after year 10.
Conclusions
The morbidity of liver transplantation is considerable and may have been under estimated. Long term survival and morbidity may improve by shifting the focus from the first post-operative year where survival rates are excellent to immune suppression related complications.

P102

Impact of patients' ethnic background on outcome after Liver transplant surgery

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Introduction: In the UK about 10-15 % of liver transplants are performed on patients from non-white background. It is not clear whether there is a survival difference for different races following liver transplantation in the UK.
Method: The UK & Ireland Liver transplant audit is a multi-centre prospective cohort study of all patients undergoing liver transplantation since 1 March 1994. All patients who received a first transplant between 1 March 1994 and 31 December 2005 were included in this study. Patient and graft survival as a function of time after transplantation was measured using Kaplan-Meier methods. The effect of ethnicity and other risk factors was determined by univariate and multivariate cox proportional hazard regression
Result: Of the 5915 patients who gad a liver transplant 5307 (90%) were whites, 473 (8%) were asians, 135 (2%) blacks. The five year patient survival for whites (73%) was significantly higher compared to asians (66%) and blacks (57%) (log rank test $p<0.05$). Ethnicity was an independent predictor of patient survival after adjusting for the potential confounders. The other significant predictors were recipient age, history of previous upper abdominal surgery, encephalopathy, serum albumin, renal support, serum creatinine, incompatible blood group, cause of liver disease and pretransplant funtional status.
Discussion: Recipients ethnic background was an independent predictor of patient survival. Higher number of black and asian patients transplanted with greater severity of illness may partly explain the findings. Further analysis of patients on the waiting list may explain the disproportionate number of sicker patients in this group. Factors like referral pattern, racial differences in comorbidities not included in our analysis, education, response to drug treatment merit further investigation.

P103

Late Mortality Following Orthotopic Liver Transplantation a Single Centre Experience.

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Background: Studies into causes of mortality following liver transplantation have predominantly focussed on the first post-operative year. Here, the causes of patient mortality are well defined and identify primary graft non-function, technical complications of the surgery, infection and cardiovascular complications as important. A lesser amount of data exists regarding mortality in OLT recipients who have survived 3 years or more.
Aim: To review the causes of death in all patients who underwent OLT in a single centre and survived 3 or more years post transplantation.
Method: Single centre retrospective observational study. We examined all-cause mortality in OLT recipients who survived at least 3 years since 1992.
Results: Out of 642 OLTs performed in our unit, 298 (46.4%) patients survived ≥ 3 years. 45 (15.1%) patients subsequently died. Causes of death in this group included: malignancy 15 (4 PTLD) (33.3%) patients, cardiovascular 4 (8.9%), sepsis 10 (22.2%), multi organ failure 3 (6.7%), recurrence of primary disease 3 (6.7%) and other causes in 10 patients (22.2%). Mean age at time of death was 58 years (range 29-74). The aetiology of liver disease in this cohort was: PBC 15 (33.3%), alcoholic liver disease 10 (22.2%), Paracetamol overdose 4 (8.9%), Autoimmune liver disease 4 (8.9%), Hepatitis C 4 (8.9%), hepatocellular carcinoma 4 (8.9%), cryptogenic cirrhosis 3 (6.7 %) and drug induced liver disease 1 (2.2%). The mean time since transplant was 2175 days (range 1107-4026).
Conclusion: Over 75% of deaths in our OTL recipients who survived ≥ 3 years were from 4 main causes; malignancy, sepsis, cardiovascular and recurrence of primary disease. These main aetiological groups have immunosuppression as a common denominator and, as graft loss from acute or chronic rejection is uncommon, strategies to progressively reduce immunosuppressive therapy with time post-OLT should be actively pursued.

P104

Correlation of Coronary Artery Calcification Scores with Features of the Metabolic Syndrome in Patients Undergoing Assessment for Orthotopic Liver Transplantation (OLT).

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Background: An increased incidence of cardiovascular (CV) events is seen in patients with end stage liver disease (ESLD). As non alcoholic fatty liver disease (NAFLD) is increasing in prevalence, with more of these patients progressing to ESLD, we aimed to assess the relationship between the presence of features of metabolic syndrome (MS) and coronary artery calcification (CAC) score, a well validated assessment tool used in the detection of subclinical coronary artery disease (CAD). We also examined if any relationship exists between insulin resistance (IR) (as assessed by HOMA-IR index), features of the MS and CAC scores in an unselected cohort of patients undergoing OLT assessment.
Method: Single centre prospective observational study. Patients undergoing OLT assessment from April 2005-May 2006 were recruited. All patients underwent CT scanning of the thorax to allow CAC scores to be generated and correlated with number of features of MS (classified by ATP III criteria) and degree of IR.
Results: 52 patients underwent CT scanning with median age of 54 years (range 24-69). Median CAC score was 102 (range 0- 3533). Features of the MS were common with 27.45%, 41.18%, 23.53% and 7.84% of patients having no, one, two and three features respectively. IR was almost universal with 19.61% having moderate and 70.59% severe IR. We identified a significant ($p=0.038$) albeit weak correlation ($r= 0.291$) between the number of features of MS and CAC score. A significant ($p=0.047$) relationship between features of the MS and HOMA ($r=0.28$) was identified.
Conclusion: The relationship between the MS, IR and CAD may be important in determining CV risk in OLT candidates. Further evaluation of these risk factors for CV disease is important and should be addressed in prospective studies.

P105

Does the Donor Risk Index help in organ allocation in the UK?
A single centre experience.

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Introduction:
Feng et al described the Donor Risk Index (DRI) as an important factor affecting outcome in North American Liver transplant recipients. Our study sought to evaluate the effect of the DRI and MELD score on liver transplant recipients from a single centre in the UK.

Method:
Prospectively collected data of all patients transplanted at our centre between 01/95 and 12/05 were included for the analysis (n=1213). The DRI and MELD scores were calculated using published methods. Outcomes evaluated included patient and death censored graft survival. Hazard Ratios were used to evaluate the outcome of liver transplantation from "high" and "low" DRI groups (DRI >1.7 and DRI<1.7 respectively) on patients categorised into low (<15), intermediate (15-30) and high (>30) MELD categories.

Results:
MELD at transplant was found to be the only significant predictor of patient survival. MELD at transplant and DRI >1.7 was found to be associated with a poorer graft survival (Hazard ratio(HR)= 1.41). This was found to be more significant when the two scores were used together. Grafts from donors with a high DRI had an increased likelihood of failing compared to low DRI grafts when transplanted in "low" and "intermediate" MELD categories. Graft failure in recipient with MELD>30 was significantly higher when compared to MELD <30 but survival was equally bad with low and high DRI grafts (HR=3.9).

Conclusion:
Patients with low and intermediate MELD at transplantation may be better served by a low DRI graft. Whereas patients with high MELD may not be compromised by receiving a high DRI graft.

P106

Perioperative Outcomes Of Liver Transplantation Performed After Liver Resection

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Introduction: A shortage of organ donors has prompted centres to adopt strategies such as liver resection for hepatocellular carcinoma as a bridge to transplantation. The impact of prior resection on the perioperative outcome of liver transplantation is still unclear.
Methods: 11 patients were identified who had undergone liver resection prior to receiving a transplant at our centre between 1998 and 2006. The operative and perioperative period (0-28 days) was analysed. Morbidity and mortality after transplantation was assessed using Clavien's classification. The liver transplants performed before and after each of the study cases served as contemporaneous controls.
Results: The indications for liver resection were primary malignancy (8 cases), hepatic inflammatory pseudotumour (1), segmental Caroli's disease (1) and secondary biliary cirrhosis (1). 6/11 cases had parenchymal liver disease. In 8/11 cases, disease recurrence was the indication for transplantation. Early complications of resection necessitated urgent transplantation in 3/11 cases. 73% cases and 82% controls had at least 1 negative outcome. In the study group, 55% had a grade 1 (minor) complication, 27% had a grade 2 (potentially life-threatening) complication. No grade 3 (residual disability or malignancy) complications were observed. 18% had a grade 4 complication (retransplantation or death), specifically, one intraoperative death due to haemorrhage and 1 primary non-function resulting in retransplantation. In the control group the corresponding results were grade 1 (41%), grade 2 (36%), grade 3 (0%) and grade 4 (14%), which included 2 graft failures and 1 death. During transplantation, construction of a portal vein conduit was necessary for technical reasons in 3 cases. Median blood transfusion requirement within 24 hours of surgery was 4 units. 10/11 transplants were completed; median operating time was 405 minutes, warm ischaemia time was 44 minutes. The median intensive care unit stay was 2 days and total post-operative hospital stay, 18 days. For each of these parameters, no statistically significant difference was demonstrated between cases and controls.
Conclusion: In patients transplanted after prior liver resection, we observed rates of perioperative morbidity and mortality that were similar to those for de novo transplantation.

P107

Chronic renal failure in liver transplantation: beyond calcineurin inhibitor toxicity

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Introduction: Long-term outcomes after liver transplantation have improved in last two decades. With this improvement long-term complications such as chronic kidney disease (CKD) now represent a major management challenge. Although CNI toxicity is an assumed major pathogenic factor in CKD in this setting, there is little data on the patterns of renal damage seen in situ. The aim of this study was to assess histological diagnoses and renal outcomes in a cohort of patients who underwent a renal biopsy for investigation of renal failure following liver transplantation.
Methods: Thirty-five liver transplants recipients at our centre who underwent a renal biopsy for investigation of deteriorating renal function were identified. The histopathological diagnoses of these biopsies were reviewed. Follow up data was obtained from the local transplant databases and renal survival was calculated, as defined by a requirement for renal replacement therapy or a fall in MDRD GFR by 50%.
Results: Renal biopsies were performed at median duration of 1468 days [228 to 5809] after transplantation with a mean MDRD GFR of 26.14 (mean serum creatinine of 274 µmol/L). Six patients were dialysis dependent at the time of biopsy. Twenty two biopsies demonstrated evidence of dominant microvascular and ischemic damage consistent with a component of CNI-toxicity. In the remaining 13 recipients the dominant cause of renal damage was secondary to other primary pathologies, including: diabetic glomerulopathy [4/13]; IgA nephropathy [3/13]; hypertensive nephropathy [2/13]; acute tubular damage [2/13]; post-infective glomerulonephritis [1/13] and membranous nephropathy [1/13]. Eleven [31.4%] recipients required long-term dialysis; one of these patients subsequently received a renal transplant. Two further patients experienced a fall in MDRD GFR by 50%. Median renal survival in the whole group was 690 days [range 11 to 3695].
Conclusion: Although CNI toxicity plays an important role in the pathogenesis of kidney disease in many liver transplant recipients, other factors may be predominant in a subset of patients [37% in our series]. Renal biopsies may be indicated in this setting in liver transplant recipients to accurately direct further management.

P108

Outcome of right lobe grafts in Liver Transplantation. A multivariate analysis.

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Introduction: We analysed our data of 98 right adult lobe grafts from a single centre. All the variables were included in a univariate and a multivariate analysis. Our objective was to find variables that are associated with poor outcome.
Methods: In the period from 1994 to 2006, 98 right adult lobe grafts were used in our centre. Our criteria for grafts that are suitable for splitting include age <40 years, weight > 50 Kg, ICU stay up to 5 days, modest inotropic requirement, haemodynamically stable donors and macroscopically normal liver. Our recipient criteria are: weight <55 Kg, patient not hospitalised at the time of transplant, MELD<25, no previous abdominal surgery and mild portal hypertension. We analysed our data using a univaraiate and a multivariate analysis to find predictors of poor outcome. The factors that we studied included; Donor factors; age, cause of death, inotropic requirement, sodium level, donor arterial anatomy, and ICU stay. Recipient factors included; age, sex, weight, indication of transplant, MELD, sodium level, cold and warm ischaemia time.
Results: Median age was 50 (17-70) years, Our patient and graft survival at 1, 3 and 12 months is 87.8, 80.6, 78.6% & 87.8, 79.6 and 74.5% respectively. In the univariate analysis factors that were associated with poor survival were: Donor sodium >150 mmol/l (p=0.03), recipient sodium < 135 mmol/l (p= 0.001), warm ischaemic time >50 minutes (p=0.003), transplantation for hepatocellular carcinoma (p= 0.001). In the multivaraiate analysis, we found that donor sodium (p=0.04), recipient sodium (p=0.001), warm ischaemia time (p=0.001), MELD >12 (p=0.028) and transplantation for hepatocellular carcinoma (p=0.002). Twelve donors were outside the split criteria (age>40 yrs) and this had no impact on patient or graft survival. Our biliary complication rate was 24.5% (24 patients): 16 patients had bile leaks and 8 developped anastomotic stricture (2 treated by stenting and 2 with Roux Y reconstruction). Biliary complications had not adversely affected the survival in this series.
Discussion: Split liver transplantation is associated with reduced survival if donor sodium >150mmol/l, recipient sodium level<135 mmol/l, transplantation for HCC and warm ischaemia time >50 minutes.

Thursday 29 March

Moderated Poster Session

Pancreas

P109

F-MRI and Headspace Gas Chromatography to Determine Penetration of Perfluorocarbon (PFC) in Pancreas Preserved by Two-Layer Method for Islet Transplantation

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INTRODUCTION : The mechanism of action of the two-layer method remains unclear. Direct measurements of pO_2 in the core of pancreas by two separate investigators have yielded conflicting results. A fundamental issue is to ascertain the likelihood of penetration of PFC into the substance of the pancreas during TLM cold storage.
MATERIALS AND METHODS : Segments of the pancreas (7.5 cm in length) were studied using a Varian Inova 9.4T MR spectrometer. Tissues were suspended in UW solution and an external standard of PFC was introduced for quantification. Four consecutive transverse images of 4mm thickness were obtained using a spin-echo sequence: repetition time (TR) of 1s, echo time (TE) of 20ms, field of view (FOV) of 45cm x 45cm, matrix size of 256 x 12 and 4 averages.^{19}F MRI was then performed using the same parameters. For headspace gas chromatography 500 mg of pancreatic tissue was transferred to 50 ml capacity Pyrex vials containing 1g anhydrous magnesium sulphate. The bottles were placed in a microwave oven and heated for 90 sec at 200° C to volatilize the PFC. One ml of headspace was analysed in a gas chromatograph equipped with a flame ionisation detector.
RESULTS : *^{19}F MRI*: In a transverse ^{1}H MRI image of the porcine pancreas after 24h storage in PFC syringe of PFC was not detected by ^{1}H MRI but readily observed by ^{19}F MRI - not surprising, as PFC has no ^{1}H for detection by ^{1}H MRI. By ^{19}F MRI, although the PFC standard can be observed, no^{19}F signals are detected from the pancreas, suggesting any PFC present in the pancreas is below the detection limit by the ^{19}F MRI experiment. *GC-MS*: With headspace the background (in control sample) concentration of perfluorodecalin was 0.025 ppm w/w (0.013nl/g) and the mean concentration in the test samples was 0.021 ± 0.013 ppm w/w (0.011 ± 0.006 nl/g), confirming that there was no PFC retained in the test samples. The positive control was a 500 mg sample of porcine pancreas spiked with 0.1 μl of perfluorodecalin. The concentration of the spiked standard was 165.15nl/g **CONCLUSIONS :**
1. ^{19}F MRI can be used in the setting of pancreas organ preservation, even though in the present work PFC was found not to penetrate the pancreas during TLM.
2. Results from ^{19}F MRI were confirmed by GC-MS.
3. Other methods of perfusion during pancreas preservation (such as intraductal or intravascular routes for PFC delivery) should be explored to improve oxygenation and organ viability.

P110

Comparison of long term outcome after transplantation between diabetic and non-diabetic patients. A UK Renal Registry data analysis

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Introduction: Renal transplant recipients whose primary renal disease is diabetes mellitus have more co-morbidity than non-diabetic patients and are more at risk from cardiovascular disease. This analysis was aimed at comparing the outcome and quality of care after renal transplantation of diabetic with non diabetic patients.
Method: A total of 3,860 patients with a functioning first renal transplant on the UK Renal Registry database at the end of 2003 were identified. After excluding 51 patients with a missing primary renal diagnosis, the cohort was divided into diabetic [424, 11%] and non diabetic groups [3385, 89%]. Sequential quarterly changes in the estimated means for haemoglobin, blood pressures, calcium, phosphate, intact parathyroid hormone (iPTH) and bicarbonate were analysed using analysis of variance after adjusting for age, gender, ethnicity, time on dialysis, year of transplantation and eGFR. The rate of decline in eGFR was also studied. Patient and graft survival rates in the two groups were compared.
Results: One, three and five year death censored graft survival rates for diabetics and non-diabetics were 91%, 88%, 81% and 91%, 88%, 85% respectively. Five year transplant survival (graft survival not censored for death) was 69% for diabetics and 78% for non-diabetics ($p = 0.003$). Five year patient survival was 85% and 91% for diabetics and non-diabetics respectively ($p < 0.0001$). Throughout the 5 year observational period, diabetics had higher SBP (5 mmHg, $p < 0.001$.) and lower cholesterol (0.5 mmol/L, $p < 0.001$). There was no difference in haemoglobin, corrected calcium, iPTH and bicarbonate levels between diabetics and non-diabetics.
Discussion: Overall the quality of care of diabetic transplant patients in UK is similar to non-diabetics. Although some cardiovascular risk factors such as cholesterol level are lower, others such as systolic blood pressure are higher. Death censored graft survival is similar in the two groups. Transplant survival is significantly lower in diabetics because a higher proportion of renal allografts are lost through patient deaths

P111

Outcomes Of Pancreas Transplantation in Recipients Age 50 and Over. A Single Centre Experience.

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INTRODUCTION: Pancreas transplantation in patients older than 50 years is presumed to have inferior outcome compared to the younger group. Some investigators argue that the scarce resources of the valuable donor pool should not be allocated to these high-risk, older individuals who often have significant comorbidity. However, little data is available regarding outcomes after pancreas transplantation (PT) in recipients aged 50 and over. The objective of this study was to compare the outcomes of PTs in patients age 50 and over (n=24) to recipients under 50 (n=72). **METHODS:** From June 2001 to November 2006, we performed 96 PTs (76 SPK, 18 PAK and 2 PTA). Clinical data was collected prospectively into an electronic database (Microsoft Excel). We grouped recipients by recipient age at transplant (< 50 vs. ≥ 50) and data were analysed retrospectively. Clinical outcomes including pre-operative and long term surgical (e.g., relaparotomy, bleed, thrombosis, infections, leaks) and medical co-morbidity (e.g. urinary and respiratory tract and CMV infections), graft and patient survival were compared between the two groups. **RESULTS:** The two groups were compared for donor and recipient demographic, immunologic and transplant characteristics (e.g. gender, weight, timing and technique of exocrine drainage of pancreas, etc). All patients received tacrolimus (TAC), mycophenolate mofetil (MMF) and steroids as maintenance therapy. Patient survival was 88% in ≥50 v 92% in <50 group and Pancreas graft survival rates were similar (79% in the ≥50 and 74% in <50 groups, respectively, p = 0.4). The incidence of acute rejection and thrombosis were higher in the <50group (35% for rejection and 17% for thrombosis) compared to the ≥50 group (25% for rejection and 8% for thrombosis) (both p = 0.26). The incidence of respiratory tract infection were significantly higher in ≥50 (46% in ≥50 vs. 10% in <50, p <0.001). Similarly higher incidence of bleed in ≥50 (25% in ≥50 vs. 8% in <50, p <0.03) occurred. The incidences of relaparotomy (54%≥50 vs. 50%in <50) and major fistula (17% vs. 10% in <50) were similar between groups.
CONCLUSIONS: These results suggest that PT in recipients aged 50 and over although associated with a higher incidence of bleed and respiratory infection with a longer hospital stay they however have comparable patient and graft survival with those younger than 50 years old.

P112

Perio-operative nutritional management of pancreatic transplant recipients-
A review of current UK practices

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Introduction
Simultaneous pancreatic-kidney (SPK) transplantation is a major challenge in a population at risk for nutritional complications. The influence of malnutrition on post-operative morbidity and mortality is well documented in the general surgery literature. However, there is little published data regarding how best to manage the pancreatic transplant recipient. This paper reviews the current approaches of all the UK centres.
Methods
A questionnaire was sent to all units involved in Pancreatic Transplantation in the UK, regarding the perio-operative nutritional management of the pancreatic transplant recipient. All 9 units responded.
Results-Summary

Drainage	100% centres use enteric / systemic drainage routinely
Enteric intake	56% commence enteral intake within 48 hrs post op
Supplements	62% administer food supplements routinely
TPN	22% commence TPN routinely
Analgesia	78% use an epidural analgesia
Nausea	22% prescribe pre-emptive anti-emetics
Gastroparesis	33% prescribe prokinetic agents post-operatively
Assessment	11% perform pre-operative nutritional screening
Protocol	0% had a perio-operative nutrition protocol
Understanding	45% felt our understanding was poor
Study	89% requested further study in this area

Conclusions
Nutritional management of the pancreatic transplant recipient varies widely in the UK. Further collaboration is needed to develop standard protocols.

P113

Complications requiring hospitalization after bladder drained simultaneous pancreas-kidney transplantation -10 years experience

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Introduction
In the first 10 years of the pancreas transplant programme bladder drainage was used exclusively to manage the exocrine secretions of simultaneous pancreas-kidney transplants (SPK). We present our experience of complications necessitating hospitalization in over 90 cases.

Methods
The data is derived from 94 cases of SPK transplantion (median follow up 37 weeks) which has been collected prospectively since the inception of the programme in August 1996. The donor and recipient selection criteria adheres to national standards and all patients receive Tacrolimus, MMF and Prednisolone maintenance immunotherapy.

Results
Complications requiring surgery or medical hospitalization

	Sepsis	Bleed	Ischaemia	Obstruction	Dehiscence	Panc'tectomy
Surg	12%	4%	3%	2%	2%	2%
	UTI	Acidosis	Haematuria	CMV	Pancreatitis	Infection
Med	30%	11%	9%	7%	6%	6%

- **Mode of dialysis** (haemodialysis vs peritoneal) did not correlate with surgical complications (P>0.05)
- **Re-laparotomy** rate was 13% in the first year post transplantation.
- **Enteric conversion** was 3% in the first year post transplantation.
- **1 year Survival**- Patient 95%, Kidney 91%, Pancreas 89%

Conclusion
Bladder drained pancreas-kidney transplantation is a successful therapy for suitable candidates but has significant morbidities associated with it

P114

Acute Inflammatory Syndrome In A Kidney-Pancreas Transplant Recipient Attributed to Mycophenolate Mofetil

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Introduction: Mycophenolate mofetil (MMF) has become a standard component of maintenance therapy in organ transplantation due to its efficacy in preventing acute rejection and improving graft survival. Generally it is well tolerated and its commonest side effects include gastrointestinal disturbance, leukopenia and cytomegalovirus infections. Very rarely MMF may be associated with an acute inflammatory syndrome first described in 2002. This condition is characterized by pyrexia, myalgia, oligoarthritis and elevated inflammatory markers. Here we describe an acute inflammatory syndrome with systemic haemodynamic instability in a kidney-pancreas transplant recipient attributed to MMF.
Case: A 30-year-old man with a simultaneous kidney-pancreas transplant developed severe acute rejection on day 85-post transplantation (p.t.) following the brief discontinuation of his MMF due to asymptomatic leukopenia. He completed a course of pulsed methylprednisolone and antithymocyte globulin and was restarted on MMF at 1.5 g per day on day 96 p.t. Five days after re-introduction of MMF he presented with pyrexia, symmetrical polyarthritis affecting the metacarpophalangeal and wrist joints, myalgia, neutrophilia and raised C-reactive protein. All initial investigations failed to reveal an infective cause for his presentation. Two days later the patient deteriorated further, displaying leukopenia and haemodynamic disturbance, and required admission to a high dependency unit. The symptoms improved on withdrawal of MMF and recurred on re-challenging. All microbiological investigations proved again negative. The patient has remained symptom-free since discontinuation of MMF.
Discussion: An acute inflammatory syndrome attributed to MMF has been previously described twice: in two patients treated for Wegener’s granulomatosis and in one patient with a kidney transplant. The case described here bears a lot of similarities with the previously reported cases, but is the first one associated with haemodynamic disturbance and leukopenia. An inflammatory syndrome secondary to MMF should be considered as a diagnosis of exclusion in the differential of systemic disturbance, fever and arthralgia in the immunosuppressed individual. The biological mechanism underlying this presentation remains to be elucidated.

P115

Prevalence Of Serological Markers Of Islet Autoimmunity Following Pancreas Transplantation.

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Introduction: Recurrence of beta cell destruction due to islet autoimmunity is an additional limitation in graft survival following pancreas transplantation. This study shows the prevalence of auto antibodies to glutamate decarboxylase (GADA) 65 and to islet cells (ICA), well recognised as markers of beta cell destruction.
Materials and methods: 58 diabetic patients (40 male, 18 female) who underwent pancreas transplantation from January 2005 to September 2006 were studied. All patients had pancreases implanted intraperitoneally with systemic venous drainage. Sera were obtained pre-transplant, and at 3, 6, 9, 12 and 15 months following transplantation. Insulin and C-peptide levels were measured using standard radioimmunoassay kits. GADA was measured using a radioimmunoassay (RSR, Cardiff, U.K.) The assay recognizes autoantibodies to GAD65 in serum and has a clinical cut-off of 1.0 units/ml with an intra-assay coefficient of variation (CV) of 3.1% and an inter-assay CV of 5.1%. ICA was measured using indirect immunofluorescence, by performing comparison with standard pancreatic islet tissue and standard islet control serum (Binding Site, UK). The results are expressed as JDF units.
Results: The incidence of GADA at the time of transplantation was 40.5%, and of ICA, 4.5%. Transplantation resulted in the disappearance of ICA in the first year following transplantation, whereas GADA persisted throughout the study period, with no discernible effects on glucose and insulin levels in the patients. Comparison of glucose tolerance curves, serum cholesterol, serum triglyceride, HbA1C, fasting C-peptide and fasting insulin levels between patients who were GADA positive and GADA negative revealed no differences during the study period.
Discussion: This study confirms observations made by other studies in islet transplantation that GADA positivity persists in long-term diabetics regardless of the duration of diabetes, and is not affected by immunosuppression. The presence of ICA or new appearance of GADA in the post-transplant period is associated with incipient graft failure, although it appears to be a late phenomenon. Sequential monitoring of these antibodies could help identify humoral immune response against beta cells non-invasively.

P116

Metabolic Outcomes Following Pancreas Transplantation Using a Steroid-Free Immunosuppressive Regimen.

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Introduction: The complications due to diabetes mellitus are a result of chronic hyperglycemia, which are gradually reversed following pancreas transplantation. Steroid use in maintenance immunosuppression may reduce or nullify these beneficial effects due to peripheral insulin resistance. This study shows the early metabolic outcomes following pancreas transplantation in a steroid-free regimen.
Materials and methods: 58 diabetic patients (40 male, 18 female) who underwent pancreas transplantation between February 2005 and September 2006 were analysed retrospectively. All patients received a steroid-free immunosuppressive regimen consisting of CAMPATH 1H induction, with Tacrolimus and mycophenolate maintenance. Serum cholesterol, triglyceride levels, HbA1c levels were measured pre-operatively as well as in the post-operative period at 3, 6, 9, 12, 15 months following transplantation. In the postoperative period, the patients also underwent an oral glucose tolerance test. The median follow-up was 11 months (range 3-15 months).

Results: The median glucose, cholesterol, triglyceride, HbA1C levels are shown below.

	Glucose (mmol/L)						
	fasting	30 mins	60 mins	120 mins	TGL	Chol	HbA1C
Pre Tx					1.62	4.5	9
3 months	5.5	9.85	8.3	6.4	0.83	3.9	4.95
6 months	5.4	8.75	8.2	5.45	1.14	4.1	5.6
9 months	5.35	8.45	7.1	6	1.28	4.2	5.6
12 months	5.4	8.5	8	5.5	1.33	4	5.8
15 months	5.4	7.7	6	5.5	1.68	2.7	5.3

Discussion: These results indicate a progressive improvement in the glucose tolerance curves, lipid profile as well as the HbA1C levels that are better than the pre-transplant values. However it remains to be seen if a steroid avoidance regimen in pancreas transplantation translates into a better metabolic outcome by earlier reversal of end-organ damage. Therefore, a randomised controlled trial comparing steroid versus non-steroid based regimen is warranted.

P117

Anticoagulation In Pancreas Transplantation – Who, How, When, and For How Long?

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Introduction: Graft thrombosis is one of the leading causes of early graft loss following pancreas transplantation. Unmonitored anticoagulation in these patients carries a risk of severe bleeding. This study reports the outcome following thromboelastography (TEG) monitored anticoagulation in these patients.

Materials and methods: From April 2004 to September 2006, 74 pancreas transplants (64 simultaneous kidney-pancreas (SPK), 9 pancreas after kidney (PAK), 1 pancreas transplant alone (PTA)) were performed. All patients had a baseline TEG pre-operatively, and anticoagulation regime with a combination of dextran, aspirin and heparin was used postoperatively, directed by daily TEG tracings. Patients were given Dalteparin 2500U subcutaneously for 6 weeks post-transplant. Kaolin activated TEG was used in the study (Haemoscope 5000) and plain and heparinase-modified TEG was performed. The Coagulation Index (CI, normal range -3 to +3; CI > +3 indicates hypercoagulability) was analysed. The aim of anticoagulation was to maintain the CI within its normal range.

Results: In the SPK group there were 44 (69%) males and 20 (31%) females; in the PAK group there were 3 (33%) males and 6 (66%) females; in the PTA group there was one male. 25 (34%) patients had a C.I. of more than +5 requiring therapeutic anticoagulation. Of these 23 (92%) patients were in the SPK group and 2 (8%) patients had the same feature in the PAK group. The one patient in the PTA group had a normal coagulation index. Gender distribution in the patients with C.I. more than five in the SPK group revealed that two-thirds were male whereas in the PAK group all of them were females, suggesting that gender did not appear to be a risk factor. One patient (1.3%) had an intra-abdominal bleed that required a laparotomy for evacuation of hematoma. Two patients who had CI >5 and anticoagulated, presented with graft failure (1 patient at 3 months, 1 at 12 months post transplant). These failures are thought to be due to an immunological cause.

Discussion: Pancreas graft thrombosis is mainly an early phenomenon. 34% patients undergoing pancreas transplantation develop profound hypercoagulability requiring therapeutic anticoagulation. The mechanism underlying this hypercoagulability is unknown, as are the risk factors associated with it. Identification of this high-risk cohort as well as the underlying mechanism will help develop targeted therapy.

P118

Outcomes Following Pancreas Transplantation In Non-uremic Type 1 Diabetics.

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Introduction: Isolated pancreas transplantation, either as a sequential pancreas after kidney transplantation (PAK), or pancreas transplant alone (PTA), has traditionally had inferior results compared to simultaneous kidney-pancreas transplantation. In this article, we present our early results with this cohort of patients.
Materials and methods: From July 2004 to October 2006, 12 patients underwent isolated pancreas transplantation (11 PAK, 1 PTA). All patients had CAMPATH 1H induction with tacrolimus and mycophenolate maintenance therapy. All grafts were placed intraperitoneally with systemic venous drainage and enteric exocrine drainage. All patients had thromboelastography directed anticoagulation in the first six weeks post transplant. Pancreatic graft function was monitored by measurement of C-peptide weekly, as well as by three-monthly oral glucose tolerance tests. Patients who presented with graft tenderness, high blood sugars in the presence of low tacrolimus levels were treated empirically for rejection.
Results: Median recipient age was 39 (range 30 – 56 years); Male: female ratio was 2:3. Median follow-up was 11 months. Median hospital stay was 11 days. 2 patients (16%) had a re-laparotomy in the post-transplant period. 3 patients (25%) had empirical treatment for rejection. 3 patients (25%) became profoundly hypercoagulable post-transplant and required therapeutic anticoagulation. Median fasting C-peptide level was 1.87 nmol/L (range 1.43 – 2.39 nmol/L). Two patients lost their grafts, one at 13 months and second patient at 3 months post transplant. Actuarial graft survival was 83.3% with 100% patient survival. In comparison, the SPK graft survival in the same period was 84.5% with 95.6% patient survival. No CMV infections, BKV nephropathy or fungal infections occurred in the cohort.
Discussion: Of the two patients who failed, the patient who failed in 3 months had a pancreas after simultaneous kidney-pancreas transplant, where the pancreas had failed in 11 months post-transplant, and it is known that these patients who undergo re-transplants have a higher risk of early graft loss.
Our results show acceptable actuarial graft and patient survival compared to patients undergoing simultaneous kidney pancreas transplantation, with good pancreatic function. Non uremic type 1 diabetics on immunosuppression should be considered for pancreas transplant.

P119

The impact of donor variables on outcomes after cadaver pancreas transplantation

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Introduction

Pancreas transplantation (PT) remains in its early stages in the U.K. with the most active unit's still totalling less than 100 transplants. Donor criteria vary widely between institutions and it remains unclear whether criteria established from larger series – predominantly in the U.S.A. – are applicable to the U.K. population. This study examines the impact of donor variables including age, body mass index (BMI), cold ischaemic time and smoking on graft outcomes including patient survival, graft survival and major surgical complications.

Methods

From June 2001 to November 2006, we performed 96 PT's, 72 simultaneous pancreas kidney transplants, 18 pancreas after kidney and 2 pancreas transplant alone. Demographic, clinical and biochemical data was prospectively collected and stored in an electronic database (Microsoft excel). The effect of donor BMI, donor age, donor cold ischaemic time, donor cause of death and donor smoking on clinical outcomes, including patient survival, graft survival, surgical and medical morbidity was analysed retrospectively.

Results

All patients received Tacrolimus, Mycophenylate mofetil and steroids as maintenance immunosuppression. There were no significant differences in recipient variables (age, sex, blood group or duration of disease) between comparison groups. Donor BMI ranged from 13.3-30.9. Donor BMI > 25 was associated with a significantly reduced patient 1 year survival, 80.0% ($p=0.007$) and higher overall major surgical morbidity ($P=0.03$). Graft survival however in this group was not significantly less than in patients with lower donor BMI. Cold ischaemic time varied between 542 and1327 minutes but was not significantly associated with graft or patient survival or major surgical complications. Donor's age range was 7 to 55 years and increasing age within this range was not associated with increased risk of any adverse outcome although the relationship to graft failure approached significance ($p=0.09$).

Discussion

In the 1st 5 years of our unit's pancreas transplant programme, a relatively narrow range of donor characteristics have been accepted based on large published series from overseas. Within the ranges utilised, increasing donor age and cold ischaemic time are not associated with any increased risk adverse outcome however higher donor BMI's, in even the sub-obese range of 25-30.9, was associated with a significant decrease in patient survival as well as major surgical morbidity. As programmes become established and donor criteria better defined, expansion may be more safely focused on the use of older or non-heart-beating donors with strict criteria for donor BMI maintained.

P120

Serum sCD30 Levels In Pancreas Patients Prior To Transplantation

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Introduction: The aim of this study was to identify if pre-transplant serum sCD30 is associated with acute rejection in patients undergoing simultaneous pancreas kidney transplantation. A high level of pre-transplant serum sCD30 (a marker for Th2 cytokine producing T cells) in patients undergoing a renal transplant has been shown to be a risk factor for acute as well as chronic rejection (Süsal *et al* 2002, Cinti *et al* 2005). There are no similar studies in pancreas transplant patients.

Methods: The serum samples of 76 patients before simultaneous pancreas kidney transplant were tested retrospectively for sCD30 level using ELISA.
All transplants were performed in the same unit between August 1996 and July 2005 using a bladder drainage technique. sCD30 concentration was correlated with the presence of kidney and/or pancreas rejection. Kidney rejection was proven by biopsy and pancreas rejection was proven by reduction in urinary amylase. Mann-Whitney U test was used to assess the relationship between absolute sCD30 concentration and rejection within one month and one year after transplantation.

Results: There were 34 female and 42 male patients. The median age was 38 years. Some 70 patients were white. Some 38 patients had ≥ 4 mismatches. At the time of transplantation the first nine patients were commenced on cyclosporine, MMF and prednisolone and the rest on tacrolimus, MMF and prednisolone. Some 34 patients had at least one episode of renal or renal and pancreas rejection at one month and 40 at twelve months after transplantation. The median sCD30 level was 60U/ml. There was no significance difference between absolute sCD30 level and rejection within one or 12 months after transplantation ($p=0.722$ & $p=0.667$ respectively).

Conclusions: Unlike previous studies in potential kidney graft recipients, this project has not shown a significant relationship between serum sCD30 in patients before simultaneous pancreas kidney transplantation and rejection up to one year after transplantation. This may be because most of these patients were on tacrolimus which unlike cyclosporine inhibits IL-10 secretion from Th2 cells and may be more effective in preventing rejection. More patients' sera will need to be tested in the future to investigate this further.

P121

Initial flow resistance can predict extent of apoptosis in Non-heart beating donor (NHBD) porcine pancreas preserved by low-pressure hypothermic machine perfusion (HMP)

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Introduction: HMP is a well-established method of preservation for NHBD kidneys. Pancreas is haemo-dynamically a low-flow organ with no definite encapsulation, leading to increased risk of baro-trauma. The role of HMP in preservation of NHB pancreases prior to islet isolation is unclear.
Aim: Study the perfusion mechanics in pancreases from a NHBD porcine model on low pressure HMP and determine whether they can be used as indicators of tissue injury.
Methods: Pancreases from five NHB pigs were retrieved by standard surgical technique. All pancreases were preserved using HMP with MPS™ (Machine preservation solution). Perfusion pressure was maintained at 10mmHg throughout the preservation period. The flow mechanics in-terms of the flow resistance (FR) and tissue flow rate (TF) were monitored. Weight gain after 6 and 24 hours of preservation was noted. Pancreas biopsies were collected at start of preservation and after 2, 4, 6 and 24 hours. Apoptosis was measured in terms of activated Caspase 3 levels (CASP3) in tissue lysate using a colorimetric substrate-based assay (reported in terms of μmoles of p Nitro-aniline released per minute per mg of tissue lysate).
Results: Median duration of warm ischaemia (WI) was 35 minutes (25-60 min). The mean flow resistance (FR) was 0.974 (0.45-1.99) at start of perfusion with a mean tissue flow rate (TF) of 0.07 ml/min/g of tissue (0.02-0.12). FR decreased to 0.426 (0.15-0.75) after 6 hours of perfusion while TF increased to 0.30 ml/min/g of tissue (0.06-0.38). Mean weight-gain at 6 hours of preservation was 20.6% (10-44%). CASP3 levels in biopsies at start of preservation were 0.473 U (0.172-0.702), which changed to 0.601 U (0.165-1.287) at 6 hours and 0.307 U (0.072-0.778) at 24 hours. There was no significant correlation between the WI duration or weight gain with TF, FR or CASP3 levels. There was significant positive correlation between the flow resistance at start of perfusion and the CASP3 at 24 hours ($p=0.012$).
Conclusion: We have been able to delineate the expected perfusion dynamics of a large animal NHBD pancreas. Initial data suggests that tissue resistance at start of HMP can be used as an indicator of the extent of apoptotic activation.

P122

Preservation of Non-heart-beating donor (NHBD) porcine pancreas- Comparison of low-pressure hypothermic machine perfusion (HMP) and static cold preservation (SCP)

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Introduction: SCP using the two-layer method (TLM) is the current standard of pancreas preservation prior to islet isolation. HMP is an established method of preserving NHBD kidneys. The role of HMP in pancreas preservation is unclear.
Aim: Compare the quality of preservation of NHBD porcine pancreases preserved with HMP or SCP.
Methods: Pancreases from eight NHBD pigs were retrieved by standard surgical technique. Pancreases were preserved using HMP at 10mmHg with MPS™ (Machine preservation solution) or using SCP (MPS™ alone or TLM with pre-oxygenated per- fluorocarbon). Weight gain after 6 and 24 hours of preservation with both preservation methods was noted. Preservation fluid samples and pancreas biopsies were collected at start of preservation (0 hours) and after 2, 4, 6 and 24 hours of preservation. Apoptosis was measured in tissue biopsies by activated Caspase 3 levels (CASP3) using a colorimetric substrate-based assay (reported as μmoles of p Nitro-aniline released per minute per mg of tissue lysate).
Results: The median duration of warm ischaemia was 35 minutes (25-60 min). Five pancreases underwent HMP while three were stored by SCP (MPS™ =1, TLM=2). Mean weight-gain at 6 hours was 20.6% (10-44%) in the HMP pancreases and 0% in the SCP pancreases. CASP3 levels in biopsies from HMP and SCP pancreases were 0.473 U (0.172-0.702) and 0.427U (0.126-0.660) respectively at start of preservation, which changed to 0.601 U (0.165-1.287) and 0.465 (0.373-0.556) at 6 hours. There was no significant difference in levels of apoptosis between the two preservation groups at start (p=0.82) or after 6 hours of preservation (p=0.55). H&E sections from pancreas biopsies at 0 and 6 hrs preservation revealed increased septal and intersititial oedema with HMP as compared to SCP. However islet morphology was preserved in both preservation groups.
Conclusion: Pancreases on HMP have a 20% weight gain due to interstitial oedema. There is no difference in apoptotic activation between the two preservation groups. The oedema in the HMP group might be advantageous to subsequent parenchymal disruption for islet isolation.

P123

Cardiac Outcomes After SPK: Do They Correlate With Preoperative Non-Invasive Imaging?

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Introduction:
Coronary artery disease (CAD) is a significant cause of death in diabetic patients. Furthermore, one third of diabetic transplant patients have clinically silent CAD. Coronary angiography has been the investigation of choice for the cardiac assessment of diabetic patients prior to transplant surgery. Myocardial perfusion imaging (MPI) is a useful non-invasive tool for the evaluation of asymptomatic diabetic patients. A recent meta-analysis suggests that diabetics with stress-induced MPI abnormalities have a significant high risk of myocardial infarction during the peri-operative period and should be investigated further by coronary angiography before listing for transplantation. Conversely, non-induced MPI abnormalities are not associated with a higher cardiac risk at the time of surgery but sometime later. MPI is now part of the protocol for the assessment of patients considered for simultaneous pancreas-kidney transplant (SPK) in our unit. The aim of the study was to correlate MPI results with cardiac events during the peri-operative period following SPK transplant.
Methods:
From January 2005 we introduced MPI in the protocol for assessment of all patients considered for SPK. Evidence of inducible and non-inducible (fixed) MPI abnormalities and cardiac events in the operative period were recorded prospectively.
Results:
28 diabetic patients underwent a simultaneous pancreas-kidney transplant following MPI as per protocol. The mean age of recipient was 38 years old. One patient had a fixed abnormality on the MPI. The remaining 27 patients had grossly normal MPI. No cardiac events were reported during the peri-operative or post-operative periods (30 days post-op). The patient with abnormal MPI died suddenly at home 36 days after the transplant procedure.
Conclusion:
Our data suggest that MPI is an accurate tool for the prediction of cardiac morbidity of patients undergoing SPK during the peri-operative period. These findings have permitted the selective use of coronary angiography on those patients with stress-induced MPI abnormalities.

P124

Comparative Study of Non-Diabetic Living Donor Kidney Transplantation (LDK) with Simultaneous Pancreas-Kidney Transplantation (SPK)

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INTRODUCTION: Some series showed that well HLA-matched diabetic recipients of SPK may have similar graft and patient survival such well HLA-matched non-diabetic recipients of LDK. The aim of this study was to investigate whether poorly HLA-matched diabetic recipients of SPK could achieve similar outcome as well HLA-matched non-diabetic recipients of LDK.
PATIENTS AND METHODS: We retrospectively analysed our cohorts of recipients of SPK transplantation and non-diabetic recipients of LDK and compared the outcome of both groups.
RESULTS: Between March 1st, 2002 and December 31st, 2005, 67 transplants were performed with kidneys from living donors (LD) and 46 organs from deceased donors (DD) were transplanted simultaneously with a pancreatic graft. SPK group received kidneys from DD donors with more CVA and hypertension but, significantly younger (31.5 +- 1.6 vs. 45.3 +-1.1) There were no difference in other recipient features. SPK group was poorly HLA-matched and there was no difference in preservation technique. However, CIT was longer in the SPK group (745 +- 55 vs 112 +- 12) Monoclonal antibody-based induction therapy was higher in the SPK group (100% vs 49.3%) In this group Campath-1 was administrated in 60.1% and Basiliximab in 39.9%. No difference in PNF (0% vs 0%), IGF (80.4% vs 83.6%) and DGF (19.5% vs 16.4%) was found. One-year graft survival was similar in both groups but, graft function at 1-year was statistically better in the SPK group. Patient survival at 1-month, 6-months and 1-year was similar.
CONCLUSION: This data suggests that deceased organs poorly HLA-matched and submitted to longer cold ischemia times could achieve similar clinical outcome as better HLA-matched organs from optimal donors. Did the use of campath-1 as induction agent in these patients contribute to these results? Further studies comparing SPK recipients with different monoclonal antibodies as induction therapy may be required to answer this question.

Thursday 29 March

Moderated Poster Session

Sensitisation

P125

Early Graft Loss And Vascular Thrombosis: Thrombophillia Or Donor Specific Antibodies?

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Introduction
In the modern era, 0.5-6% of grafts are lost early often secondary to arterial and venous thrombosis. Previously thought largely the result of technical complications, recent publications have suggested that vascular thrombosis (VT) in CDC crossmatch negative kidney transplants may also be due to the presence of circulating donor specific antibodies (DSA).
Method
We conducted a nested case control study of VT in our centre between 1995-2006. All patients had CDC negative cross matches at the time of transplantation. Both groups were assessed for their thrombophilic potential and their HLA antibody profiles were studied using FACS and xMAP™ multiple bead based technology (LUMINEX).
Results
26 cases of VT were identified. There were no differences between the VT group and their controls in terms of age, gender, historical PRA, dialysis modality and cold ischaemia time. The VT group had more beneficially matched grafts compared to controls (<1,1,0 mismatch, $p<0.05$). Donor factors were also similar in the 2 groups (age, sex, % cadaveric donors). The results failed to identify an association between VT and Factor V Leiden mutation, Prothrombin-Factor II gene mutations or antiphospholipid antibodies. The presence of DSA (using LUMINEX) immediately pretransplant was similar in both groups, being present in 5 of 26 patients in the VT group and 4 of 26 in the control group (p=NS). Of the 5 patients with DSA in the VT group only 1 showed additional signs of rejection in the explanted kidney, the others having pure vascular thrombosis as a cause of graft loss.
Conclusion
Low level circulating DSA at the time of transplantation are not associated with VT in the context of a negative CDC crossmatch.

P126

Early Graft Dysfunction After HLA Incompatible Transplantation; How Important Are Low Levels Of Donor-Specific Antibody?

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The presence of donor-specific HLA antibodies (DSA) in recipients of renal allografts may be associated with acute humoral rejection. Treatment with plasmapheresis pre-transplantation has been used with some success to reduce the level of DSA. Between June 2003 and October 2006 we transplanted 30 patients with DSA aged between 22 and 66 years 21 of whom (70%) were female. Pre-treatment 9 patients had complement dependant cytotoxic (CDC) +ve crossmatch (XM), 14 had flow cytometric (FC) +ve XM and 7 had DSA detectable only by Luminex beads. 25 patients underwent treatment with plasmapheresis pre-transplant. 8 developed early graft dysfunction (ED), defined as urine output <1000 mls per 24 hours in any one of the first 2 post-transplant days. 28 patients were evaluated after 2 patients died in the first week.
Of the 6 patients who developed ED, 4/9 (56%) were CDC XM +ve and 2/12 (17%) FC XM +ve pre-plasmapheresis. No patient with DSA detectable by Luminex alone developed ED. At transplantation, after plasmapheresis, 3 patients had antibody levels compatible with a CDC +ve XM, one of whom developed ED (33%). In patients with FC XM +ve at transplantation, 5/13 (38%) had ED, compared with 1/15 (7%) who were FC XM –ve.
5 of 6 patients (83%) with ED were subsequently diagnosed to have rejection requiring additional immune-modulating treatment compared with 6 of 22 patients (27%) who did not have ED.
Other risk factors for ED investigated (but not found to be significant) included number of years on dialysis prior to transplantation in the presence of DSA – mean 6.2 years with ED vs 5.6 years with no ED. In those with significant pre-transplant co-morbidity, 3/12 (25%) had ED, compared with 4/15 (27%) with no co-morbidity.
In conclusion, ED after antibody incompatible plantation was associated with pre-treatment antibody levels and residual antibody present at the time of transplantation, but not to other recipient factors. Post-perfusion renal biopsies showed minor glomerulitis in some patients, also suggesting that low levels of DSA caused graft dysfunction in our patients. Further work is required to define the level of DSA at which it is safe to perform a renal transplant.

P127

Indirect Allorecognition of HLA Public T cell Epitopes: Implications for the Mechanisms of Graft Rejection and Acceptance

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Indirect allorecognition provides T cell help for the generation of class-switched anti-HLA antibody and T cell activation through this pathway is independently associated with chronic allograft nephropathy. It is therefore likely to be important in 'chronic rejection' but has also been associated with graft acceptance in experimental models of transplantation. The identification of indirectly presented peptide epitopes has been confined to highly polymorphic sequences in the membrane distal domain(s) of MHC class I & II. We have systematically studied responses to peptides derived from the complete sequence of a single MHC class I molecule: HLA-A2. 53 overlapping 15mer peptides that spanned the primary sequence of HLA*020101 were made using F-moc technology. Their binding affinity to 13 different MHC class II molecules was studied in a competition assay by ELISA. Peptides from several locations exhibited promiscuous binding to MHC class II, some correlated with previously recognised α1 & α2 domain sequences but others lay in the non-polymorphic α3 domain. 30 peptides that bound one or more MHC class II were used to stimulate PBMCs from 55 transplant listed patients with known antibody sensitisation histories. Their responses were assessed by γ-interferon elispot. The findings are summarised in the table below. 22/55 patients responded to peptides from HLA-A2 and this was associated with but not confined to, those who had made antibody to HLA-A2 (14/18). 19/22 patients responded to peptides derived from the polymorphic α1 and α2 domains and 18/22 responded to peptides from the α3 and transmembrane domain, the sequence of which shows little polymorphism, such that the epitopes so identified may reasonably be termed 'public'. In 6 patients, the sequence of such 'public' T cell epitopes was identical to self; the response was autoimmune. The finding of responses to indirect 'public' T cell epitopes derived from MHC class I has implications for the immune response to alloantigen, its regulation and the application of antigen specific immunotherapy to transplantation.

	Number of patients responding in elispot	
Patient anti-HLA antibody status	**Patient HLA type**	
	A2 positive	**A2 negative**
Sensitised with anti-HLA A2		**14/18**
Sensitised with no anti-HLA A2	**1/9**	**3/8**
Unsensitised	**1/10**	**3/10**

P128

Monocytes And Acute Rejection - The Role Of A Neglected Cell Type In Transplant Immunology

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Introduction: Macrophages are known to infiltrate allografts during acute rejection. Macrophage precursors are circulating peripheral blood monocytes, which play a pivotal role in the immune system via potent antigen presentation, phagocytic and migratory activity. The aim of this pilot study was to investigate possible correlations between peripheral blood monocytes and acute rejection following heart transplantation.
Methods: Fifty four heart transplant recipients were enrolled into the study. Clinical data including immunosuppression was collected from patient notes. Cytomegalovirus (CMV) activation was determined by real time PCR. Acute allograft rejection was diagnosed histopathologically according to the ISHLT classification.
Results: 13% of our patients experienced an episode of acute rejection. Using independent sample T-Test we found a significantly lower monocyte count in patients with acute rejection in comparison to stable heart transplant recipients (0.379G/l vs 0.526G/l [normal range 0.1-0.8G/l] respectively $p=0.025$). We found no correlation between peripheral blood monocyte count, patient demographics, immunosuppressive drug regimen or CMV activation.
Conclusions: This is the first study in the literature to describe an association between circulating monocytes and acute rejection following heart transplantation. Our data is suggestive of a peripheral migration of monocytes to rejecting tissue (where the potential differentiation into macrophages would occur). This pilot study reveals a novel finding, implicating a role for monocytes in the acute rejection cascade, and may lead to a new focus in transplant immunology on this neglected cell type.

P129

Post-Transplant Donor Antigen-Specifc Antibody Modulation In HLA Antibody Incompatible (Ait) Renal Transplantation

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Introduction. Antibody removal is increasingly being used to overcome the barrier of a positive crossmatch in renal transplantation. With modern Luminex bead assays for HLA-specific antibody detection it is clear that complete removal of donor specific antibody (DSA) is difficult to achieve. DSA persistance can also be detected post transplant using these methods but its relevance to graft accomodation and function is unclear. We have sought to characterise DSA persistence and modulation in patients transplanted with pre-existing DSA.

Methods. In 30 AiT transplants there was no DSA response in 3 and follow-up was less than 3 months in a further 8. In the remaining 19 a DSA response was seen, peaking at a median of 12.5 days (range 2-30) post transplant. Antibody levels were measured as median fluorescence intensity (MFI) using a commercial bead assay. We defined modulation where an antibody declined to an MFI<1000.

Results. In all cases the post-transplant response involved an initial rise in all pretreatment specificities (DSA and 3rd party antibodies, TPA). 15/19 cases had HLA Class I DSA with persistence (> 3 months) observed in 6 of these and modulation in 9. This contrasts with persistence of Class I TPA in 9/15 patients. 10 patients had Class II DSA and these persisted in 5 patients, but were modulated by 3 months in a further 4. In the remaining case the HLA DRB1 DSA modulated while the DQ DSA persisted. In 11/12 patients Class II TPA persisted. The comparison between DSA and TPA reveals that antibody modulation is donor HLA driven and is most marked for DRB1 DSA (5/7 vs 1/10, p=0.018). In addition modulation is more marked for HLA A and B DSA compared with TPA (6/11 vs 2/10 and 6/8 vs 6/13, respectively, p=ns). Modulation of DQ and DP antibody, either DSA or TPA was not observed. For antibodies specific for the low expression DRB loci DRB3/4 there was also a low rate of modulation (1/3 DSA, 0/3 TPA).

Discussion. There are too few cases studied here to indicate if antibody persistence relates to graft failure. Rejection was diagnosed in 10/19 cases and in these we observed modulation of 13/20 DSAs compared with 6/18 DSAs in those that did not suffer rejection (p=0.052). The association of DSA persistence with no rejection is intriguing and may be relevent to the process of graft accomodation. Alternatively, the process of rejection or its treatment may intiate DSA modulation.

P130

Influence Of Single Nucleotide Polymorphisms On HLA Specific Antibody Production in Kidney Allograft Recipients

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The production of donor specific HLA antibodies post transplantation in renal allograft recipients is thought to play a role in the development of humoral rejection and ultimately graft failure. However, the production of such antibodies does not occur in all recipients, including those who have received mismatched donor kidneys. The mechanisms underlying this variation in immune responsiveness are not completely clear. Genetic factors, such as single nucleotide polymorphisms (SNPs) may be responsible, in part, to the propensity of some recipients to produce antibodies directed against their graft. The aim of this preliminary study was to investigate the influence of SNPs in the Class II Transactivator (CIITA; the master regulator of HLA class II gene expression) and Interleukin-6 (IL-6) genes on HLA specific antibody production in renal allograft recipients.
A cohort of 105 adult recipient and donor pairs, of primary renal transplants were genotyped using TaqMan® at the three SNPs of interest (CIITA rs3087456, rs4774; IL-6 rs1800795). Recipients had been monitored for HLA specific antibody production pre- and post transplantation. 31% of the recipients produced HLA specific antibodies post-transplantation, of which 91% of these produced donor specific HLA antibodies. Statistical analysis was performed using Chi Square and Fisher's Exact tests.
The recipient IL-6 rs1800795 CC genotype was significantly associated with a lack of HLA specific antibody production post transplantation ($P = 0.018$). The recipient CIITA SNP genotypes showed no significant association with HLA specific antibody production, although a trend was observed for the rs4774 CC genotype and a lack of antibody production. The donor CIITA rs4774 and IL-6 rs1800795 SNP genotypes were found to be significantly associated with HLA-DQ specific antibody production in the recipients ($P = 0.041$ and $P = 0.036$, respectively.) No association was observed between the SNP genotypes and graft outcome.
Further investigations in a larger cohort, un-sensitised prior to transplantation, is required to assess the role of CIITA and IL-6 genotyping as a predictor of immune responsiveness, as part of a patients pre-transplantation risk assessment.

P131

HLA-DP Specific Antibodies in a Group of Renal Transplant Recipients

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Introduction The detection of HLA-DP specific antibodies in renal transplant recipients has recently been reported (Qiu et al, 2005). Between September 1990 and December 2003, 1818 kidney alone transplants were carried out at our centre. 225 of these had zero mismatches at HLA-A, -B and -DR (0:0:0 transplants). 140 donor/recipient pairs were HLA-DP typed and formed the study group for the production of HLA-DP specific antibodies (DP abs).

Methods A pretransplant sample and a range of posttransplant serum samples for 127 of the 140 transplant recipients (81 primary, 46 re-transplants) were screened for HLA class II specific antibodies using the FlowPRA™ class II screening test (One Lambda, Inc.). 38 recipients with class II specific antibodies were tested for DP abs using FlowPRA™ DP-specific Single Antigen (SA) beads (One Lambda, Inc.).

Results 45 (35.4%) of 127 recipients tested were class II specific antibody positive. 26 of the 45 patients had received a DP mismatched transplant and were tested for DP abs. 4 of 26 patients had DP abs. All 4 had had more than one transplant. 2 of 4 had > 85% HLA antibody reactivity. In 3 of 4, DP abs were present pre- and post-0:0:0 transplant. 3 of the transplants are functioning and one has failed. For 1 of the 4, analysis of the SA bead results showed that antigens to which antibody had bound shared the epitope DEAV at the 6^{th} hypervariable region of the DP amino acid sequence, one antigen of which (DPB1*0101) was a DP mismatch from the 0:0:0 transplant. The two antigens to which there was no antibody binding (DPB1*0201 and DPB1*0401) both had the GGPM epitope. The recipient was DPB1*0401.

12 of the 45 class II specific antibody positive patients received no DP mismatches from their 0:0:0 transplant. 5 of 12 had DP abs. 3 of 5 had had more than one transplant and the remaining 2 were female with the possibility of pregnancy related sensitisation to DP.

Discussion DP abs have been found in sensitised patients, often those who have had more than one transplant. Testing for DP abs in sensitised patients, especially those who require a repeat transplant and selecting DP compatible recipients may avoid positive crossmatches.

Reference: J. Qiu, Cai J., Terasaki P., El-Awar and Lee J-H. 2005, *Transplantation,* **80**, 1511.

P132

Low levels of donor-specific and non-donor-specific HLA-specific antibodies of different IgG subclasses on transplant outcome

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Sensitised patients with preformed IgG anti-HLA antibodies have an increased risk of graft rejection. The novel xMap (Luminex™) technology for the detection of anti-HLA class I and class II is now available, and we have developed an IgG subclass-specific modification of this technique. The aim of this project was to evaluate the correlation between renal transplant outcome and the presence of pre-transplant anti-HLA IgG (total and subclass) detected using xMap technology on graft outcome and also to determine the impact of donor-specific (detected by xMap, but not complement-dependent-cytotoxicity (CDC) or flow cytometry (FCXM)) and non-donor-specific antibodies.We identified 39 sensitised renal transplant recipients (PRA > 30%) who had been transplanted with negative CDC and FXCM cross matches. To detect the presence of IgG class I- and class II-specific antibodies of both complement-fixing and non-complement-fixing subclasses of IgG, we reanalysed the same pre-transplant sera from these patients (a) on a panel of cells in a CDC assay and (b) using an xMap technology-based screening kit. As expected, given the raised PRA, all 39 samples had anti-HLA antibodies by both CDC and xMap. In the xMap screening assay, 19 samples had both anti-class I and anti-class II antibodies, 13 samples had anti-class I antibodies alone and 7 samples had anti-class II antibodies alone. We next analysed the 32 samples with anti-class I antibodies and the 26 samples with anti-class II antibodies for specificities using the xMap identification assay. This gave a higher yield of specificities than the CDC screening analysis. Of the 32 samples in which the xMap screening assay had determined anti-class I antibodies were present, we were able to define specificities in only 12 using the identification kit. The corresponding figure for the 26 samples in which the xMap screening assay identified anti-class II antibodies, the identification kit allowed us only to define specificities in 9. The xMap assays allowed us to distinguish between donor-specific and non-donor specific specificities. A higher proportion of those with acute rejection had donor-specific specificities (8 vs 4) than those who did not suffer acute rejection (12 vs 15). The subclass skewing of these antibodies appeared to be different for anti-class I and anti-class II in that the latter group was dominated by antibodies of IgG3 subclass. xMap technology is a more sensitive technique than flow cytometry and CDC in detecting low-level anti-HLA donor-specific antibodies which were present in pre-transplant patients' sera at the time of transplantation. In addition, the presence of donor-specific antibodies detected by xMap, but missed by CDC and flow cytometry against donor cells may have a significant effect on graft outcome.

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