Bootcongres 2011

wetenschappelijke voorjaarsvergadering

Nederlandse Transplantatie Vereniging

6 en 7 april 2011

i.s.m.

AMC en VUmc

Locatie:

Koninklijk Instituut voor de Tropen - Amsterdam

Inhoudsopgave

In het programma vindt u achter de titel van de voordracht een verwijzing naar de pagina waar u het betreffende abstract kunt vinden.

Welkom op het 23ste bootcongres!

Dit jaar legt de boot van de Nederlandse Transplantatie Vereniging aan in Amsterdam. Een stad die zijn rijkdom en schoonheid verwierf in verre streken, waarvan het Koninklijk instituut voor de Tropen een fraaie afspiegeling is.
Dit kennisinstituut werkt internationaal samen aan duurzame ontwikkeling, armoedebestrijding en diversiteit. Waar anders dan hier had de NTV boot kunnen afmeren.
Het congresprogramma volgt dit jaar de thema's waar het Tropeninstituut garant voor staat. In totaal 115 abstracts vanuit de meest diverse disciplines, zoals interne geneeskunde en chirurgie alsook immunologische, moleculair- en celbiologische richting zijn ingestuurd. We hebben de kans gehad om veel van dit enthousiasme te belonen: de meeste inzendingen met een voordracht en de minderheid met een poster.
De gastsprekers zijn eveneens uiterst gevarieerd: Op de eerste dag kruipen wij in het brein van de mensen die niet willen doneren; vervolgens leren we wat onder het tapijt van onze darmen huist, om dan via een naburige VOC stad weer terug te keren naar de potentiële krakers van het centraal zenuwstelsel. Aan het einde van de dag schepen we ons in om naar een plek te varen waar een multicultureel cohort kansarme jongeren ons culinair zal verwennen.
Het diner wordt muzikaal omlijst met wereldmuziek.
Op de tweede dag worden de touwtjes weer strak aangetrokken met een lezing over onze wettelijke rechten en plichten. Tussen de middag is de leden-vergadering van de NTV en sluiten we af met twee voordrachten waaruit blijkt hoeveel er nog te verbeteren valt.
In het kader van de armoedebestrijding worden er behalve diverse grote prijzen zoals de Gauke Kootstra prijs, ook een aanzienlijk aantal kleinere prijzen uitgereikt: na elke sessie een prijs voor de beste spreker, en ook een prijs voor de beste poster.

Wij wensen u goede en behouden vaart!

Frederike Bemelman,
Voorzitter lokaal organisatiecomité

Organisatiecommissie Bootcongres 2011:

F.J. Bemelman
R.J.M. ten Berge
K.A. Donselaar

F.J. van Ittersum
S.A. Nurmohamed

N.M. Lardy

Vanuit het secretariaat NTV te Haarlem
Jeanine Gies
Marie José van Gijtenbeek
Marja Weber

Accreditatie is toegekend door de volgende verenigingen

Nederlandse Vereniging voor Heelkunde	12 punten
Nederlandse Vereniging voor Immunologie	12 punten
Nederlandse Vereniging van Maag-Darm-Leverartsen	12 punten
Nederlandsche Internisten Vereeniging	12 punten
Nederlandse Vereniging voor Kindergeneeskunde	in behandeling

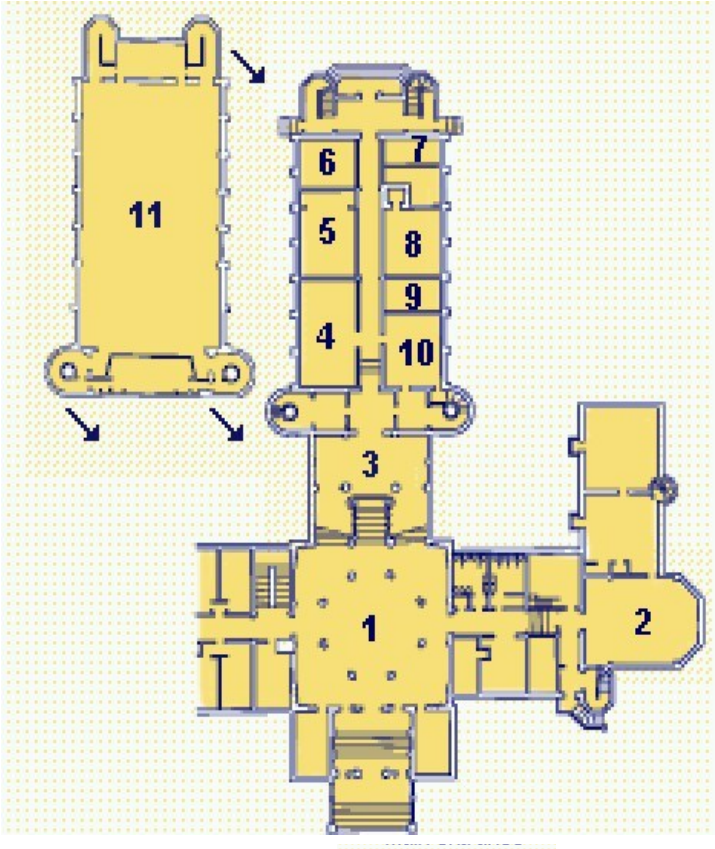
Op individuele basis kan accreditatie worden aangevraagd bij:

Nederlandse Vereniging van Artsen voor Longziekten en Tuberculose

Nederlandse Vereniging voor Cardiologie

Koninklijk Instituut voor de Tropen
Mauritskade 63,
1092 AD Amsterdam
www.kit.nl

FLOOR PLAN KIT



1. Marmeren Hal
2. Mauritszaal
3. Onder de Bogen
4. Raadzaal
5. Bestuurskamer
6. Regentenkamer
7. Wilhelminazaal
8. Emmazaal
9. Antichambre
10. Clauszaal
11. Grote Zaal
12. Kleine Zaal

Locatie en tijdstippen van de maaltijden

Woensdag

Ontbijt woensdag in de diverse hotels	07.00 - 09.30 uur
Lunch KIT – marmeren hal	12.30 - 14.00 uur
Lunch onderwijssessie Mauritszaal (lunchpakket)	12.30 - 14.00 uur
Congresborrel aan boord van de salonboten	18.30 - 19.30 uur
Diner en feest Restaurant Fifteen, Amsterdam	19.45 - 00.30 uur

Donderdag

Ontbijt donderdag in de diverse hotels	07.00 - 08.30 uur
Lunch KIT- marmeren hal	12.30 - 13.30 uur

Bijeenkomsten tijdens Bootcongres

Dinsdag 5 april 2011

17.00 – 19.30	Landelijk Overleg Levertransplantatie *Locatie: Arenahotel*
17.00 – 19.30	Landelijk Overleg Niertransplantatie *Locatie: Arenahotel*
17.00 – 19.30	Landelijke Werkgroep Transplantatie Verpleegkunde *Locatie: Indonesiëzaal NH Tropenhotel*

Woensdag 6 april 2011

08.00 – 10.00 uur	Transplantatie Werkgroep Nederland *Locatie: Bestuurskamer Koninklijk Instituut voor de Tropen*
12.30 – 14.00 uur	Landelijk Overleg Transplantatie Thoracale Organen *Locatie: Bestuurskamer Koninklijk Instituut voor de Tropen*

Schematisch overzicht programma
woensdag 6 april 2011

Woensdag 6 april 2011		**Grote zaal**	**Mauritszaal**	**Raadszaal**
08.00 – 10.00	Vergadering TWN			
10.00 – 11.25		Opening congres door F.J. Bemelman Lezing gastspreker V.A.F. Lamme, AMC, Amsterdam		
		Plenaire sessie I		
11.25 – 11.45	Koffiepauze			
11.45 – 12.35		Plenaire sessie II Lezing gastspreker N. v.d. Kar, gevolgd door vrije voordrachten		
12.40 – 13.50	Lunchbuffet + postersessie		Onderwijssessie	
14.00 – 16.00		Parallelsessie III – Klinisch	Parallelsessie III - Basaal	Parallelsessie III – Verpleegk./Donatie
16.00 – 16.25	Theepauze			
16.25 – 18.10		Plenaire sessie IV Lezingen gastsprekers: E.E.S. Nieuwenhuis, UMC Utrecht D. van de Beek, AMC Amsterdam M.H.H. Raasveld, Westfries Gasthuis Lezing winnaar ATRP 2010		
18.10 – 18.30		Uitreiking prijzen: Novartis Transplantation Grant 2011 Uitreiking ATRP 2011 Uitreiking Gauke Kootstraprijs 2011		
18.30 – 18.45 19.45 – 01.00	Gasten aan boord, borrel Novartis Dinerbuffet en feestavond Fifteen			

Schematisch overzicht programma
donderdag 7 april 2011

Donderdag 7 april 2011		**Grote zaal**	**Mauritszaal**	**Raadszaal**
08.30 – 10.00		Plenaire sessie V- voordrachten Gastspreker: J.J.A. van Boven, gezondheidsjuriste		
10.00 – 10.30	Koffiepauze			
10.30 – 12.30		Parallelsessie VI – Klinisch	Parallelsessie VI – Basaal	Parallelsessie VI – Verpleegk./Donatie
12.30 – 13.30	Lunchpauze + postersessie			
13.30 – 14.30		**Ledenvergadering NTV**		
14.30 – 15.30		Plenaire sessie VII		
15.30 – 16.00	Theepauze			
16.00 – 17.00		Plenaire sessie VIII Lezingen gastsprekers: J. Groothoff, Emma Kinderziekenhuis: "Niet-westerse kinderen in Nederland en België: langer op de wachtlijst en meer kans op afstoting" R.J. Ploeg, UMC Groningen: "Strategieën ter verbetering van de kwaliteit van het donor orgaan"		
		Afsluiting door LOC 10 min.		
17.00 – 18.00	Vertrek congresdeelnemers			

Sessie I - plenair **Grote zaal**

09.00 Ontvangst en registratie

10.00 Opening F.J. Bemelman, voorzitter lokaal organisatiecomité Amsterdam

10.05 **De vrije wil bestaat niet**
Wat is er mis met de marketing van donorschap?
Prof. dr. V.A.F. Lamme
hoogleraar cognitieve neurowetenschap
Afdeling Psychologie, Universiteit van Amsterdam

Voordrachten in het Nederlands, spreektijd 7 minuten, discussietijd 3 minuten.

Voorzitters: S.A. Nurmohamed en R. de Weger

10.45 Pediatric kidney transplantation in the Netherlands: CMV prophylaxis up to revision? (p. 47)
H. Jongsma[1], A.H. Bouts[2], E.A.M. Cornelissen[3], M.R. Lilien[4], M. Beersma[5], K. Cransberg[1], Dept. of Pediatric Nephrology, [1]Erasmus Medical Centre, Sophia Children's Hospital, Rotterdam, [2]Emma Children's Hospital, Academic Medical Centre, Amsterdam, [3]University Medical Centre St. Radboud, Nijmegen, [4]Wilhelmina Children's Hospital, University Medical Centre, Utrecht, [5]Dept. of Virology, Erasmus Medical Centre, Rotterdam, The Netherlands

10.55 A Dutch multi-center study on the decision-making process of families requested for organ and/or tissue donation (p. 48)
N.E. Jansen[1], H.A. van Leiden[1], B.J.J.M. Haase-Kromwijk[1], Nardo J.M. van der Meer[2], Edwin Vorstius Kruijff[2], Netty van der Lely[3], Hans van Zon[3], Arend-Jan Meinders[4], Machteld Mosselman[4], A.J. Hoitsma[5], [1]Dutch Transplant Foundation Leiden, [2]Dept. of Intensive Care, Amphia Hospital Breda, [3]Dept. of Intensive Care, Sint Elisabeth Hospital Tilburg, [4]Dept. of Intensive Care, Sint Antonius Hospital Nieuwegein, [5]Dept. of Nephrology, University Medical Centre Nijmegen, The Netherlands

Sessie I - plenair vervolg **Grote zaal**

11.05 Excessive premature ageing of T lymphocytes in end-stage renal disease: an important factor to consider in pre-transplant immunological risk assessment (p. 49)
N.H. Litjens[1], E.A. de Wit[1], A. Langerak[2], A. van de Spek[2], W. Weimar[3] and M.G. Betjes[1], Depts. of [1]Nephrology, [2]Immunology and [3]Transplantation, Erasmus Medical Centre, Rotterdam, The Netherlands

11.15 Hand-Assisted Retroperitoneoscopic versus Standard Laparoscopic Donor Nephrectomy: Single Blind, Randomised Controlled Trial (p. 50)
L.F.C. Dols[1], N.F.M. Kok[1], T.C.K. Tran[1], T. Terkivatan[1], F.C.H. d'Ancona[2], J.F. Langenhuijsen[2], F.J.M.F. Dor[1], W. Weimar[3], J.N.M. IJzermans[1], [1]Dept. of Surgery, Erasmus Medical Centre, Rotterdam, [2]Dept. of Urology, Radboud University Nijmegen, [3]Dept. of Internal Medicine, Erasmus Medical Centre, Rotterdam, The Netherlands

11.25 Koffiepauze

Sessie II - plenair **Grote zaal**

Voorzitters: S.P. Berger en C. van Kooten

11.45 **Nieuwe inzichten in de behandeling van patiënten met atypische vorm van Hemolytisch Uremisch Syndroom (aHUS)**
N. van de Kar, kindernefroloog,
afdeling kindernefrologie, UMC St. Radboud, Nijmegen

12.05 Meningococcal polysaccharide vaccine fails to protect a renal transplant recipient receiving eculizumab from developing meningococcal disease (p. 51)
G.H. Struijk[1], A.H.M. Bouts[2], G.T. Rijkers[3], E.A.C. Kuin[1], H.L. Zaaijer[4], I.J.M. ten Berge[1], F.J. Bemelman[1], [1]Renal Transplant Unit, Dept. of Nephrology, Div. of Internal Medicine, [2]Dept. of Paediatric Nephrology, Academic Medical Centre, Amsterdam, [3]Dept. of Medical Microbiology and Immunology, St. Antonius Hospital, Nieuwegein, [4]Dept. of Virology, Academic Medical Centre, Amsterdam, The Netherlands

12.15 Prophylactic plasmapheresis (PE) and eculizumab (EC) allow long term renal function preservation in *FH* mutation related atypical haemolytic uremic syndrome (aHUS) (p. 52)
J-C. Davin[1,2], J.W. Groothoff[1], F.J. Bemelman,[3,]A.H. Bouts[1]. [1]Pediatric Nephrology, Emma Children's Hospital / Academic Medical Centre, Amsterdam Z-O, Netherlands; [2]Pediatric Nephrology, Queen Fabiola Academic Children's Hospital/ULB, Brussels, Belgium, and [3]Nephrology, Academic Medical Centre, Amsterdam Z-O, Netherlands.

12.25 CD46-associated atypical HUS with uncommon course caused by mutations in the cblC MMACHC gene (p. 53)
A.H.M. Bouts[1], G.S. Salomons[2], B.Straver[3], V. Gracchi[1], J.W. Groothoff[1], J.C. Davin[1], [1]Dept. of Pediatric Nephrology, [3]Dept. of Pediatric Cardiology, Emma Children's Hospital, Academic Medical Centre, Amsterdam, [2]Department of Clinical Chemistry, Metabolic Unit, VU Medical Centre, Amsterdam, The Netherlands

12.35 Einde sessie II, lunchpauze en postersessie

Onderwijssessie **Mauritszaal**

12.40 Lunchpakket bij ingang van de zaal
voor alle **geregistreerde** deelnemers aan de onderwijssessie

Voorzitters: J. Vervelde en M. Wessels

12.45 "Eurotransplant als verbinder van donor en ontvanger - De principes van orgaanallocatie door ET".
Dr. A. Rahmel, medical director Eurotransplant

13.10 Alles wat u altijd al over antilichamen heeft willen weten
Dr. D.L. Roelen, immunoloog,
Afd. immunohematologie & bloedtransfusie, Leids Universitair Medisch Centrum

13.35 Nierdonatie bij leven: welke programma's maken het mogelijk?
Dr. J.I. Roodnat, internist-nefroloog
Afd. nefrologie-niertransplantatie, Erasmus MC, Rotterdam

14.00 Einde onderwijssessie

Parallelsessie III - klinisch — Grote zaal

Voordrachten in het Nederlands, spreektijd 7 minuten, discussietijd 3 minuten.

Voorzitters: K.A. van Donselaar en A. Hoksbergen

14.00 Vaccine Induced Allo-HLA reactive Memory T-cells in a Kidney Transplantation Candidate (p. 54)

E.M.W. van der Meer-Prins[1], N.M. van Besouw[2], L.J.A. D'Orsogna[1], P. van der Pol[3], M. Franke-van Dijk[1], Y. M. Zoet[1], A. van der Slik[1], W. Weimar[2], C. van Kooten[3], A. Mulder[1], D. L. Roelen[1], I. I.N. Doxiadis[1], F.H.J. Claas[1], [1]Dept. of Immunohaematology and Blood Transfusion, Leiden University Medical Centre, [2]Dept. of Internal Medicine, Erasmus Medical Centre, Rotterdam, [3]Dept. of Nephrology, Leiden University Medical Centre, The Netherlands

14.10 A randomized, prospective, open-label, multicenter study comparing the efficacy and safety of conversion to Sirolimus in stable renal transplant recipients with cutaneous squamous cell carcinoma (p. 55)

J.M. Hoogendijk-van den Akker[1], J.N. Bouwes-Bavinck[2], J.W.de Fijter[3], P.N. Harden[4], A.J. Hoitsma[5], [1]Dept. of Internal Medicine, Isala Clinics Zwolle, [2]Dept. of Dermatology, Leiden University Medical Center, [3]Dept. of Nephrology, Leiden University Medical Centre, [4]Dept. of Nephrology, Churchill Hospital Oxford, United Kingdom, [5]Dept. of Nephrology, Radboud University Nijmegen Medical Centre, The Netherlands. (On behave of the members of the RESCUE study group)

14.20 A single intra-operative high-dose of anti-T-lymphocyte immune-globulin in DCD donor renal allograft recipients: randomized, open, multicenter study on efficacy and safety to prevent delayed graft function (p. 56)

M.W.F. van den Hoogen[1], A.D. van Zuilen[2], J.J. Homan van der Heide[3], M.M.L. Kho[4] W. Weimar[4], L.H. Hilbrands[1], A.J. Hoitsma[1], [1]Dept. of Nephrology, Radboud University Nijmegen Medical Centre, [2]Dept. of Nephrology, University Medical Centre Utrecht, [3]Dept. of Nephrology, University Medical Centre Groningen, [4]Dept. of Nephrology, Erasmus Medical Centre Rotterdam, The Netherlands

Parallelsessie III - klinisch - vervolg **Grote zaal**

14.30 Survival prognosis of patients starting renal replacement therapy in the Netherlands (p. 57)
A.C. Hemke[1], M.B.A. Heemskerk[1], B.J.J.M. Haase-Kromwijk[1], W. Weimar[2], A.J. Hoitsma[1,3], [1]Dutch Transplant Foundation, Leiden, [2]Erasmus Medical Centre, Rotterdam, [3]Radboud University Medical Centre, Nijmegen, The Netherlands

14.40 Interstitial pneumonitis caused by everolimus: a case control study (p. 58)
M.C. Baas[1], G.H. Struijk[1], D.J. Moes[4], I.A.H. van den Berk[2], R.E. Jonkers[3], J.W. de Fijter[5], J.J. Homan van der Heide[6], I.J.M. ten Berge[1], F.J. Bemelman[1], [1]Renal Transplant Unit, [2]Dept. of Radiology; [3]Dept. of Pulmonology, Academic Medical Centre, Amsterdam, [4]Dept. of Clinical Pharmacy and Toxicology, [5]Dept. of Nephrology, Leiden University Medical Centre, [6]Renal Transplant Unit, Groningen University Hospital, The Netherlands

14.50 What to do with a failed renal allograft:Take it or leave it? (p. 59)
D.G.M. Gommers, L.B. Hilbrands, Dept. of Nephrology, Radboud University Nijmegen Medical Centre, The Netherlands

15.00 Identification of Patients at High Risk for Infections after Liver Transplantation (p. 60)
S.H. van Olphen[1], I.C.A.W. Konings[1], L.H. de Grim[2], G. Kazemier[3], B.E. Hansen[1], R.A. de Man[1], X. Rogiers[2], C.A.M. Schurink[4] and H.J. Metselaar[1], [1]Dept. of Gastroenterology and Hepatology, Erasmus University Medical Centre Rotterdam, [2]Dept. of Liver Transplantation, University Hospital Ghent, Belgium, [3]Depst. of Surgery, [4]Dept. of Medical Microbiology and Infectious Diseases, Erasmus University Medical Centre, Rotterdam, The Netherlands

15.10 Hypertensive kidney donors perform well at short term post-donation follow-up (p. 61)
H. Tent[1], E. van den Berg[1], H.S. Hofker[2], R.J. Ploeg[2], G.J. Navis[1], J.J. Homan van der Heide[1], [1]Dept. of Internal Medicine Division of Nephrology and [2]Dept. of Surgery, University Medical Centre Groningen, The Netherlands

Parallelsessie III - klinisch - vervolg **Grote zaal**

15.20 The effect of ritonavir on pharmacokinetics of tacrolimus in pre-transplant kidney failure patients with HIV (p. 62)
H.A. Crommelin[1], A.D. van Zuilen[2], T. Mudrikova[3], M.P.H. van den Broek[1], E.M. van Maarseveen[1], [1]Dept. of Clinical Pharmacy, [2]Dept. of Nephrology and Hypertension, [3]Dept. of Internal Medicine and Infectious Diseases, University Medical Centre Utrecht, The Netherlands

15.30 Effect of routinely inserted gentamycin-containing collagen sponges on surgical site infections after hand-assisted laparoscopic donor nephrectomy (p. 63)
V. P. Alberts[1], R.C. Minnee[1], F.J. Bemelman[2], K.A.M.I. van Donselaar – van der Pant[2], M.M. Idu[1], [1]Dept. of Surgery, [2]Renal Transplant Unit, Department of Nephrology, Academic Medical Centre, Amsterdam, The Netherlands

15.40 The effect of rituximab infusion on cytokine levels in renal transplant patients (p. 64)
M.W.F. van den Hoogen, J.W. Dieker, J. van der Vlag, L.B. Hilbrands, Dept. of Nephrology, Radboud University Nijmegen Medical Centre, The Netherlands

15.50 Characterization of urinary T-cells in kidney transplantation patients with polyomavirus associated nephropathy or allograft rejection (p. 65)
W.B. van Doesum, W.H. Abdulahad, W.J. van Son, C.A. Stegeman, J.S. Sanders, Dept. of Nephrology, University Medical Centre Groningen, The Netherlands

16.00 Theepauze

Parallelsessie III – basaal **Mauritszaal**

Voordrachten in het Nederlands, spreektijd 7 minuten, discussietijd 3 minuten

Voorzitters: L. Hilbrands en I. Joosten

14.00 The role of graft-resident hematopoietic progenitor cells in intragraft leukocyte chimerism after liver transplantation (p. 66)
V. Moroso[1], Q. Pan[1], F. Famili[1], T. Cupedo[2], G. Kazemier[3], H.W. Tilanus[3], H.L.A. Janssen[1], H.J. Metselaar[1], L.J.W. van der Laan[3] and J. Kwekkeboom[1], Depts. of [1]Gastroenterology and Hepatology, [2]Hematology and [3]Surgery and Laboratory of Experimental Transplantation and Intestinal Surgery, Erasmus Medical Centre, Rotterdam, The Netherlands

14.10 Living Mesenchymal Stem Cells Disappear Rapidly after Intravenous Infusion (p. 67)
M.J. Hoogduijn[1], E. Eggenhofer[2], F.C. Popp[2], P. Renner[2], W. Weimar[1], C.C. Baan[1], M.H. Dahlke[2], [1]Dept. of Internal Medicine, Erasmus Medical Centre, Rotterdam, The Netherlands, [2]Dept. of Surgery, University Medical Centre Regensburg, Regensburg, Germany

14.20 Spontaneous tumorigenic transformation of mesenchymal stem cells caution clinical application (p. 68)
Q. Pan[1], S.M.G. Fouraschen[2], J. de Jonge[2], G. Kazemier[2], J. Kwekkeboom[1], H.J. Metselaar[1], H.W. Tilanus[2], H.L.A. Janssen[1], L.J.W. van der Laan[2], Depts. of [1]Gastroenterology and Hepatology and [3]Surgery and Laboratory of Experimental Transplantation and Intestinal Surgery, Erasmus Medical Centre, Rotterdam, The Netherlands

14.30 Mannose-binding lectin induces tubular epithelial cell death following renal ischemia reperfusion injury independent of complement activation (p. 69)
P. van der Pol[1], N. Schlagwein[1], D.J. van Gijlswijk[1], I.M. Bajema[2], M.R. Daha[1], C. van Kooten[1], Depts. of [1]Nephrology and [2]Pathology, Leiden University Medical Centre, The Netherlands

Parallelsessie III – basaal - vervolg **Mauritszaal**

14.40 IL-2-independent induction of novel CD4+CD25+CD127-FOXP3+ T cells by mesenchymal stem cells and natural regulatory T cells (p. 70)
A.U. Grohnert, M.J. Hoogduijn, W. Weimar, C.C. Baan, Dept. of Internal Medicine, Erasmus Medical Centre, Rotterdam, The Netherlands

14.50 Expression of dsRNA sensors in the renal transplant is increased during cytomegalovirus, Epstein-Barr virus and BK virus infection (p. 71)
K.M. Heutinck[1,2], J. Kassies[1,2], N. Claessen[3], K.A.M.I. van Donselaar-van der Pant[2], F.J. Bemelman[2], S. Florquin[3], J. Hamann[1], I.J.M. ten Berge[2], [1]Dept. of Experimental Immunology, [2]Renal Transplant Unit, Dept. of Internal Medicine and [3]Dept. of Pathology, Academic Medical Centre, Amsterdam, The Netherlands

15.00 Induction of VZV-specific effector memory T-cell response by herpes zoster infection after lung transplantation (p. 72)
N.M. van Besouw[1], P.Th.W. van Hal[3], G.M.G.M. Verjans[2], J.M. Zuijderwijk[1], W. Weimar[1], Depts. of [1]Internal Medicine – Transplantation, [2]Virology, [3]Respiratory Medicine, Erasmus Medical Centre, Rotterdam, The Netherlands

15.10 ABCB1 expressing memory CD8+ T cells; a new memory CD8+ T cell subset? (p. 73)
S.H.C. Havenith[1,2], S.L. Yong[1,2], B. Piet[2], S.D. Koch[1,2], R.A.W. van Lier[2], R.J.M. ten Berge[1], [1]Renal Transplant Unit, Dept. of Internal Medicine and [2]Dept. of Experimental Immunology, Academic Medical Centre, Amsterdam, The Netherlands

15.20 Viability of the human small bowel graft in the scope of intestinal transplantation (ITx) (p. 74)
A.M. Roskott[1], H.G.D. Leuvenink[1], G. Dijkstra[2], R.J. Ploeg[1], H. v. Goor[3], V.B. Nieuwenhuijs[1], Depts. of [1]Surgery, [2]Gastroenterology and Hepatology and [3]Pathology, Groningen University Medical Centre, Groningen, The Netherlands

Parallelsessie III – basaal - vervolg **Mauritszaal**

15.30 Adverse effects of mTOR inhibition on liver regeneration (p. 75)
S.M.G. Fouraschen[1], J. de Jonge[1], P.E. de Ruiter[1], G. Kazemier[1], R.W.F. de Bruin[1], H.J. Metselaar[2], J. Kwekkeboom[2], H.W. Tilanus[1] and L.J.W. van der Laan[1], Depts. of [1]Surgery and Laboratory of Experimental Transplantation and Intestinal Surgery and [2]Gastroenterology & Hepatology, Erasmus Medical Centre, University Medical Centre Rotterdam, The Netherlands

15.40 Functional paralysis of CD8 memory T Cells in rATG treated kidney transplant patients (p. 76)
A.P. Bouvy[1], M.M.L Kho[1], M. Klepper[1], J.N.M. IJzermans[2], W. Weimar[1], C.C. Baan[1], Depts. of [1]Internal Medicine and [2]Surgery, Erasmus Medical Centre, University Medical Centre Rotterdam, The Netherlands

15.50 Dexamethasone increases ROS production and T cell suppressive capacity by anti-inflammatory macrophages (p. 77)
M.D. Kraaij, S.W. van der Kooij, M.E.J. Reinders, K. Koekkoek, A.J. Rabelink, C. van Kooten, K.A. Gelderman, Dept. of Nephrology, Leiden University Medical Centre, The Netherlands

16.00 Theepauze

Parallelsessie III – Transplantatieverpleegkunde / Donatie Raadszaal

Voordrachten in het Nederlands, spreektijd 10 minuten, discussietijd 5 minuten.

Voorzitters: B. Hepkema en R.J. Ploeg

14.00 Renovascular resistance of machine perfused DCD kidneys is associated with primary non-function (p. 78)
E.E. de Vries[1], E.R.P. Hoogland[1], B. Winkens[2], M.G. Snoeijs[1], L.W.E. van Heurn[1], [1]Dept. of General Surgery, [2]Department of Methodology and Statistics, Maastricht University Medical Centre, The Netherlands

14.15 Long term postoperative complaints recorded after donation in 509 living kidney donors in a single centre (p. 79)
F. van de Logt[1], H.J. Kloke[1], J.F. Langenhuijsen[2], F.C.H. D'Ancona[2], J.A. van der Vliet[3], Ph.M.M. Dooper[1], A.J. Hoitsma[1], [1]Dept. of Nephrology, [2]Dept. of Urology, [3]Dept. of Surgery, Radboud University Nijmegen Medical Centre, The Netherlands

14.30 Living donor exchange remains the main solution for incompatible couples by its direct and indirect effects (p. 80)
M. de Klerk, for the 8 kidney transplant centers, Dutch Transplant Foundation and National Reference Laboratory for Histocompatibility

14.45 Validation of the Donor Risk Index (DRI) in orthotopic liver transplantation within the Eurotransplant region (p. 81)
J.J. Blok[1], J. Ringers[1], R. Adam[2], A.K. Burroughs[3], N.G. Kooreman[1], J. Dubbeld[1], H. Putter[4], A.O. Rahmel[5], R.J. Porte[6], X. Rogiers[7], A.E. Braat[1], [1]Dept. of Surgery, [4]Dept. of Medical Statistics, Leiden University Medical Centre, [2]Centre Hépato-Biliaire, Hôpital Paul Brousse, Villejuif, France, [3]Liver Transplantation and Hepatobiliary Medicine, Royal Free Hospital, London, United Kingdom, [5]Eurotransplant Int. Foundation, Leiden, [6]Dept. of Surgery, University Medical Centre Groningen, [7]Dept. of Surgery, Ghent University Hospital Medical School, Belgium

Parallelsessie III – Transplantatieverpleegkunde / Donatie Raadszaal

15.00 Living kidney donation among ethnic minorities: a Dutch qualitative study on attitudes, communication and knowledge of kidney patients (p. 82)
S.Y. Ismail[1], L. Claassens[1], E.K. Massey[2], A.E. Luchtenburg[2], W. Weimar[2], J.J. Busschbach[1], Depts. of [1]Medical Psychology and Psychotherapy and [2]Internal Medicine, Erasmus Medical Centre, Rotterdam, The Netherlands

15.15 The influence of ethnicity on re-hospitalization and complications after kidney transplantation (p. 83)
L. Maasdam[1], E.K. Massey[1], M.M.L. Kho[1], J.N.M. IJzermans[2], W. Weimar[1], Depts. of [1]Internal Medicine and [2]General Surgery, Erasmus Medical Centre Rotterdam, The Netherlands

15.30 Psychosociale screening bij partnerniertransplantatie (p. 84)
E.C.M. Berendsen, T. Winkel, A. D. van Zuilen, F. E. van Reekum. Dept. of Nephrology, University Hospital Utrecht, The Netherlands

15.45 Transitie; zelfmanagement en zelfredzaamheid bij jongeren met een donornier (p. 85)
J.L. Knoll[1], M. van Helden[2], R. Scholten[1], E.A.M. Cornelissen[1], I. Dooper[2], E. Ensink[1], S. van Duin[2], G. Reuhl[1], [1]Dept. of pediatric nephrology, [2]Dept. of nephrology, Radboud University Nijmegen Medical Centre, The Netherlands

16.00 Theepauze

Sessie IV - plenair — Grote zaal

Voorzitters: F.J. Bemelman en S.A. Nurmohamed

16.25 **Darmstamceltransplantatie: een nieuw tapijt**
Prof. dr. E.E.S. Nieuwenhuis, Afd. Kindergeneeskunde
UMC Utrecht

17.00 **Central nervous system infections in transplant recipients**
Dr. D. van de Beek, Afdeling Neurologie,
Academisch Medisch Centrum, Amsterdam

17.35 **Lange termijn zorg na niertransplantatie in de periferie: van stiefkind naar speerpunt**
Dr. M.H.H. Raasveld, Afdeling Interne Geneeskunde,
Westfries Gasthuis

17.55 **Lezing ATRP-winnaar 2010:**
Viability of the intestinal graft within the scope of Intestinal Transplantation
A.M.C. Roskott, Afd. Chirurgie - orgaandonatie en transplantatie UMCG

Prijsuitreikingen — Grote zaal

18.05 Uitreiking van Novartis Transplantation Grant 2011

Uitreiking Astellas Trans(p)la(n)t(at)ionele Research Prize 2011

18.10 Uitreiking Gauke Kootstraprijs 2011,
gevolgd door voordracht door de prijswinnaar

Sociaal programma

18.25 Inschepen voor vertrek naar locatie diner
Congresborrel aan boord aangeboden door Novartis

19.30 Diner en feestavond

Plenaire sessie V — Grote Zaal

Voorzitters: F.J. Bemelman en F.E. van Reekum

Voordrachten in het Nederlands, spreektijd 7 minuten, discussietijd 3 minuten.

08.30 Development of new onset diabetes after lung transplantation in patients with cystic fibrosis compared with patients suffering from other lung diseases (p. 86)
G. van Meerkerk[1,2], E.A. van de Graaf[1], J.W.J. Lammers[1], D.H. Biesma[2], H.W. de Valk[2], Depts. of [1]Respiratory Medicine and [2]Internal Medicine, University Medical Centre Utrecht, The Netherlands

08.40 Dysbalance of angiopoietins and a decrease in pericytes in a rat model of renal ischemia reperfusion injury (p. 87)
M. Khairoun[1], P. van der Pol[1], E. Lievers[1], N. Schlagwein[1], H.C. de Boer[1], D.K. de Vries[3], A. J. van Zonneveld[1,2], T.J. Rabelink[1,2], C. van Kooten[1], M.E.J. Reinders[1], [1]Dept. of Nephrology, [2]Einthoven Laboratory for Experimental Vascular Research, [3]Dept. of Surgery, Leiden University Medical Centre, The Netherlands

08.50 High Throughput Sequencing of hCMV-pp65 reactive CD8-clones formed during primary infection and subsequent reactivation (p. 88)
E.B.M. Remmerswaal[1,2], P.L. Klarenbeek[3], S. Koch[1,2], M.E. Doorenspleet[3], B.D.C. van Schaik[4], K. van Donselaar[2], F. Bemelman[2], R.E.E. Esveldt[3], A.H. van Kampen[4], F. Baas[5], A. ten Brinke[6], R.A.W. van Lier[1], N. de Vries[3], I.J.M. ten Berge[2], [1]Dept. of Exp Immunology, [2]Renal Transplant Unit, Dept. of Nephrology, Div of Int Medicine, [3]Dept. of Clin Immunology and Rheumatology, [4]Dept. of Clin Epidemiology, Biostatistics and Bioinformatics, [5]Dept. of Genome Analysis, [6]Sanquin Research, Dept. of Immunopathology, Academic Medical Centre, Amsterdam, The Netherlands

09.00 Who benefits from alternative living kidney donation programs? (p. 89)
J.I. Roodnat, J. Wetering, J.A. Kal van Gestel, M. de Klerk, W. Zuidema, J.N.M. IJzermans, M. van Agteren, W. Weimar, Dept. of Internal Medicine and General Surgery, Erasmus Medical Centre, Rotterdam, The Netherlands

Plenaire sessie V – vervolg **Grote Zaal**

09.10 Adenosine and renal dendritic cells; integration of tissue integrity, danger signals and immune regulatory processes (p. 90)
C. van Kooten, S. Kamerling, M. Reinders, Dept. of Nephrology, Leiden University Medical Centre, The Netherlands

09.20 Anatomical suitability of the iliac fossa for implantation of living donor kidneys with a short renal vein (p. 91)
J. Hellegering[1], R. van Es[2], H.J. Kloke[3], F.C.H. D'Ancona[4], A.J. Hoitsma[3], J.A. van der Vliet[1], L.J. Schultze Kool[2], M.C. Warlé[1], [1]Dept. of Surgery, Division of Vascular- and Transplant Surgery, [2]Dept. of Radiology, [3]Dept. of Nephrology, [4]Dept. of Urology, Radboud University Nijmegen Medical Centre, The Netherlands

09.30 **De hoofdbehandelaar en het protocol**
mr. J.J.A. van Boven, gezondheidsjuriste
directeur juridisch adviesbureau voor de gezondheidszorg

10.00 Koffiepauze

Parallelsessie VI - Klinisch **Grote zaal**

Voordrachten in het Nederlands, spreektijd 7 minuten, discussietijd 3 minuten.

Voorzitters: M.H.L. Christiaans en M.M. Idu

10.30 Case report: successful lung transplantation with a positive cross match due to HLA class II antibodies (p. 92)
B.G. Hepkema[1], I. Bouwman[1], T. Jongsma[1], C. Roozendaal[1], L. Bungener[1], G. Nossent[2], E. Verschuuren[2], W. van der Bij[2], M. Erasmus[3], S.P.M. Lems[1], [1]Transplantation Immunology, Dept. of Laboratory Medicine, [2]Lung transplantation, Dept. of Internal medicine, [3]Dept. of Cardiothoracic Surgery, University Medical Centre Groningen, The Netherlands

10.40 Long term follow-up of overweight and obese living kidney donors (p. 93)
H. Tent[1], M. Rook[1], H.S. Hofker[2], R.J. Ploeg [2], G.J. Navis[1], J.J. Homan van der Heide[1], Depts. of [1]Internal Medicine Division of Nephrology and [2]Surgery, University Medical Centre Groningen, The Netherlands

10.50 The natural course of donor chimerism including the NK-cell fraction after liver transplantation: a prospective study (p. 94)
R.C. Verdonk[1], E.B. Haagsma[1], T. Jongsma [2], R.J. Porte[3], C. Roozendaal[2], A.P. v.d. Berg[1], B.G. Hepkema[2], [1]Dept. of Gastroenterology and Hepatology, [2]Dept. of Laboratory Medicine, [3]Dept. of Surgery, Section of Hepatobiliary Surgery and Liver Transplantation, University Medical Centre Groningen, The Netherlands

11.00 Adiponectin paradox in renal transplant recipients (p. 95)
L.V. de Vries, J.J. Homan van der Heide, W.J. van Son, R.T. Gansevoort, G.J. Navis, R.O.B. Gans, S.J.L. Bakker, Dept. of Internal Medicine, University Medical Centre Groningen, The Netherlands

11.10 Improvement of microvascular tortuosity after combined kidney-pancreas transplantation (p. 96)
M. Khairoun[1], R.N. de Boer[1], J.I. Rotmans[1], B.M van den Berg[1], D.K. de Vries[2], H.C. de Boer[1], E. Lievers[1], A.J. van Zonneveld[1,3], E.J. de Koning[1], J.W. de Fijter[1], T.J. Rabelink[1,3], M.E.J. Reinders[1], [1]Dept. of Nephrology, [2]Dept. of Surgery, [3]Einthoven Laboratory for Experimental Vascular Research, Leiden University Medical Centre, The Netherlands

Parallelsessie VI - Klinisch - vervolg **Grote zaal**

11.20 Risk of infectious complications after renal transplantation; awareness and attitude of renal transplant recipients (p. 97)
G.H. Struijk[1], R. Brinkman[1], M. van Vugt[2], I.J.M. ten Berge[1], F.J. Bemelman[1], [1]Renal Transplant Unit, Dept. of Nephrology, Div. of Internal Medicine, [2]Dept. of Infectious Diseases, Tropical Medicine & AIDS, Academic Medical Centre, Amsterdam, The Netherlands

11.30 Islet-after-kidney transplantation using alemtuzumab induction therapy (p. 98)
E.J.P. de Koning[1,2], M.A. Engelse[1], J. Oostendorp[3], J.J. Zwaginga[4], C. Loomans[1], H.J. Guchelaar[3], H. Van Bockel[5], A. Baranski[5], S. Schaapherder[5], J.A. Romijn[2], W. Fibbe[4], O. Korsgren[6], T. Lundquist[7], R. Ploeg[8], P.J.M. van der Boog[1], H.J. de Fijter[1], J. Ringers[5], T.J. Rabelink[1], Depts. of [1]Nephrology, [2]Endocrinology, [3]Clinical Pharmacy & Toxicology, [4]IHB, [5]Surgery, Leiden University Medical Centre, [6]Dept. of Clinical Immunology, Uppsala University, [7]Dept. of Surgery, Karolinska Hospital, Stockholm, Sweden, [8]Dept. of Surgery, University Medical Centre Groningen, The Netherlands

11.40 Slow graft function in living donor kidney transplantation: an issue to be addressed (p. 99)
J. Hellegering[1], J. Visser[1], H.J. Kloke[2], F.C.H.D'Ancona[3], A.J. Hoitsma[2], J.A. van der Vliet[1], M.C. Warlé[1], [1]Dept. of Surgery, Division of Vascular- and Transplant Surgery, [2]Dept. of Nephrology, [3]Dept. of Urology, Radboud University Nijmegen Medical Centre, The Netherlands

11.50 Patient survival after the diagnosis of cancer in renal transplant recipients: a nested case control study (p. 100)
J. van de Wetering[1], J.I. Roodnat[1], A.C. Hemke[2], A.J. Hoitsma[2], W. Weimar[1,2], [1]Internal Medicine and Transplantation, Erasmus University Medical Centre Rotterdam, [2]Dutch Transplant Foundation, Leiden, The Netherlands

Parallelsessie VI - Klinisch - vervolg **Grote zaal**

12.00 mTOR inhibition enhances the procoagulant state of renal transplant recipients (p. 101)
M.C. Baas[1], V.E.A. Gerdes[2, 3], I.J.M. ten Berge[1], J.C.M. Meijers[2], F.J. Bemelman[1], [1]Renal Transplant Unit, Dept. of Nephrology, Div of Internal Medicine, [2]Dept. of Vascular Medicine, Academic Medical Centre, Amsterdam, [3]Dept. of Internal Medicine, Slotervaartziekenhuis, Amsterdam, The Netherlands

12.10 The impact of donor age in living and deceased donor kidney transplantation (p. 102)
M. Laging[1], J.A. Kal-van Gestel[1], J. van de Wetering[1], J.N.M. IJzermans[2], W. Weimar[1], J.I. Roodnat[1], Depts. of [1]Internal Medicine and [2]General Surgery, Erasmus Medical Centre Rotterdam, The Netherlands

12.20 A functional polymorphism in Ficolin-2 in the donor kidney is associated with improved renal transplant outcome (p. 103)
M. Eikmans[1], I. de Canck[2], P. van der Pol[3], C.C. Baan[4], G.W. Haasnoot[1], M.J.K. Mallat[3], M. Bryson-Vergunst[1], E. de Meester[2], J.I. Roodnat[4], J.D.H. Anholts[1], M. van Thielen[2], I.I.N. Doxiadis[1], J.W. de Fijter[3], P.J.E. van der Linden[1], E. van Beelen[1], C. van Kooten[3], J. Kal-van Gestel[4], A.M.A. Peeters[4], W. Weimar[4], D.L. Roelen[1], R. Rossau[2], F.H.J. Claas[1], [1]Dept. of Immunohematology, Leiden University Medical Centre, [2]Dept. of Innogenetics, Belgium, [3]Dept. of Nephrology, Leiden University Medical Centre, [4]Dept. of internal Medicine, Erasmus University Medical Center, Rotterdam, The Netherlands

12.30 Lunchbuffet, postersessie

Parallelsessie VI - Basaal **Mauritszaal**

Voordrachten in het Nederlands, spreektijd 7 minuten, discussietijd 3 minuten.

Voorzitters: M. Betjes en L. van der Laan

10.30 In vitro skewing of the human KIR repertoire leads to enhanced NK cell alloreactivity (p. 104)
D.N. Eissens[1], F.W.M.B. Preijers[2], B. van Cranenbroek[1], K. van Houwelingen[1], A. van der Meer[1], I. Joosten[1], [1]Dept. of Laboratory Medicine - Laboratory of Medical Immunology, [2]Dept. of Laboratory Medicine - Laboratory of Hematology, Radboud University Nijmegen Medical Centre, The Netherlands

10.40 Oxygenated In Situ Cold Perfusion of DCD Kidneys in Pigs (p. 105)
H.G.D. Leuvenink, C. Krikke, S. Hofker, V. Nieuwenhuijs, H. ten Cate Hoedemaker, R. Ploeg, Dept. of Surgery, University Medical Centre Groningen, The Netherlands

10.50 The antioxidant dogma in human ischemia-reperfusion injury: no evidence for free radical mediated damage (p. 106)
D.K. de Vries[1], K.A. Kortekaas[2], D. Tsikas[3], R.J.M. Klautz[2], A.F.M. Schaapherder[1] and J.H.N. Lindeman[1], Depts. of [1]Surgery and [2]Cardio-thoracic Surgery, Leiden University Medical Centre, The Netherlands, [3]Institute of Clinical Pharmacology, Hannover Medical School, Germany

11.00 Activated tubular epithelial cells produce chemokines that attrack Th1-, but not Th17 cells (p. 107)
M.W.H.J. Demmers, C.C. Baan, W. Weimar, A.T. Rowshani, Dept. of Internal Medicine, Division of Renal Transplantation, Erasmus University Medical Centre Rotterdam, The Netherlands

11.10 Factors secreted by liver-derived mesenchymal stem cells promote liver regeneration after partial hepatectomy (p. 108)
S.M.G. Fouraschen[1], J. de Jonge[1], Q. Pan[2], G. Kazemier[1], J. Kwekkeboom[2], H.J. Metselaar[2], H.W. Tilanus[1], L.J.W. van der Laan[1], Depts. of [1]Surgery and Laboratory of Experimental Transplantation and Intestinal Surgery and [2]Gastroenterology & Hepatology, Erasmus University Medical Centre, Rotterdam, The Netherlands

Parallelsessie VI - Basaal - vervolg **Mauritszaal**

11.20 Phosphospecific flow cytometry to monitor P38 MAP kinase activity in T lymphocytes of renal transplant patients (p. 109)
R. Vafadari, M.M. Kho, M. Wabbijn, W. Weimar, C.C. Baan, Dept. of Internal Medicine, Erasmus Medical Centre Rotterdam, The Netherlands

11.30 Adipose Tissue Derived Mesenchymal Stem Cells Are Not Affected by End Stage Renal Disease (p. 110)
M. van Rhijn[1], M.E.J.Reinders[3], S.S. Korevaar[1], F.J.M.F. Dor[2], J.N.M. IJzermans[2], C.C. Baan[1], W. Weimar[1], M.J. Hoogduijn[1], Depts. of [1]Internal Medicine and [2]General Surgery, Erasmus University Medical Centre Rotterdam, [3]Dept. of Nephrology, Leiden University Medical Centre, The Netherlands

11.40 Optimizing alloantigen presentation as a tool to monitor indirect alloantigen presentation in renal transplant recipients (p. 111)
E. Breman[1], M.H. Heemskerk[2], F.H. Claas[3], C. van Kooten[1], Depts. of [1]Nephrology, [2]Hematology, [3]Immunohematology and Blood Transfusion, Leiden University Medical Centre, The Netherlands

11.50 Exosomes can mediate transmission of Hepatitis C virus in the presence of neutralizing antibodies: relevance for Hepatitis C recurrence? (p. 112)
V. Ramakrishnaiah[1], P.E. de Ruiter[1], R. Willemsen[2], J. Demmers[2], D. Diederick[2], G. Jenster[2], J. de Jonge[1], G. Kazmier[1], J. Kwekkeboom[3], H.J. Metselaar[3], H.W. Tilanus[1], L.J.W van der Laan[1], [1]Dept. of Surgery and Laboratory of Experimental Transplantation and Intestinal Surgery, [2]Dept. of Cell Biology and Genetics and [3]Dept. of Gastroenterology & Hepatology, Erasmus University Medical Centre, Rotterdam, The Netherlands

12.00 Lysis of Mesenchymal Stem Cells by NK Cells cannot be Prevented by Immunosuppressive Drugs (p. 113)
M.J. Hoogduijn, S.S. Korevaar, A. Grohnert, M. van Rhijn, W. Weimar, C.C. Baan, Dept. of Internal Medicine, Erasmus Medical Centre Rotterdam, The Netherlands

Parallelsessie VI - Basaal **Mauritszaal**

12.10 Cardiac allograft vasculopathy: a quantitative analysis of changes in coronary artery wall architecture after heart transplantation (p. 114)
M.M.H. Huibers[1], J. Kaldeway[1], A. Huisman[1], H.F.J. Dullens[1], M.E.I. Schipper[1], N. de Jonge[2], R.A. de Weger[1], Depts. of [1]Pathology, and [2]Cardiology, University Medical Centre Utrecht, The Netherlands

12.20 Microwell scaffolds for extrahepatic islets of Langerhans transplantation in type 1 diabêtes (p. 115)
M. Buitinga[1], E.J.P. de Koning[2], M.A. Engelse[2], C.J.M. Loomans[2], R. Truckenmüller[1], L. Moroni[1], C.A. van Blitterswijk[1], A.A. van Apeldoorn[1], M.Karperien[1], [1]Dept. of Tissue Regeneration, University of Twente, [2]Dept. of Nephrology, University Medical Centre Leiden, The Netherlands

12.30 Lunchbuffet, postersessie

Parallelsessie VI – Transplantatieverpleegkunde / Donatie Raadszaal

Voordrachten in het Nederlands, spreektijd 10 minuten, discussietijd 5 minuten.

Voorzitters: A.E. Braat en F.J. van Ittersum

10.30 Preservation Solution and Method Affect Organ Temperature during Procurement (p. 116)
E. Buiter[1],C. Billault[1,2], B. Barrou[2], R.J. Ploeg[1], H.G.D. Leuvenink[1], [1]Dept. of Surgery, University Medical Centre Groningen, The Netherlands, [2]Dept. of Service d'Urologie et de Transplantation Rénale, Hôpital de la Pitié Salpêtrière, Paris, France

10.45 The emotional response to the receipt of an organ in liver transplant recipients (p. 117)
J.H. Annema[1], P.F. Roodbol[1], R.J. Porte[2], A.V. Ranchor[3], [1]Wenckebach Institute, School of Nursing & Health, [2]Dept. of Surgery, [3]Dept. of Health Psychology, University Medical Centre Groningen, The Netherlands

11.00 Donation after cardiac death in liver transplantation: a calculated risk (p. 118)
J.J. Blok[1], J. Ringers[1], R. Adam[2], A.K. Burroughs[3], N.G. Kooreman[1], J. Dubbeld[1], H. Putter[4], A.O. Rahmel[5], R.J. Porte[6], X. Rogiers[7], A.E. Braat[1], [1]Dept. of Surgery, Leiden University Medical Centre, [2]Centre Hépato-Biliaire, Hôpital Paul Brousse, Villejuif, France, [3]Liver Transplantation and Hepatobiliary Medicine, Royal Free Hospital, London, United Kingdom, [4]Dept. of Medical Statistics, Leiden University Medical Centre, [5]Eurotransplant Int. Foundation, Leiden, [6]Dept. of Surgery, University Medical Centre Groningen, [7]Dept. of Surgery, Ghent University Hospital Medical School, Belgium

11.15 Unspecified and specified living kidney donation to unrelated recipients (p. 119)
W. Zuidema, J. van de Wetering, F. Dor, J. Roodnat, E. Massey, J. IJzermans, W. Weimar, Depts. of Internal Medicine and General Surgery, Erasmus Medical Centre Rotterdam, The Netherlands

Parallelsessie VI – Transplantatieverpleegkunde / Donatie Raadszaal

11.30 Overgewicht voor en na nierdonatie bij leven (p. 120)
E.C.M. Berendsen, A.G.E. Vink, A. Moazenni, F.E. van Reekum, P.F. Vos, A.D. van Zuilen, Dept. of Nephrology, University Medical Centre Utrecht, The Netherlands

11.45 Zelfstandig Uitname Team,1 jaar operationeel (p. 121)
J. Dubbeld[1], E. Luijer[1], S. Hamelinck[2], Y.M.L. Verwer[2], J.Ringers[1]. [1]Afdeling Heelkunde, Leids Universitair Medisch Centrum, [2]Afdeling Operatie Kamer, Leids Universitair Medisch Centrum, Nederland

12.00 A preoperative protein deficient diet protects against renal and hepatic ischemia and reperfusion injury (p. 122)
T.C Saat[1], T.M van Ginhoven[1], M. Verweij[1], J.N.M. IJzermans[1], J.H.J. Hoeijmakers[2], R.W.F. de Bruin[1], Depts. of [1]Surgery and [2]Genetics, Erasmus University Medical Centre, Rotterdam, The Netherlands

12.15 Clinical and experimental monitoring of temperature during cold static preservation of kidney grafts with a new organ preservation container (p. 123)
C. Billault[1,2], H.G.D. Leuvenink[1], R.J. Ploeg[1], B. Barrou[2], [1]Dept. of Surgery, University Medical Centre Groningen, The Netherlands, [2]Service d'Urologie et de Transplantation Rénale, Hôpital de la Pitié Salpêtrière, Paris, France

12.30 Lunchbuffet, postersessie

Ledenvergadering — Grote zaal

13.30 Ledenvergadering
Nederlandse Transplantatie Vereniging

Plenaire sessie VII — Grote zaal

Voordrachten in het Nederlands, spreektijd 7 minuten, discussietijd 3 minuten.

Voorzitters: G. Kazemier en R.J. Porte

14.30 Gaseous hydrogen sulfide (H2S) is protective during cardiac ischemia/reperfusion (p. 124)
P.M. Snijder[1,2], R.A. de Boer[3], E.M. Bos[1,2], J.C. van den Born[1,2], W.T. Ruifrok[3], I. Vreeswijk-Baudoin[3], M.C.R.F. van Dijk[1], H.G.D. Leuvenink[2], H. van Goor[1], [1]Dept. of Pathology and Medical Biology, [2]Dept.of Surgery, [3]Dept. of Cardiology, University Medical Centre Groningen, The Netherlands

14.40 Quantification of demethylated FOXP3 DNA demonstrates a lower proportion of natural regulatory T cells 1 year after kidney transplantation (p. 125)
K. Boer, A.M.A. Peeters, W. Weimar, C.C. Baan, Dept. of Internal Medicine, Erasmus Medical Centre Rotterdam, The Netherlands

14.50 Donor serum angiopoietin 2 is an independent predictor of kidney transplant outcome (p. 126)
L.G. Koudstaal[1,2] ,C. Moers[1], J.G.M. Burgerhof[3], H. van Goor[2], A.O. Rahmel[4], A. Paul[5], J. Treckmann[5], D. Monbaliu[6], J. Pirenne[6], R.J. Ploeg[1] and H.G.D. Leuvenink[1], Depts. of [1]Surgery, [2]Pathology and [3]Epide-miology, University Medical Centre Groningen, [4]Eurotransplant Foundation, Leiden, The Netherlands, [5]Abdominal Transplant Surgery, University Hospital Essen, Germany, [6]Abdominal Transplant Surgery, University Hospital Leuven, Belgium

Plenaire sessie VII - vervolg **Grote zaal**

15.00 Transplantation of right living donor kidneys in obese recipients correlates with a decreased graft survival (p. 127)
J. Hellegering[1], J. Visser[1], F.C.H. D'Ancona[2], J.F. Langenhuijsen[2], A.J. Hoitsma[3], J.A. van der Vliet[1], M.C. Warlé[1], [1]Dept. of Surgery, Division of Vascular- and Transplant Surgery, [2]Dept. of Urology, [3]Dept. of Nephrology, Radboud University Nijmegen Medical Centre, The Netherlands

15.10 Effects of rituximab-treated B cells on T cell proliferation and cytokine production in vitro (p.128)
E.G. Kamburova[1], H.J. Koenen[1], L.B. Hilbrands[2], I. Joosten[1], [1]Dept. of Laboratory Medicine, Laboratory of Medical Immunology, [2]Dept. of Nephrology, Radboud University Nijmegen Medical Centre, The Netherlands

15.20 *Hepatocyte-derived MicroRNAs in Human Serum are Sensitive Markers for Hepatic Injury in Liver Transplantation* (p. 129)
W.R.R. Farid[1], Q. Pan[2], A.J.P. van der Meer[2], P.E. de Ruiter[1], V.Ramakrishnaiah[1], J. de Jonge[1], J. Kwekkeboom[2], H.L.A. Janssen[2], H.J. Metselaar[2], H.W. Tilanus[1], G. Kazemier[1] and L.J.W. van der Laan[1] [1]Department of Surgery and Laboratory of Experimental Transplantation and Intestinal Surgery and [2]Department of Gastroenterology & Hepatology, Erasmus MC - University Medical Center, Rotterdam, The Netherlands

15.30 Theepauze

Plenaire sessie VIII **Grote zaal**

Voorzitters: R.J.M. ten Berge en F.J. van Ittersum

16.00 **Niet-westerse kinderen in Nederland en België: langer op de wachtlijst en meer kans op afstoting**
Dr. J. Groothoff, Afdeling Kindernefrologie, Emma Kinderziekenhuis Amsterdam.

16.30 **Strategieën ter verbetering van de kwaliteit van het donor orgaan**
Prof. dr. R.J. Ploeg, Afdeling Heelkunde, UMC Groningen

17.00 Afsluiting congres

Posters

1. Influence of living donor transplantation on the composition of the population that remains dependent on deceased donor trans-plantation
   J.I. Roodnat , M. Laging, J. Wetering, M. Kho, J.A. Kal van Gestel, J.N.M. IJzermans, W. Weimar. Depts. of Internal Medicine and General Surgery, Erasmus Medical Centre, Rotterdam, The Netherlands

2. Risk factors for incisional hernia after J-shaped subcostal incision after liver transplantation: a prospective study
   B. de Goede[1], H.H. Eker[1], P.J. Klitsie[1] H.W. Tilanus[1], H.J. Metselaar[2] , R.A. de Man[2], J.F. Lange[1], G. Kazemier[1] .[1]Erasmus University Medical Center, Dept. of Surgery, [2] Erasmus University Medical Center, Dept. of Gastroenterology and Hepatology, The Netherlands

3. Validation of a Fungal Infection Prediction Model in 2 European Liver Transplant Centers
   I.C.A.W. Konings[1], S.H. van Olphen[1], L.H. de Grim[2], G. Kazemier[3], B.E. Hansen[1], R.A. de Man[1], X. Rogiers[2], C.A.M. Schurink[4] and H.J. Metselaar[1], [1] Dept of Gastroenterology and Hepatology, Erasmus University MC Rotterdam, The Netherlands; [2] Dept of Liver Transplantation, University Hospital Ghent, Belgium; [3]Dept of Surgery, Erasmus University MC, Rotterdam, The Netherlands; [4] Dept of Medical Microbiology and Infectious Diseases, Erasmus University MC Rotterdam, The Netherlands

4. Improved treatment satisfaction in renal transplant patients using a simplified medication regimen with the use of tacrolimus OD (ADVAGRAF®)
   G.A.J. van Boekel, C.H.H. Kerkhofs, L.B. Hilbrands Dept. of Nephrology, Radboud University Nijmegen Medical Center

5. The impact of participation in randomized clinical trials after kidney transplantation
   J. A Kal-van Gestel[1], N. de Leeuw van Weenen[1], E. A.F.J. van Gurp[3], J.N.M. IJzermans[2] and W. Weimar[1]. [1]Internal Medicine, Section Kidney Transplantation, Erasmus MC, Rotterdam, [2]General Surgery Erasmus MC, Rotterdam, [3]Ziekenhuis De Lievensberg, Bergen Op Zoom, The Netherlands

6. Circulating biomarkers of reverse remodeling during continuous flow LVAD support and after heart transplantation
S.I. Lok[1], F.M.A. Nous[2], P. van der Weide[2], J. Kuik[2], B. Winkens[3], M.E.I. Schipper[2] , H. Kemperman[2], P.A.F. Doevendans[1], R. de Weger[2], N. de Jonge[1]. Depts. of [1]Cardiology, [2]Pathology,University Medical Center Utrecht, Utrecht, Netherlands and [3] Dept. of Methodology & Statistics, Academic Hospital Maastricht, Maastricht, Netherlands

7. Alpha-1-antichymotrypsin, a new player in reverse remodeling of the human heart?
S.I. Lok[1], Niels Bovenschen[2], F.M.A. Nous[2], R. Quadir[2], J. van Kuik[2], B. Winkens[3], P.A.F. Doevendans[1], N. de Jonge[1] and R. de Weger[2]. Depts. of [1]Cardiology, [2]Pathology, University Medical Center Utrecht, Utrecht, Netherlands and [3] Dept. of Methodology & Statistics, Academic Hospital Maastricht, Maastricht, Netherlands

8. Prolonged treatment with everolimus does not induce podocyte damage and leaves the glomerular basementmembrane intact
M.C. Baas[1], J.Kers[2], S. Florquin[2], J.W. de Fijter[3], J.J.Homan van der Heide[4], M.A. van den Bergh Weerman[2], I.J.M. ten Berge[1], F.J.Bemelman[1].Renal Transplant Unit, Dept of Nephrology, Div of Internal Medicine[1], Academic Medical Center, Amsterdam, the Netherlands; Dept of Pathology[2], Academic Medical Center, Amsterdam, the Netherlands, Dept of Nephrology[3], Leiden University Medical Center, the Netherlands; Dept of Nephrology, Div[4], Groningen University Hospital, The Netherlands

9. Quality control of pancreatic islet preparations for transplantation.
M.A. Engelse [1,2], J. Oostendorp[3], E.H van Rossenberg[1], H.A.M Töns[1], C. Vermeulen[1], J. Ringers[4], A. Braat[4], A. Baranski[4], J. Dubbeld[4], S. Schaapherder[4], R. Ploeg[5], A.J Rabelink[1], J.J. Zwaginga[2], E.J.P. de Koning[1,2]. Leiden University Medical Center, Dept. of Nephrology[1], Pharmacotherapy, Surgery[3], Immunohematology[4], University Medical Center Groningen, Dept of Surgery[5], The Netherlands

10. Effect of mild diarrhea on tacrolimus exposure.
G.A.J. van Boekel[1], R.E. Aarnoutse[2], J.J. van der Heijden[3], K.E.J. Hoogtanders[3], L.B. Hilbrands[1]. Dept. of Nephrology[1], Dept. of Clinical Pharmacy[2], Radboud University Nijmegen Medical Center, Dept. of Clinical Pharmacy[3], Maastricht University Medical Center, The Netherlands

11. Skin AGE (Advanced Glycation End products) is not affected by immunosuppressive therapy in kidney transplant recipients
M. van Dijk[1], A. M. van Roon[2], E.F. de Maar[1], M.A.J. Seelen[1], W.J. van Son[1], F.J. Bemelman[3], K.A. van Donselaar-v.d. Pant[3], R. J. Ploeg[4] , J. Homan van der Heide[1]. Dept of Nephrology[1], University Medical Center Groningen, Dept of Internal medicine[2], University Medical Center Groningen, Renal Transplant Unit[3], Academic Medical Center, Amsterdam, Dept of abdominal and transplant surgery[4], University Medical Center Groningen, The Netherlands

12. Virus specific CTL do not compete for space in lymph nodes.
E.B.M. Remmerswaal[1,2], S.H.Havenith[1,2], A. ten Brinke[3], M.M. Idu[4], K.A.M.I. van Donselaar-van der Pant[1], F.J. Bemelman[1], R.A.W. van Lier[2], I.J.M. ten Berge[1] [1]Dept. of Experimental Immunology, [2]Renal Transplant Unit, Dept. of Nephrology, Div. of Internal Medicine, [3]Sanquin Research and Landsteiner Laboratory, Dept. of Immunopathology, [4]Dept. of Vascular Surgery, Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands

13. Prehabilitation of living-donor kidney transplant candidates
K. Valkenet[1], F. van Reekum[2], D. Zinger D[1], I.G.L. van de Port.[1] [1]University Medical Centre Utrecht, Dept. of Rehabilitation, Nursing Science and Sport. [2]University Medical Centre Utrecht, Dept. of Nephrology

14. Circulating microRNAs in patients with cardiac allograft vasculopathy after heart transplantation
H. Vroman[*], M.M.H. Huibers[*], J. van Kuik[*], N. de Jonge[#] and R.A. de Weger[*], Dept. of Pathology[*] and Cardiology[#], University Medical Centre Utrecht, The Netherlands

15. Expression of circulating miRNAs in end-stage heart failure patients with continuous flow left ventricular assist device support.
S.I. Lok[1], D.M. Hamerpagt[2], J. van Kuik[2], N. de Jonge[1], R.A. de Weger[2]. Dept of Cardiology[1], University Medical Centre Utrecht, Utrecht, Netherlands, Dept of Pathology[2], University Medical Centre Utrecht, Utrecht, Netherlands

16. No evidence for involvement of donor or recipient NK-cell allo-reactivity in liver transplantation outcome
V. Moroso[1], A. van der Meer[2], G. Kazemier[3], L.J.W. van der Laan[3], H.J. Metselaar[1], I. Joosten[2], J. Kwekkeboom[1]. Depts. of Gastroenterology and Hepatology[1] and Surgery[3], Erasmus MC University Medical Center, Rotterdam, [2]Dept. of Laboratory Medicine – Laboratory of Medical Immunology, Radboud University Nijmegen Medical Center, Nijmegen, The Netherlands

17. The effect of normothermic recirculation before cold preservation on posttransplant injury of ischemically damaged donor kidneys
C. Moers[1], G. van Rijt[1,2], M. Weij[1,3], R. Gras[1], A. Smit-van Oosten[3], A.H. Zandvoort[3], R.J. Ploeg[1], H.G.D. Leuvenink[1]. Surgery Research Laboratory[1], Dept. of Surgery, University Medical Center Groningen, University of Groningen, The Netherlands, Pathology Research Laboratory[2], Dept. of Pathology, University Medical Center Groningen, University of Groningen, The Netherlands, Central Animal Laboratory[3], University Medical Center Groningen, University of Groningen, The Netherlands

18. Endothelial and Thrombocyte Activation are Not Mediators in Early Ischemia-Reperfusion Injury in Human Kidney Transplantation
D.K. de Vries[1], M. Roest[2], M. Khairoun[3], J.H.N. Lindeman[1], T. Holten[2], J.Ringers[1], T.J. Rabelink[3], P.G. de Groot[2], M.E.J. Reinders[3], A.F.M. Schaapherder[1],[1]Dept. of Surgery, Leiden University Medical Center, Leiden, Netherlands; [2]Dept. of Haematology, University Medical Center Utrecht, Utrecht, Netherlands; [3]Dept. of Nephrology, Leiden University Medical Center, Leiden, Netherlands.

19. Conversion to the once-daily tacrolimus formulation in renal transplant recipients leads to higher P38 MAPK activity in T lymphocytes
R. Vafadari[1], D.A. Hesselink[1], M.E. Quaedackers[1], M.M. Cadogan[1], T. van Gelder[1], W. Weimar[1] and C.C. Baan[1], Dept of Internal Medicine[1], Erasmus Medical Center Rotterdam, The Netherlands

20. Rapamycin and MPA, but not CsA, impair human NK-cell cytotoxicity due to differential effects on NK-cell phenotype
D.N. Eissens[1], A. van der Meer[1], B. van Cranenbroek[1], F. W.M.B. Preijers[2], I. Joosten[1]Dept. of Laboratory Medicine - [1] Laboratory of Medical Immunology and [2] Laboratory of Hematology, Radboud University Nijmegen Medical Centre, Nijmegen, the Netherlands.

21. Psychosocial characteristics predictive of post-operative mental health in living-related liver or kidney donors: a systematic literature review
J.B. van Gogh[1], N. Duerinckx[2], E. Massey[3], S. Y. Ismail[1], J.V. Busschbach[1],F. Dobbels[2]. Dept. of Medical Psychology & Psychotherapy[1], Erasmus Medical Center, Centre for Health Services and Nursing Research[2], KU Leuven. Dept. of Internal Medicine[3], Erasmus Medical Center, The Netherlands

22. Activation of hemostasis in brain-dead organ donors
T. Lisman, H.G.D. Leuvenink, R. J. Porte, R.J. Ploeg, Dept. of Surgery, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands

23. IL-17 producing cells home to the graft early after heart transplantation
N.M. van Besouw[1], A.M.A. Peeters[1], M. Dieterich[1], K. Caliskan[2], A.P.W.M. Maat[3], A.H.M.M. Balk[2], W. Weimar[1], and C.C. Baan[1], Depts. of Internal Medicine – Transplantation[1], Cardiology[2], Thoracic Surgery[3], Erasmus MC, University Medical Center Rotterdam, Rotterdam, The Netherlands.

24. Selective proliferation of human CD28null effector memory T cells induced by primary renal tubular epithelial cells
M.W.H.J. Demmers, C.C. Baan, W. Weimar and A.T. Rowshani
Dept. of Internal Medicine, Division of Renal Transplantation, Erasmus MC, University Medical Center Rotterdam, the Netherlands

25. ELPAT's new classification for living donor organ donation
F.J.M.F. Dor[1], E.K. Massey[2], M. Frunza[3], R. Johnson[4], A. Lennerling[5], C. Lovén[5], N. Mamode[6], A. Pascalev[7], S. Sterckx S[8,9], K. Van Assche[8], W.C. Zuidema[2], W. Weimar[2]. [1]Dept of Surgery [2]Dept of Internal Medicine, Erasmus MC, Rotterdam [3]Babes-Bolyai University, Cluj, Romania [4]NHS Blood and Transplant, Bristol, UK [5]University Hospital Göteborg, Sweden [6]Guy's Hospital, London, UK [7]Bulgarian Center for Bioethics, Sofia, Bulgaria [8]Free University of Brussels, Belgium, [9]Bioethics Institute Ghent, Belgium.

26. Skype saved the ELPAT congress
M.A.A. van Noord-Haubrich, J.A.E. Ambagtsheer, J.A. Kal-van Gestel, W. Zuidema and W. Weimar. Dept of Internal Medicine, Section Kidney Transplantation, Erasmus Medical Center Rotterdam, Rotterdam, The Netherlands

27. The paradox of organ trafficking prohibition: how to control the potential adverse effects of the Declaration of Istanbul
J.A.E. Ambagtsheer[1], D. Zaitch[2], W. Weimar[1] Dept. of Internal Medicine, Kidney Transplant Unit, Erasmus MC, University Medical Center Rotterdam, the Netherlands[1] Willem Pompe Institute for Criminal Law and Criminology, Utrecht University, Utrecht, The Netherlands[2]

28. Gewicht in evenwicht: of toch niet na een longtransplantatie?
M. Quak, J. den Ouden, G.A.M. Tuijtelaars, J.J. van Weezel, P.Th.W. van Hal. Dept of Respiratory Medicine, Erasmus Medical Center Rotterdam, The Netherlands.

29. Knowledge on kidney disease and renal replacement therapy among renal patients: Development of the Rotterdam Kidney Knowledge Questionnaire (RKKQ)
E.K. Massey[1], S.Y. Ismail[2], A. Luchtenburg[1], P.J.H. Smak Gregoor[3], R.W. Nette[4], M.A. van den Dorpel[5], W. Zuidema[1], R. Zietse[1], J.J. van Busschbach[2], W. Weimar[1]. Depts. of Internal Medicine[1], Erasmus Medical Centre Rotterdam, Medical Psychology[2], Erasmus Medical Centre Rotterdam, Internal Medicine[3], Albert Schweitzer Ziekenhuis, Dordrecht, Internal Medicine[4], Sint Franciscus Gasthuis, Rotterdam, Internal Medicine[5], Maasstadziekenhuis, Rotterdam, The Netherlands.

Pediatric kidney transplantation in the Netherlands: CMV prophylaxis up to revision?

H. Jongsma[1], A.H. Bouts[2], E.A.M. Cornelissen[3], MR Lilien[4], M. Beersma[5], K. Cransberg[1], Dept. of Pediatric Nephrology, [1]Erasmus Medical Centre, Sophia Children's Hospital, Rotterdam, [2]Emma Children's Hospital, Academic Medical Centre, Amsterdam, [3]University Medical Centre St. Radboud, Nijmegen, [4]Wilhelmina Children's Hospital, University Medical Centre, Utrecht, [5]Dept. of Virology, Erasmus Medical Centre, Rotterdam, The Netherlands

Background: A large proportion of children receiving a kidney transplant are seronegative for CMV and EBV and therefore highly susceptible to infection with these viruses. The aim of this study is to evaluate the incidence, timing and severity of CMV and EBV infections in the first year post-transplantation since the introduction of CMV prophylaxis. Design: a retrospective, observational, multicentre study. Methods: We included 198 pediatric kidney transplantations performed in the Netherlands between 1999 and 2010 after which PCR assays were performed; the time of introduction of PCR assays varied between the hospitals. Clinical data and PCR measurements of CMV and EBV over 12 months post-transplant were collected. Prophylaxis in high risk patients (serostatus CMV D+R-) consisted of 3 months Valacyclovir and Megalotect, and Valgancyclovir at a later stage. Intermediate risk patients (R+) received Valacyclovir and Megalotect, and Valacyclovir at a later stage. Low risk patients (D-R-) did not receive any prophylaxis. Infection was defined as more than 1000 copies/ml plasma.
Results: CMV: 24 of 65 high risk patients (37%) experienced a CMV infection; 17 of 78 with intermediate risk (22%), and 6 of 55 with low risk (11%). Infection occurred within 3 months in 24 (51%) of cases, equally distributed over the risk groups. Infections after 3 months mostly occurred in the high risk group: 17 of 23 (71%). Valgancyclovir provided substantially better protection than did Valacyclovir + Megalotect. Introduction of an IL2MoAb in the immunosuppressive regimen did not affect the incidence of CMV infection.
EBV: 15 of 167 patients with monitored EBV PCR (9%) developed an EBV infection. All 15 had received basiliximab induction (n.s.); 3 developed PTLD. Eight infections occurred within 3 months. The numbers are too small to draw conclusions on the effect of CMV prophylaxis on EBV infection.
Conclusion: Despite CMV prophylaxis a high proportion of children experience CMV and EBV infection within one year after kidney transplantation. We recommend lengthening CMV prophylaxis from 3 to 6 months in D+R- seropairs to prevent infection and disease.

A Dutch multi-center study on the decision-making process of families requested for organ and/or tissue donation

N.E. Jansen[1], H.A. van Leiden[1], B.J.J.M. Haase-Kromwijk[1], Nardo J.M. van der Meer[2], Edwin Vorstius Kruijff[2], Netty van der Lely[3], Hans van Zon[3], Arend-Jan Meinders[4], Machteld Mosselman[4], A.J. Hoitsma[5], [1]Dutch Transplant Foundation Leiden, [2]Dept. of Intensive Care, Amphia Hospital Breda, [3]Dept. of Intensive Care, Sint Elisabeth Hospital Tilburg, [4]Dept. of Intensive Care, Sint Antonius Hospital Nieuwegein, [5]Dept. of Nephrology, University Medical Centre Nijmegen, The Netherlands

Purpose: The consent process for organ donation is complex not only for the family members who have to make decisions under emotionally stressful circumstances, but also for professionals who must ask the family if their relative was willing to donate. As a result family refusal is seen as a frequent outcome. In the Netherlands this is the main reason for the loss of potential donors. The Dutch Transplant Foundation therefore performed a multi-center study in an attempt to decrease the refusal rate.
Methods: Three hospitals participated in our study. In the intervention hospital a special group of health-care professionals was trained according to the 'Communication about Donation' programme. We named them '*trained donation practioners*' (TDP), and their role was to guide the family throughout the time in the ICU until a decision regarding donation had been reached. The first control hospital had no special professionals for family care and donation was requested by the physician without any extra support. The second control hospital had 'hostesses' for family support but without any special training related to donation. The primary outcome measurement was the donation consent rate, and second was the experiences of families measured by use of a questionnaire with items like 'demographic profile', 'satisfaction with care provided by health care professionals', 'the decision-making process', and 'factors that could have influenced the decision'. Results: The family consent rate was significantly higher in the intervention hospital with the TDP (57.6%) compared to the control hospital without hostesses (34.6%), and the control hospital with hostesses, but without special training (39.4%). Even after excluding 'consent', as a preference of the potential donor registered in the Donor Register. No significant differences were seen between the participating hospitals based on the outcomes of the questionnaire, therefore no confounding variables could have influenced the consent rate.
Conclusion: It was possible to achieve higher consent rates with the implementation of the TDP, even though families in the intervention hospitals were not more satisfied compared to the control group. The training and long and extensive contact between the TDP and the next of kin were the decisive factors in the statistically significant higher consent rate.

Excessive premature ageing of T lymphocytes in end-stage renal disease: an important factor to consider in pre-transplant immunological risk assessment.

N.H. Litjens[1], E.A. de Wit[1], A. Langerak[2], A. van de Spek[2], W. Weimar[3] and M.G. Betjes[1], Depts. of [1]Nephrology, [2]Immunology and [3]Transplantation, Erasmus Medical Centre, Rotterdam, The Netherlands

Introduction: End-stage renal disease (ESRD) causes an impaired T cell-mediated immune function, which is associated with marked changes in T cell numbers and differentiation. We tested the hypothesis that these changes are compatible with the concept of premature immunological ageing. Such a finding would be relevant to patients undergoing kidney transplantation, as the degree of premature immunological ageing may influence the risk for allograft rejection and/or infection.
Methods: Three different approaches were chosen to assess the immunological age of T cells in 75 stable ESRD patients and age-matched healthy controls (HC) with an age range from 20-80 years. First, total numbers of circulating T cells and their differentiation pattern into well-characterized subsets of naive and memory T cells were analyzed by flowcytometry. In addition, the T cell receptor excision circle (TREC) content by real-time qPCR and relative telomere length (RTL) of CD4 and CD8 T lymphocytes was assessed. TRECs are generated during T cell receptor rearrangement in the thymus and are diluted with every cell division after the T cell has exited the thymus into the circulation. Results: An age-dependent decrease in absolute T cell numbers and increased terminal differentiation was observed in both HC and ESRD patients. However, at all ages the phenotype of the ESRD T cell compartment was similar to HC 30 years older. Particularly the subset of recent thymic emigrants (CD31pos naive T cells) decreased sharply in ESRD patients. This loss was counteracted by significantly more Ki67pos cells, indicating a higher T cell proliferation index. TREC content of T cells decreased with increasing age (Rs=0.70, P=0.001). A significantly greater decrease in TREC content was observed in ESRD patients compared to HC (p=0.01), yielding an average difference in immunological age of 15-20 years. The RTL of CD4+ and CD8+ T lymphocytes gave similar findings as the TREC assay but resulted in a greater immunological age difference of almost 30 years.
Conclusion: ESRD increases the immunological age of T lymphocytes by approximately 20-30 years compared to age-matched HC. A decreased thymic output with increased homeostatic proliferation of T cells seems to be the underlying mechanism.

Hand-Assisted Retroperitoneoscopic versus Standard Laparoscopic Donor Nephrectomy: Single Blind, Randomised Controlled Trial

L.F.C. Dols[1], N.F.M. Kok[1], T.C. Khe Tran[1], T. Terkivatan[1], F.C.H. d'Ancona[2], J.F. Langenhuijsen[2], F.J.M.F. Dor[1], W. Weimar[3], J.N.M. IJzermans[1], [1]Dept. of Surgery, Erasmus Medical Centre, Rotterdam, [2]Dept. of Urology, Radboud University Nijmegen, [3]Dept. of Internal Medicine, Erasmus Medical Centre, Rotterdam, The Netherlands

Background: Live kidney donation is an important alternative for patients with end-stage renal failure. Laparoscopic donor nephrectomy (LDN) has become the preferred method to procure kidneys because of the reduced surgical trauma and reduced pain subsequently, shorter convalescence time and superior quality of life as compared with open approaches. However, safety issues of LDN have been debated. In theory, hand-assisted retroperitoneoscopic (HARP) combines the control, dexterity and speed of the hand-guided surgery with the benefits of minimal invasive surgery, benefits of LDN including retroperitoneal access and reduced surgical trauma. The objective is to determine the best approach for live donor nephrectomy to optimise donor's safety and comfort.
Methods: This multicenter, randomised controlled trial compares the hand-assisted retroperitoneoscopic approach with standard laparoscopic donor nephrectomy. From July 2008 to September 2010, 190 consecutive donors were randomly assigned to left-sided HARP procedure or left-sided LDN. Intra and postoperative data were prospectively collected and analysis on outcome was performed. Results: Baseline characteristics were not significantly different. Compared with LDN, HARP donor nephrectomy resulted in shorter skin to skin time (median 162 vs. 190 minutes, $p < 0.001$), shorter warm ischemia time (2 vs. 4 minutes, $p < 0.001$), more blood loss (160 vs. 104 ml, $p = 0.063$), and a lower number of intraoperative complications (7% vs. 20%, $p < 0.001$). In the LDN group two conversions occurred, one to hand-assisted laparoscopic, and the other to an open donor nephrectomy. One conversion to a LDN occurred in the HARP group. Total morphine require-ment was not significantly different between HARP and LDN (11 vs. 12 mg, $p = 0.833$). Postoperative compli-cations and hospital stay were not significantly different (both 8%; both 3 days, $p = 0.135$). During follow-up estimated glomerular filtration rates in donors and recipients and graft- and recipient survival did not differ between groups.
Conclusion: Hand-assisted retroperitoneoscopic donor nephrectomy reduces operation and warm ischemia times, and provides better intraoperative safety. Hand-assisted retroperitoneoscopic is an important alternative for left-sided LDN.

Meningococcal polysaccharide vaccine fails to protect a renal transplant recipient receiving eculizumab from developing meningococcal disease

G.H. Struijk[1], A.H.M. Bouts[2], G.T. Rijkers[3], E.A.C. Kuin[1], H.L. Zaaijer[4], I.J.M. ten Berge[1], F.J. Bemelman[1], [1]Renal Transplant Unit, Dept. of Nephrology, Div of Internal Medicine, [2]Dept. of Paediatric Nephrology, Academic Medical Centre, Amsterdam, [3]Dept. of Medical Microbiology and Immunology, St. Antonius Hospital, Nieuwegein, [4]Dept. of Virology, Academic Medical Centre, Amsterdam, The Netherlands

Guidelines for the use of eculizumab, a monoclonal antibody against complement factor C5, recommend vaccination against meningococcal disease, because *N. meningitidis* establishes systemic infections in patients deficient in complement components. Here, we describe failure of a tetravalent meningococcal polysaccharide vaccine to protect against meningococcal disease in a 19-year old renal transplant recipient receiving eculizumab to prevent atypical haemolytic-uremic syndrome (aHUS) recurrence.

Our patient received her third transplant in February 2008. Her immunesuppressive therapy consisted of basiliximab, prednisolone, mycophenolate mofetil and tacrolimus. To prevent aHUS recurrence she was initially treated with plasma exchange (PE). However, due to severe allergic reactions to plasma, PE was substituted for eculizumab in January 2009. Two weeks before initiating eculizumab therapy, patient was vaccinated with polysaccharide vaccine Mencevax® (ACYW135). In June 2010 patient developed meningococcal sepsis (serotype W135) which was treated with penicillin G intravenously. Fortunately, she recovered completely; her renal function decreased only temporarily and eculizumab therapy was continued.

Since our patient developed meningococcal sepsis with serotype W135, for which she was vaccinated 1.5 years prior to this disease episode, we analysed *N. meningitides*-specific immunoglobulin (Ig) G in plasma in several pre- en postvaccination samples. The results showed that our patient had only made a humoral response against *N. meningitides* serotype C, but not against serotypes A, Y and W135.

We hypothesize that our patient was not able to mount a humoral response after vaccination due to the use of immunosuppressive therapy, possibly in combination with PE, since several studies have shown that different immunesuppressive regimens vary in their effects on immune responses after vaccination. We therefore, strongly advice transplant physicians to monitor meningococcal vaccination efficacy after initiation of eculizumab therapy and to regularly check IgG levels since protective immunity induced after vaccination may wane more rapidly in renal transplant recipients.

Prophylactic plasmapheresis (PE) and eculizumab (EC) allow long term renal function preservation in *FH* mutation related atypical haemolytic uremic syndrome (aHUS)

J-C Davin [1,2], JW Groothoff[1], FJ Bemelman,[3,]AH Bouts[1]. [1]Pediatric Nephrology, Emma Children's Hospital / Academic Medical Centre, Amsterdam Z-O, Netherlands, 1105 AZ; [2]Pediatric Nephrology, Queen Fabiola Academic Children's Hospital/ULB, Brussels, Belgium, 1020 and [3]Nephrology, Academic Medical Centre, Amsterdam Z-O, Netherlands.

Background: In patients with atypical hemolytic uremic syndrome (aHUS) known to have a mutation in the complement factor H gene (*CFH),* there is a 75% risk of ESRF, a 80% risk of a renal allograft lost to recurrent disease within 2 years of transplant and a 100% risk of graft loss after recurrence.
Patients: We have had the unique opportunity to follow over a 18 y period 3 sisters with aHUS associated with a *CFH* mutation. Two of the sisters are monozygotic twins. A similar natural evolution and response to treatment would be expected for the three patients, as they all presented with the same at risk polymorphisms for *CFH* and *CD46* and no identifiable mutation in either *CD46* or *CFI*.
Method: Because of previous experience of immediate ESRF at the first aHUS episode and loss of 2Tx by recurrence under no or insufficient plasma therapy in the older sister, intensive PE was used at first episode or recurrence: daily sessions until pl.creat normalisation followed by progressive tapering and indefinitely prolongation at a frequency depending on patient necessity; in case of Tx, one pre-Tx session followed by daily PE for one week and progressive tapering and indefinitely prolongation.
Results: a/ older sister: after 14 y dialysis and 2 immediate Tx losses by recurrence, successful third Tx (Tx3) despite recurrence at month 8. Severe cerebral artery stenosis present after 12 y dialysis. At month 12 post-Tx3, PE was stopped and patient was shift to EC because of allergy to plasma. Pl.creat: 125 µmol/L 3 years post Tx3, at 20 y age; b/ twin 1: after 2 years dialysis, successful first Tx (Tx1) despite several CMV infection-associated recurrences. Pl. creat: 150 µmol/L at age 17 y, 8 y after Tx1. c/ twin 2: complete recovery after first episode. Pl.creat. 58 µmol/L at age 17 y, 10 y after first HUS episode. No cerebral artery stenosis demonstrated in both twins after 10 y evolution.
Conclusions: Intensive en prophylactic PE, eventually shifted to EC allow longterm preservation of renal function of native kidney and of transplant and might prevent large vessels stenosis in *FH* mutation-related aHUS.

CD46-associated atypical HUS with uncommon course caused by mutations in the cblC MMACHC gene

A.H.M. Bouts[1], G.S. Salomons[2], B.Straver[3], V. Gracchi[1], J.W. Groothoff[1], J.C.Davin[1], [1]Dept. of Pediatric Nephrology, [3]Dept. of Pediatric Cardiology, Emma Children's Hospital, Academic Medical Centre, Amsterdam, [2]Department of Clinical Chemistry, Metabolic Unit, VU Medical Centre, Amsterdam, The Netherlands

Membrane cofactor protein (CD46) mutation-associated aHUS has a less severe course than other mutations of complement system factors. We reported recently a child with CD46-associated aHUS who developed an unusual evolution characterized by slowly progressive on-going aHUS leading to end stage renal failure within 12 months. Mutation screening of complement factors showed a missense mutation in exon 11 of CD46. 17 months after starting HD, at age 11, he received a cadaver kidney transplant.
Immunosuppression: prednisolone, cyclosporine, MMF, basiliximab. No HUS relapse occurred after transplantation (Plasma creatinine 80 µmol/L). 24 months after transplantation he developed a progressive fatigue, polypnea and hypoxia without any clinical or laboratory signs of HUS recurrence. Ultrasound of the heart led to the diagnosis of pulmonary hypertension. Etiological investigation of a suspected pulmonary embolism led to the finding of hyper-homo-cysteinemia (plasma 185 µg/L). He died of rapidly cardio-respiratory failure. Necropsy analysis of the lungs showed a massive endothelial proliferation in post-capillary venules pleading for a diagnosis of pulmonary veno-occlusive disease (PVOD). Subsequent DNA analysis revealed two heterozygous mutations of the methylmalonic aciduria cblC with homocystinuria type C gene (MMACHC, NM_015506.2)
Conclusion: Progressive on-going HUS leading to end stage renal failure as well as fatal PVOD observed in this patient probably resulted from the combination of different pathogenic mechanisms of endothelial dysfunction associated with CD46 and cblC MMACHC gene mutations. It indicates that, aside mutations for genes coding for complement factors, investigations to cbl disorders via homocysteine and methylmalonic acid determination should be added to the work-up of every aHUS patient.

Vaccine Induced Allo-HLA reactive Memory T-cells in a Kidney Transplantation Candidate

E.M.W. van der Meer-Prins[1], N.M. van Besouw[2], L.J.A. D'Orsogna[1], P. van der Pol[3], M. Franke-van Dijk[1], Y. M. Zoet[1], A. van der Slik[1], W. Weimar[2], C. van Kooten[3], A. Mulder[1], D. L. Roelen[1], I. I.N. Doxiadis[1], F.H.J. Claas[1], [1]Dept. of Immunohaematology and Blood Transfusion, Leiden University Medical Centre, [2]Dept. of Internal Medicine, Erasmus Medical Centre, Rotterdam, [3]Dept. of Nephrology, Leiden University Medical Centre, The Netherlands

Background: Allo-HLA reactivity by naturally acquired viral specific memory T-cells is common. However, the effect of successful vaccination on the alloreactive memory T-cell repertoire is unclear. We hypothesized that vaccination could specifically induce allo-HLA reactive memory T-cells. Methods: A varicella zoster virus (VZV) IE62 specific CD8 memory T-cell clone was single cell sorted from a VZV seronegative renal transplant candidate, following response to live attenuated varicella vaccination. To analyze the allo-HLA reactivity, the VZV IE62 specific T-cell clone was tested against HLA typed target cells and target cells transfected with HLA molecules, in both cytokine production and cytotoxicity assays. Results: The varicella vaccine induced VZV IE62 specific T-cell clone specifically produced IFNγ when stimulated with HLA-B*55:01 expressing Epstein-Barr virus (EBV) transformed B-cells and HLA-B*55:01 transfected K562 cells (SALs) only. The clone also demonstrated specific cytolytic effector function against HLA-B*55:01 SALs and PHA Blasts. Cytotoxicity assays using proximal tubular epithelial cell (PTEC) and human umbilical cord endothelial cell (HUVEC) targets confirmed the kidney tissue specificity of the allo-HLA-B*55:01 reactivity, and the relevance of the cross-reactivity to clinical kidney transplantation. The results also suggest that molecular mimicry, and not bystander proliferation, is the mechanism underlying vaccine induced alloreactivity.
Conclusions: Varicella vaccination generated a *de novo* alloreactive kidney cell specific cytolytic effector memory T-cell in a patient awaiting renal transplantation. Vaccination induced alloreactivity may have important clinical implications, especially for vaccine timing and recipient monitoring.

A randomized, prospective, open-label, multicenter study comparing the efficacy and safety of conversion to Sirolimus in stable renal transplant recipients with cutaneous squamous cell carcinoma

J.M. Hoogendijk-van den Akker[1], J.N. Bouwes-Bavinck[2], J.W.de Fijter[3], P.N. Harden[4], A.J. Hoitsma[5], [1]Dept. of Internal Medicine, Isala Clinics Zwolle, [2]Dept. of Dermatology, Leiden University Medical Center, [3]Dept. of Nephrology, Leiden University Medical Centre, [4]Dept. of Nephrology, Churchill Hospital Oxford, United Kingdom, [5]Dept. of Nephrology, Radboud University Nijmegen Medical Centre, The Netherlands. (On behave of the members of the RESCUE study group)

Nonmelanoma skin cancer (NMSC) causes significant morbidity and mortality in renal transplant recipients (RTR). Available evidence suggests that conversion to a regimen with Sirolimus may inhibit skin tumor growth. This multi-center, prospective, randomized trial investigated if switching to Sirolimus could diminish the recurrence rate of NMSC. One-hundred-forty-four RTR in the Netherlands and the United Kingdom with at least one biopsy-confirmed cutaneous squamous cell carcinoma (SSC) were randomized to Sirolimus or continuation of their original immunosuppression (mean age 57 years and mean duration of immunosuppression 18 years). They were evaluated every three months for 2 years by a dermatologist for NMSC and hyperkeratotic skin lesions. Many patients in the Sirolimus treatment group stopped using Sirolimus because of different adverse events (n=35). One patient on Sirolimus died of a SCC and one patient developed an acute transplant rejection. Of the patients who completed the 2 year period of follow-up on therapy (Sirolimus n=31; control n=53) less SCC developed in the Sirolimus treatment arm compared with the patients who continued their original immunosuppression (1.7 ± 2.9 versus 3.6 ± 6.3). The time till the first NMSC occurred was significantly longer in the Sirolimus treatment group. We conclude that conversion to Sirolimus-based immunosuppression in RTR can delay the development of NMSC. Strict supervision is, however, necessary to avoid complications.

A single intra-operative high-dose of anti-T-lymphocyte immunoglobulin in DCD donor renal allograft recipients: randomized, open, multicenter study on efficacy and safety to prevent delayed graft function

M.W.F. van den Hoogen[1], A.D. van Zuilen[2], J.J. Homan van der Heide[3], M.M.L. Kho[4] W. Weimar[4], L.H. Hilbrands[1], A.J. Hoitsma[1], [1]Dept. of Nephrology, Radboud University Nijmegen Medical Centre, [2]Dept. of Nephrology, University Medical Centre Utrecht, [3]Dept. of Nephrology, University Medical Centre Groningen, [4]Dept. of Nephrology, Erasmus Medical Centre Rotterdam, The Netherlands

Introduction: Transplantation of DCD (donation after cardiac death) donor kidneys is associated with a high (50-80%) incidence of delayed graft function (DGF) because of extended ischemia reperfusion injury. This injury is modulated by different cells, including T-cells. Currently different anti-T cell antibodies are available. This study evaluated the efficacy and safety of a single intra-operative high-dose of the polyclonal T-cell depleting antibody ATG-Fresenius added to triple immunosuppression to decrease the incidence of DGF and rejection. Methods: We performed a multicenter, randomized, open label study in which all eligible patients (at least 18 years-of-age and recipients of a first renal allograft from a DCD donor) were randomly assigned to receive either ATG-Fresenius i.v. (9 mg/kg body weight) intra-operatively or no induction therapy. Immunosuppression afterwards consisted of tacrolimus, mycophenolate mofetil and steroids. The primary endpoint was the incidence of DGF. Secondary endpoints included incidence of rejection, patient and allograft survival, incidence of infections, and serious adverse events (SAE), all within 3 months after transplantation. Results: The study was prematurely terminated due to a slow inclusion rate. After randomization, 27 patients were treated with ATG-Fresenius and 24 patients served as control group. The groups showed no difference with respect to donor or recipient characteristics. Induction treatment with ATG-Fresenius did not reduce the incidence of DGF (ATG-Fresenius 78% vs. control group 54%, NS). Moreover there was no significant difference in the incidence of clinically suspect rejection (ATG-Fresenius 22% vs. control group 29%), biopsy-proven rejection (ATG-Fresenius 7% vs. control group 8%), allograft survival (ATG-Fresenius 96% vs. control group 83%), and patient survival (ATG-Fresenius 100% vs. control group 96%). Infections were more frequent in the ATG-Fresenius group (65% vs. 38%, P=0.05). Finally, SAE were reported more frequently in the ATG-Fresenius group (59% of patients vs. 29%, P=0.031). Conclusion: Intra-operative administration of a single high-dose of ATG-Fresenius in DCD donor renal allograft recipients, followed by triple immunesuppression appears did not reduce the incidence of DGF or rejection, which is in contrast with studies using other anti-T cell antibodies. More-over ATG-Fresenius appears to be associated with more adverse outcomes. (EudraCT, Number 2007-000210-36)

Survival prognosis of patients starting renal replacement therapy in the Netherlands

A.C. Hemke[1], M.B.A. Heemskerk[1], B.J.J.M. Haase-Kromwijk[1], W. Weimar[2], A.J. Hoitsma[1,3], [1]Dutch Transplant Foundation, Leiden, [2]Erasmus Medical Centre, Rotterdam, [3]Radboud University Medical Centre, Nijmegen, The Netherlands

More than 40 years after the introduction of renal replacement therapy (RRT) in the Netherlands, it is still difficult to predict the prognosis for an individual patient. We analysed survival for a cohort of end stage renal disease patients that started chronic RRT between 1995-2005 (N=16545) from the Renine-database; follow-up was until 1/1/2010. We stratified for age, primary disease, waitlisting (defined as registered at Eurotransplant), transplantation and type of RRT at 90 days after the start of RRT. Patients that were not waitlisted (N=9339) had a 10-year survival of 5%; patients that were waitlisted, but not transplanted (N=1890) had a survival of 16%. Best results were found in the group of transplanted patients (N=5316) with a 10-year survival of 85%. These are overall figures; a very good prognosis from start RRT can be given to the younger transplantable patients with glomerulonephritis, starting with peritoneal dialysis (e.g. age 16-44, N=293, 10 year survival: 92%); poor results from start RRT are seen for instance in older, not transplantable, patients with diabetes, starting with hemodialysis (e.g. age 75+, N=278, 10 year survival: 2%) . Transplantable patients can positively influence their survival by bringing in a living donor. With help of the analysed data the influence of time on dialysis before a living donor kidney transplantation (N=1738), can be estimated. The survival of the waitlisted patients, censored by transplantation is used to estimate the survival on dialysis (10 year survival of 36%) and is combined with the results of transplantation at various time intervals; this resulted in a 22% survival difference from the start of RRT between the pre-emptive (92%) and the late (>3 year) transplantations (70%); this differs from the usual comparison of transplant results counted from the time of transplantation (6-8% survival difference), due to the chance of dying on dialysis before transplantation.
Based on the analysed data a survival prognosis can be given for every patient group stratified for age and primary renal disease; for the transplantable patients with a living donor the effect of dialysis before transplantation on survival chances can be predicted.

Interstitial pneumonitis caused by everolimus: a case control study

M.C. Baas[1], G.H. Struijk[1], D.J. Moes[4], I.A.H. van den Berk[2], R.E. Jonkers[3], J.W. de Fijter[5], J.J. Homan van der Heide[6], I.J.M. ten Berge[1], F.J. Bemelman[1], [1]Renal Transplant Unit, [2]Dept. of Radiology; [3]Dept. of Pulmonology, Academic Medical Centre, Amsterdam, [4]Dept. of Clinical Pharmacy and Toxicology, [5]Dept. of Nephrology, Leiden University Medical Centre, [6]Renal Transplant Unit, Groningen University Hospital, The Netherlands

Background: Inhibitors of the mammalian target of rapamycin (mTORi), sirolimus and everolimus (EVL), are potent immunosuppressive drugs widely used after organ transplantation. They have been introduced in renal transplantation because of their supposed lack of nephrotoxicity and potential anti-oncogenic and anti-atherosclerotic effects. Unfortunately, the use of mTORi is associated with many side effects; one of the most severe is interstitial pneumonitis. Many reports are published on sirolimus-induced pneumonitis; however on everolimus-induced pneumonits (EIP) only case reports exist and the etiology remains unclear. With this case-control study in renal transplant recipients (RTR), we aimed to identify risk factors for the development of an EIP after renal transplantation. Methods: This study was retrospectively conducted as a substudy of a multi-center randomized controlled trial (MECANO). All patients treated with prednisolone/EVL were included in the substudy. RTR, who developed a probable EIP, were identified as cases. We used the following criteria for EIP: (1) exposure to EVL before the onset of pulmonary symptoms, (2) exclusion of infection, (3) radiographic findings on computed tomography (CT) of the chest not compatible with another diagnosis. RTR without pulmonary symptoms served as control patients. Results: 13/102 patients (12.7%) developed an EIP. We found no predisposing factors for the development of EIP, especially no correlation with EVL trough levels or AUC (target 12 µg/l and 150 µg*hr/ml respectively), prior pulmonary condition or smoking. On pulmonary CT, EIP presented as a cryptogenic organizing pneumonia, a non-specific interstitial pneumonitis or a combination of both. Median time (range) to development of EIP after start of EVL was 109 (14-385) days. Pulmonary function tests were performed just after the onset of symptoms in 6/13 cases, showing normal spirometric values with a median (range) TLCO of 56 (38-75)%. All patients recovered clinically within one year after cessation of EVL.
Conclusion: EIP is a common side-effect of EVL in RTR, with an incidence in our study cohort of 12.7%. No clear predisposing factors could be identified in this case-control study. Pulmonary CT showed cryptogenic organizing pneumonia and/or non-specific interstitial pneumonia. The course of EIP is usually benign with disappearance of symptoms within one year after discontinuation of EVL.

What to do with a failed renal allograft: Take it or leave it?

D.G.M. Gommers, L.B. Hilbrands, Dept. of Nephrology, Radboud University Nijmegen Medical Centre, The Netherlands

Background: Whether a failed renal allograft has to be removed uniformly, or can be left in situ until it causes complaints is still a matter of debate. The influence of transplantectomy on the outcome of a subsequent renal transplantation is an important issue in this respect. It is known that anti-HLA antibodies are more readily detected after graft removal. A better characterization of the antibody profile of the candidate for retransplantation, might aid to a better selection of a subsequent graft and thus improve graft survival. In this retrospective study we examined the effect of removal of a failed first allograft on the results of a second transplantation. Methods: We reviewed 145 medical records of patients who experienced failure of their first renal allograft and received a second graft between August 1973 and December 2009. Cases of early failure (within 3 months after transplantation) were excluded. Patients were divided in a group with removal of the first graft before retransplantation (n=70) and a group without transplantectomy (n=75). Multivariate analysis was used to compare the outcome after retransplantation.
Results: The median time between failure of the first renal graft and transplantectomy was 1.9 months (range 0-27 months). The most frequent reasons for graft removal were pain at the site of the failed graft, unexplained fever, and hematuria. Patients who underwent graft removal had a shorter survival of the first graft and more frequently lost the first graft due to an acute rejection as compared to patients without graft removal. In addition, patients who underwent graft removal were younger at the time of the second transplantation and more often received a second graft from a cadaveric donor. The median time of follow-up after the second transplantation was 7.0 years. After adjustment for relevant covariables in multivariate analyses, there were no statistically significant differences in incidence of delayed graft function, acute rejection rate, graft survival, and patient survival between the two groups.
Conclusion: Our data indicate that removal of a failed first allograft does not influence the outcome of a second renal transplantation. However, other factors such as the opportunity to discontinue immunosuppression, and the avoidance of a chronic state of low grade inflammation, may favour a policy of pre-emptive graft removal in all cases.

Identification of Patients at High Risk for Infections after Liver Transplantation

S.H. van Olphen[1], I.C.A.W. Konings[1], L.H. de Grim[2], G. Kazemier[3], B.E. Hansen[1], R.A. de Man[1], X. Rogiers[2], C.A.M. Schurink[4] and H.J. Metselaar[1], [1]Dept. of Gastroenterology and Hepatology, Erasmus University Medical Centre Rotterdam, [2]Dept. of Liver Transplantation, University Hospital Ghent, Belgium, [3]Depst. of Surgery, [4]Dept. of Medical Microbiology and Infectious Diseases, Erasmus University Medical Centre, Rotterdam, The Netherlands

Objectives Liver transplantation (LTx) is a successful therapy for patients with end-stage liver disease. Infections are an important cause of morbidity and mortality in the first three months after transplantation with a reported incidence up to 60 %. In order to reduce infection rates, one option is to identify patients at high risk for early post-operative infection and adapting standard postoperative therapy accordingly.
This study was conducted to develop a model for predicting both bacterial and fungal infections. Methods: Medical records of 200 LTx recipients transplanted between 2005 and 2009 at the Erasmus MC Rotterdam were reviewed. We registered all infections according to CDC definitions during the first three months after LTx and noted potential risk factors for developing infections. Multivariate logistic regression was used to create a predictive model for infections in general. Subsequently, we validated this model in another cohort of 94 LTx recipients transplanted between 2007 and 2009 at the Ghent University Hospital. Results: The model consists the following parameters: (1) preoperative haemodialysis; (2) preoperative *Candida* colonization; (3) history of abdominal surgery; (4) Sodium < 130 mmol/l on day of LTx; (5) intubation $\geq$ 3 days after LTx; (6) relaparotomy within 5 days for intra-abdominal bleeding, anastomosis leakage, vascular insufficiency or (7) retransplantation. In high risk patients 2 or more conditions were present. In the Rotterdam cohort 81% of high risk patients developed an infection versus 50% of low risk patients [OR 4.273 (2.1-8.9)]. Surgical site infections were the most frequent and 41 out of 109 bacterial infections (38 %) were caused by 41 Enterococcus species. In the Ghent cohort 80 % of the high-risk patients developed an infection compared to 48 % of the low-risk patients [OR 4.3 (CI 1.3-14.2)]
Conclusion: This model based on 7 clinical parameters identifies patients at high risk for bacterial and fungal infections in the first 3 months after liver transplantation. Close monitoring, starting anti-bacterial and fungal prophylactic treatment and minimization of immunosuppressive therapy should be considered in these high risk patients.

Hypertensive kidney donors perform well at short term post-donation follow-up

H. Tent[1], E. van den Berg[1], H.S. Hofker[2], R.J. Ploeg[2], G.J. Navis[1], J.J. Homan van der Heide[1], [1]Dept. of Internal Medicine Division of Nephrology and [2]Dept. of Surgery, University Medical Centre Groningen, The Netherlands

Due to donor organ shortage, living kidney donor selection has become more liberal with acceptation of hypertensive donors. This raises a new set of issues. Little is known whether hypertensive donors are at increased risk for impaired residual renal function post-donation. Furthermore, the course of blood pressure following kidney donation in preexistent hypertensive donors is also poorly documented. We compared short term outcome of hypertensive donors to sex, age and BMI matched control donors. Hypertension was defined as pre-donation antihypertensive drug use. All donors had GFR (^{125}I-iothalamate) and ERPF (^{131}I-hippuran) measured 4 months prior and 2 months post-donation. Renal reserve capacity (GFR_{RC} and $ERPF_{RC}$) was measured by use of dopamine and was calculated as [stimulated renal function – basal renal function]. A subset of donors had serum creatinine and spot-urine protein excretion measured one year post-donation. Included were 46 hypertensive donors and 68 control donors (both 54% male, mean age and BMI 57±8 years and 28±3 kg/m^2). Pre-donation MAP was significantly higher in hypertensive donors compared to control donors 101±11 *vs.* 94±9 mmHg. There were no differences in basal renal function or reserve capacity: GFR and ERPF 118±20 *vs.* 113±18 and 419±88 *vs.* 412±74 mL/min, and GFR_{RC} and $ERPF_{RC}$ 10±10 *vs.* 9±10 and 95±70 *vs.* 96±50 ml/min respectively (all $p>0.15$). Post-donation, hypertensive donors had similar MAP compared to controls: 99±9 *vs.* 96±10 mmHg respectively. The previously described increase in blood pressure could not be detected in hypertensive donors, while in control donors MAP increased ($p<0.05$). Again, there were no differences in basal renal function and reserve capacity between hypertensive donors and controls: GFR and ERPF 73±113 *vs.* 70±13 and 266±50 *vs.* 264±46 ml/min, and GFR_{RC} and $ERPF_{RC}$ 1±4 *vs.* 2±4, and 38±33 *vs.* 40±21 ml/min respectively. One year follow-up was available for 25 hypertensive donors and 25 controls. There was no difference in serum creatinine, urinary protein excretion or renal function by MDRD: 108±23 *vs.* 114±22 µmol/L, 0.1[0] *vs.* 0.1[0] g/L, and 54±12 *vs.* 49±11 ml/min/1.73m^2.

In summary, hypertensive living kidney donors perform similarly to control donors early and one year post-donation. Despite these reassuring findings we like to emphasize that these donors were strictly selected and well regulated with strict blood pressure management. More long term data are necessary to ensure long term donor safety.

The effect of ritonavir on pharmacokinetics of tacrolimus in pre-transplant kidney failure patients with HIV

H.A. Crommelin[1], A.D. van Zuilen[2], T. Mudrikova[3], M.P.H. van den Broek[1], E.M. van Maarseveen[1], [1]Dept. of Clinical Pharmacy, [2]Dept. of Nephrology and Hypertension, [3]Dept. of Internal Medicine and Infectious Diseases, University Medical Centre Utrecht, The Netherlands

Background: The introduction of highly active antiretroviral therapy (HAART) has improved life expectancy of HIV patients and therefore chronic complications such as kidney failure are seen more frequently. An increasing number of HIV patients is accepted for kidney transplantation. Ritonavir-boosted protease inhibitors are frequently used in HAART. Ritonavir inhibits the cytochrome P450 CYP 3A enzyme and transporting protein P-glycoprotein (Pgp). In kidney transplantation the calcineurin inhibitor tacrolimus, which is a substrate for both CYP 3A and Pgp, is predominantly used for transplant rejecttion prophylaxis. Here we present data on the influence of ritonavir on tacrolimus pharmacokinetics in pretransplant kidney failure patients with HIV.
Methods: Six HIV patients accepted for kidney transplantation and treated with a ritonavir-containing regimen were included. At least 12 blood samples were drawn in each patient after an oral test dose of tacrolimus (Prograft®). Pharmacokinetic curves of tacrolimus in all patients were analyzed. A population model was created using Monte Carlo-simulation in MW\Pharm (PK Software edition 3.60, Medi\Ware). Results: In ritonavir users the area under the curve (AUC) after a 5 mg dose of tacrolimus was 50-fold higher than in non-ritonavir users (8680 vs 174 ng·h/mL). The mean oral clearance (CL/F) in ritonavir users was 25-fold lower than in non-ritonavir users (0.98 vs 24.2 L/h). The pharmacokinetic curve of tacrolimus in ritonavir users did not show the usual peak and trough pattern, but rather resembled a flat line with a half life up to 20 days. This resulted in a 40% lower estimated AUC when conventional target trough levels were applied. In four patients who were monitored longer than 24 hours, tacrolimus concentrations were above 3 ng/mL for at least one week after administration of a single oral dose.
Conclusion: Ritonavir changes pharmacokinetics of tacrolimus in pretransplant kidney failure patients with HIV dramatically, requiring lower dosing and close pharmacokinetic monitoring in these patients. As a result of "flat line" pharmacokinetic curves due to extremely prolonged half lives, target tacrolimus trough levels should be higher (17.5 ng/mL one month and 10 ng/mL one year after transplantation) in these patients compared to non-ritonavir users in order to achieve an equal exposure in terms of AUC.

Effect of routinely inserted gentamycin-containing collagen sponges on surgical site infections after hand-assisted laparoscopic donor nephrectomy

V. P. Alberts[1], R.C. Minnee[1], F.J. Bemelman[2], K.A.M.I. van Donselaar – van der Pant[2], M.M. Idu[1], [1]Dept. of Surgery, [2]Renal Transplant Unit, Department of Nephrology, Academic Medical Centre, Amsterdam, The Netherlands

Introduction: Advances in surgical methods have reduced the incidence of postoperative surgical site infections (SSI's) after renal transplantation. However, the rise of hand-assisted laparoscopic donor nephrectomy (HALDN) might have increased the infection rate compared to laparoscopic nephrictomy. Since 2007, our centre routinely applies gentamycin-containing collagen sponges (GCCS) when closing the wound. The effect of GCCS on SSI's is not clearly elucidated. In this study we assess the effects of GCCS on postoperative SSI's. Patients and methods: A single-center retrospective cohort analysis of 200 (100 without GCCS and 100 with GCCS) living HALDN's was performed. Between December 2004 and November 2007 we included 100 patients without GCCS and from November 2007 to July 2010 we included 100 patients with GCCS. An SSI was defined according to clinical manifestation; a painful, red, swollen wound with or without purulence or fever, within 60 days after surgery. Results: Patient characteristics were comparable between both groups. In the group without GCCS 11 postoperative complications occurred (11%), of which 6 SSI's (6%). In the group with GCCS, we found 4 complications (4%) without infections. We calculated a phi-coefficient of -0.18 (P=0.01), which indicates a significant protective effect of GCCS on SSI's. Postoperative creatinine levels after three months were 1.17 mg/dL without GCCS and 1.19 with GCCS (P=0.68). Conclusion: The use of gentamycin-containing collagen sponges significantly reduces the risk of postoperative surgical site infections, without compromising kidney function.

The effect of rituximab infusion on cytokine levels in renal transplant patients

M.W.F. van den Hoogen, J.W. Dieker, J. van der Vlag, L.B. Hilbrands, Dept. of Nephrology, Radboud University Nijmegen Medical Centre, The Netherlands

Introduction: In a randomized, placebo controlled trial, we evaluate the efficacy and safety of a single dose (375 mg/m2) of the B-cell depleting anti-CD20 antibody rituximab, added to standard immunosuppression, to prevent acute rejection after renal transplantation (ClinicalTrials.gov NCT00565331). However, infusion of rituximab can be accompanied by a cytokine release syndrome. These cytokines can modulate the immune system and thereby affect clinical outcome after transplantation. We therefore performed a detailed study on cytokine levels after infusion of rituximab. Methods: At the start of transplant surgery, patients received 100 mg prednisolone and 2 mg clemastin i.v., after which rituximab or placebo was administered at an increasing infusion rate. Blood samples were drawn in 20 recipients of a living donor kidney (10 rituximab, 10 placebo) at the morning of transplantation (baseline), at 2 and 4 hours after the start of infusion (t=2 and t=4), and the next morning (t=24). Sera were tested for IL-2, IL-6, IL-10, IL-12, IL-17, TNF-α, and IFN-γ by a commercial ELISA kit. A p-value of < 0.05 was considered significant. Results: Baseline cytokine levels did not differ between the rituximab and placebo group. A significant rise in the levels of IL-6 and IL-10 was observed in both groups at all time points. However, at t=2, the levels of IL-6 and IL-10 were significantly higher in the rituximab group than in the placebo group. Moreover, at t=24 the levels of all cytokines were significantly higher compared with baseline in the rituximab group, while in the placebo group only IFN-γ and IL-17 levels were elevated. IL-2 levels were significantly decreased at all time points compared with baseline in the rituximab group, but only at t=2 in the placebo group.
Conclusion: Rituximab infusion in renal transplant patients is associated with marked changes in the levels of pro- and anti-inflammatory cytokines. This means that administration of rituximab may have clinically relevant immunological effects beyond B-cell depletion.

Characterization of urinary T-cells in kidney transplantation patients with polyomavirus associated nephropathy or allograft rejection

W.B. van Doesum, W.H. Abdulahad, W.J. van Son, C.A. Stegeman, J.S. Sanders, Dept. of Nephrology, University Medical Centre Groningen, The Netherlands

Objective: In the last two decades, with the development of better immunosuppressive drugs, polyoma virus associated nephropathy (PVAN) has emerged as a major problem in renal transplantation. It has been proven that fluorescent assisted cell sorting can be used for characterization of immune cells in urine, which presumably reflects the immune status in the kidney of a patient. The objective of this study is to characterize different T-cell populations in renal transplant patients who experience PVAN (BK-nephropathy) or an episode of allograft rejection. Methods: Using four color flow cytometric analysis $CD4^+T_{CM}$ cells ($CD45RO^+CCR7^+CD3^+CD4^+$ T cells), $CD8^+T_{CM}$ cells ($CD45RO^+CCR7^+CD3^+CD8^+$ T cells), $CD4^+T_{EM}$ cells ($CD45RO^+CCR7^-CD3^+CD4^+$ T cells) and $CD8^+T_{EM}$ cells ($CD45RO^+CCR7^-CD3^+CD8^+$ T cells) were quantified in urine and peripheral blood of renal transplant patients with BK viruria (n =2), BK viraemia (n = 5) and biopsy proven BK nephropathy (n= 4), patients with biopsy proven allograft rejection (n = 10) and renal transplant patients with an uncomplicated course post transplantation (n = 11). Results: In patients with allograft rejection the number of urine $CD8^+T_{CM}$ cells was significantly increased compared to patients with BK-nephropathy (P = 0.017) or patients with no complications (P = 0.019). Between the patient group with BK-nephropathy and the controls no significant change in urinary $CD8^+T_{CM}$ cells was found. The number of $CD4^+T_{CM}$ cells in urine was not different between the three groups.

In peripheral blood of patients with BK-nephropathy a significant decrease of $CD4^+T_{CM}$ cells (P = 0.002) and $CD4^+T_{EM}$ cells (P = 0.012) was found compared to peripheral blood of renal transplant patients with uncomplicated course. In peripheral blood of patients with allograft rejection a significant decrease of $CD4^+T_{CM}$ cells (P = 0.020), $CD4^+T_{EM}$ cells (P = 0.008), $CD8^+T_{CM}$ cells (P = 0.008) and $CD8^+T_{EM}$ cells (P = 0.023) was found compared to peripheral blood of renal transplant patients with no complications.

Conclusions: A decrease of $CD4^+T_{EM}$ cells and $CD8^+T_{EM}$ cells in the blood of renal transplant patients with rejection or BK-nephropathy could indicate a migration of these cells from the blood to the kidney.

The appearance of $CD8^+T_{CM}$ cells in urine could be a diagnostic tool to distinguish between allograft rejection and BK-nephropathy in renal transplant patients.

The role of graft-resident hematopoietic progenitor cells in intragraft leukocyte chimerism after liver transplantation

V. Moroso[1], Q. Pan[1], F. Famili[1], T. Cupedo[2], G. Kazemier[3], H.W. Tilanus[3], H.L.A. Janssen[1], H.J. Metselaar[1], L.J.W. van der Laan[3] and J. Kwekkeboom[1], Depts. of [1]Gastroenterology and Hepatology, [2]Hematology and [3]Surgery and Laboratory of Experimental Transplantation and Intestinal Surgery, Erasmus Medical Centre, Rotterdam, The Netherlands

Sustained leukocyte chimerism within the liver graft after LTx may have regulatory effects on recipient immune responses to the allograft. In this study we analyzed the duration of leukocyte chimerism within human liver grafts after LTx and studied the role of hepatic hematopoietic stem cells (HSC) in this phenomenon. Using explants of non-functioning liver grafts obtained during re-transplantation (n=5), we observed that mature donor-derived lymphocytes, among which NK cells, NKT cells, T cells, and $CD14^+$ monocytes/Kupffer cells, remained detectable in liver grafts up to 2 years after LTx. Mononuclear cells isolated from liver grafts before transplantation contained $CD34^+$ HSC, among which we detected early NK cell precursors and all sequential stages leading to the generation of mature NK cells (n=15). Isolated hepatic HSC gave rise to granulocyte/monocyte colonies (CFU-GM), while specific *in vitro* culture of NK cell progenitors generated functional NK cells. Surprisingly, one week after LTx donor-derived HSC were fully replaced by recipient-derived $CD34^+$ HSC, indicating that persistence of donor-derived leukocytes within liver grafts after LTx is not caused by sustained intragraft persistence of donor HSC. Interestingly, during the first weeks post-LTX donor HSC migrated from the graft and were detected in the recipient circulation (~2-8% of peripheral blood $CD34^+$ cells, n=5). Thereafter, donor HSC were not detected in the recipient circulation, consistently with the observation that all intragraft HSC were replaced by recipient-derived ones. To study whether human hepatic HSC can give rise to mature progeny in the liver, luciferease-transduced human liver $CD34^+$ cells were transferred into irradiated NOD/SCID mice. Substantial numbers of CFU-GM were detected in the mouse bone marrow, but a robust luciferase signal, indicating presence of progeny, was only observed in the liver.
In summary, our results show that donor-derived leukocytes remain present in human liver grafts for at least 2 years after LTx. In contrast, hepatic HSC are rapidly replaced by recipient-derived HSC after LTx. Sustained leukocyte chimerism within liver grafts after LTx may be derived from donor-derived HSC that engrafted into the recipient bone marrow and give rise to progeny which home to the liver graft.

Living Mesenchymal Stem Cells Disappear Rapidly after Intravenous Infusion

M.J. Hoogduijn[1], E. Eggenhofer[2], F.C. Popp[2], P. Renner[2], W. Weimar[1], C.C. Baan[1], M.H. Dahlke[2], [1]Dept. of Internal Medicine, Erasmus Medical Centre, Rotterdam, The Netherlands, [2]Dept. of Surgery, University Medical Centre Regensburg, Regensburg, Germany

Introduction: Mesenchymal stem cells (MSC) have potential for application in organ transplantation as an immunomodulatory and regenerative agent. The survival and localization of MSC after infusion is however not clear and studies have been limited to tracking of label, rather than of MSC. In the present study we re-isolated MSC after infusion and brought them into culture to confirm their viability. Methods: $0.5x10^6$ MSC of C57Bl6 mice expressing red-fluorescent protein (RFP) were infused into syngeneic wild-type mice via tail vein injections. After 5 min, 1h and 24h, blood, lungs, spleen, liver, kidneys, and bone marrow were collected, and processed for the establishment of cultures. After 10 days the cultures were examined by microscopy and flow cytometry for the detection of living RFP-MSC. Results: Microscopic analysis demonstrated the presence of multiple colonies of RFP-MSC in cultures from lung tissue harvested 5 min and 1h after MSC infusion. Lung cultures established after 24h showed strongly reduced numbers of RFP-MSC. No RFP-MSC were found in cultures of all other tissues at any other time point. Flow cytometric analysis of the cultures demonstrated the expression of the MSC markers CD44 and CD73 on a subset of cells in cultures of lung, spleen, kidney and bone marrow tissue. In lung cultures established 5 min and 1h after MSC infusion, 0.2-1% of $CD44^+CD73^+$ cells expressed RFP. The number of RFP-MSC was strongly reduced in lung cultures established 24h after MSC infusion and in spleen, kidney and bone marrow cultures $CD44^+CD73^+$ cells were of recipient origin only.
Conclusions: These results indicate that intravenously infused MSC primarily localize to the lungs. The majority of viable MSC disappear within 24h. As viable MSC are not traced back in other organs, they are unlikely to survive for more than 24h after infusion. This suggests that effects of MSC after infusion are mediated via secondary mechanisms.

Spontaneous tumorigenic transformation of mesenchymal stem cells caution clinical application

Q. Pan[1], S.M.G. Fouraschen[2], J. de Jonge[2], G. Kazemier[2], J. Kwekkeboom[1], H.J. Metselaar[1], H.W. Tilanus[2], H.L.A. Janssen[1], L.J.W. van der Laan[2], Depts. of [1]Gastroenterology and Hepatology and [3]Surgery and Laboratory of Experimental Transplantation and Intestinal Surgery, Erasmus Medical Centre, Rotterdam, The Netherlands

Objective: Bone marrow (BM)-derived mesenchymal stem cells (MSC) have tissue repair and immunomodulatory capacities and therefore have high therapeutic potential for end-stage organ failure in the context of organ transplantation. The aim of this study is to investigate the potential concern of spontaneous tumorigenic transformation of *in vitro* expanded MSC derived from BM and adult human liver. Methods and Results: We observed spontaneous transformation of human BM MSC in seven cultures beyond passage eleven. In contrast, we did not observe spontaneous transformation of liver-derived MSC in the same culture condition. However, transformation of liver MSC occurred during the process of undergoing hepatic differentiation using serum-free culture conditions containing growth facts, including HGF, bFGF and EGF. Transformed stem cells formed typical mammospheres, as previously reported for cancer stem cells. These mammospheres can be detached and maintained in serum-free medium, whereas the transformed cells displayed an epithelial-like morphology and rapidly expanded at least 30 passages in serum-containing medium. Normal MSC highly express CD44, CD73, CD166 and CD105, but transformed MSC were found negative for these markers. Subcutaneous engraftment of transformed MSC in immunodeficient NOD/SCID mice demonstrated their tumorigenic potential and resulted in solid tumors showing liposarcoma-like histology. High-resolution genome-wide DNA analysis using the Affymetrix Cytogenetics Array showed an identical copy number variation pattern between parental and transformed MSC, excluding the possibility of tumor contamination.
Conclusion: In this study, we showed the spontaneous tumorigenic transformation of both BM and liver-derived MSC occur rather frequently at advanced passages. This cautions the clinical application of MSC. Currently, we are attempting to search markers to identify transformed MSC, which could be potentially used for screening of transformed cells in clinical grade cultures for MSC therapy.

Mannose-binding lectin induces tubular epithelial cell death following renal ischemia reperfusion injury independent of complement activation

P. van der Pol[1], N. Schlagwein[1], D.J. van Gijlswijk[1], I.M. Bajema[2], M.R. Daha[1], C. van Kooten[1], Depts. of [1]Nephrology and [2]Pathology, Leiden University Medical Centre, The Netherlands

Background: Ischemia/reperfusion (I/R) injury is an inevitable event in kidney transplantation and has a major impact on short- and long-term graft survival. Recently, we showed that transient inhibition of mannose-binding lectin (MBL) preserved tubular integrity and renal function in a rat model of renal I/R, whereas downstream inhibition of C3 and C5 was not protective. In the present study we explored the harmful role of MBL in renal I/R injury. Methods: In vivo, rats were subjected to 45 minutes of unilateral renal ischemia. Rats were sacrificed at different time points after reperfusion and kidneys were harvested for PCR, histology and staining for complement and tubular injury marker KIM-1. Additionally, immediately following reperfusion rats were injected with purified human MBL (50 µg) and 3 hours later both control and ischemic kidney were harvested and stained for human MBL. To investigate direct effects of MBL, human proximal tubular epithelial cells (PTEC) and endothelial cells were incubated with purified human MBL (0-20µg/ml) and after 24 hours cell death was determined by propidium iodide (PI) staining. Results**:** Despite absence of a protective effect of C3 and C5 inhibition in renal I/R, specific staining for complement components showed strong deposition of C3 and C5b-9 in ischemic kidneys. However, this was a relatively late process and only observed from 24 hours onwards. In contrast, induction of I/R resulted in extensive tubular expression of KIM-1, accompanied by acute tubular necrosis (ATN), within 24 hours. Injection of human MBL after reperfusion resulted in extensive vascular leakage of MBL into the interstitium reaching the tubular epithelial cells (mainly in the cortico-medullary border) in the ischemic, but not in the control kidney. Exposure of cultured PTEC (HK-2 and primary cells) to purified MBL resulted in a dose-dependent detaching and death of cells within 24 hours. In contrast, endothelial cells (HUVEC and ECRF) were not affected by addition of MBL. MBL-induced epithelial cell death could be completely abrogated by the specific inhibitor D-Mannose.
Conclusions: Renal I/R is accompanied by vascular leakage of MBL into the interstitial space. Exposure of tubular epithelial cells to MBL induces epithelial cell death, one of the earliest events in I/R and associated with renal function loss. Therefore, in kidney transplantation short interference with MBL may have important therapeutical implications.

IL-2-independent induction of novel CD4+CD25+CD127-FOXP3+ T cells by mesenchymal stem cells and natural regulatory T cells

A.U. Grohnert, M.J. Hoogduijn, W. Weimar, C.C. Baan, Dept. of Internal Medicine, Erasmus Medical Centre, Rotterdam, The Netherlands

Introduction: Mesenchymal stem cells (MSC) and CD4+CD25+CD127-FOXP3+ natural regulatory T cells (nTreg) represent candidates for cellular therapy in organ transplant patients due to their immunosuppressive functions. Hence, it is essential to investigate the interactions between these cell types and existing immunosuppressive medication to circumvent mutual impairment. An immunomodulatory mechanism employed by MSC is the induction of T cells with a regulatory phenotype, associated with elevated levels of IL-2. The present study aimed to elucidate whether a similar effect is evoked by nTreg and whether the effect is influenced by basiliximab, an anti-IL-2 receptor antibody. Methods: MSC were isolated from perirenal fat tissue of kidney donors. Peripheral blood mononuclear cells (PBMC) and nTreg were obtained from blood bank donors. The immunomodulatory effect of MSC (1:2.5) and nTreg (1:10) on PBMC subsets was studied without and in the presence of basiliximab (4µg/mL) by means of mixed lymphocyte reactions (MLR) and subsequent flow cytometric analysis. nTreg were labeled with PKH26 to allow discrimination from newly generated T cells with a regulatory phenotype. Results: MSC and nTreg dose-dependently decreased the proliferation of allo-activated PBMC subsets. MSC and nTreg in combination resulted in a cumulative inhibition of proliferation. Further, it was observed that MSC and nTreg induced the generation of CD4+CD25+CD127-FOXP3+ T cells which were not of nTreg origin. MSC and nTreg attained a 5.6-fold ($p=0.02$) and a 2.6-fold ($p=0.01$) increase, respectively. The addition of basiliximab maintained this phenomenon with MSC and nTreg achieving a respective induction of CD4+CD25+CD127-FOXP3+ T cells by 6.2-fold ($p<0.001$) and 2.3-fold ($p=0.005$).
Conclusion: This study demonstrates that MSC and nTreg contribute to the generation of an immunosuppressive environment via two shared mechanisms: i. inhibition of allo-activated effector T cells and ii. induction of T cells with a regulatory phenotype. The fact that basiliximab does not hamper the induction of novel CD4+CD25+CD127-FOXP3+ T cells by MSC and nTreg indicates promising prospects for combined cellular- and drug-mediated immunotherapy in organ transplant patients.

Expression of dsRNA sensors in the renal transplant is increased during cytomegalovirus, Epstein-Barr virus and BK virus infection

K.M. Heutinck[1,2], J. Kassies[1,2], N. Claessen[3], K.A.M.I. van Donselaar-van der Pant[2], F.J. Bemelman[2], S. Florquin[3], J. Hamann[1], I.J.M. ten Berge[2], [1]Dept. of Experimental Immunology, [2]Renal Transplant Unit, Dept. of Internal Medicine and [3]Dept. of Pathology, Academic Medical Centre, Amsterdam, The Netherlands

Background: Viral infection can cause severe interstitial nephritis associated with injury of renal tubular epithelial cells and lymphocyte influx. Sensors that recognize dsRNA, an intermediate formed during viral replication, can be expressed by immune and non-immune cells. The dsRNA receptors Toll-like receptor 3 (TLR3), melanoma differentiation associated protein 5 (MDA5) and retinoic acid inducible gene-I (RIG-I) promote anti-viral and pro-inflammatory responses and their expression is enhanced by dsRNA. Methods: Here, we studied the expression of these dsRNA receptors in renal transplant biopsies during infection with cytomegalovirus (CMV, n=7), Epstein-Barr virus (EBV, n=4) and BK virus (BKV, n=7). Viral infection was diagnosed by positive peripheral blood PCR, specific antibody conversion and/or immunohistochemistry. Expression of TLR3, MDA5 and RIG-I was analyzed by PCR in total biopsy lysates and by immunohistochemical staining to determine which cell types expressed the receptors. Results: TLR3 transcript levels were significantly elevated during CMV ($p=0.02$), EBV ($p=0.03$) and BKV ($p<0.01$) infection compared to levels found in stable graft biopsies (n=5). Transcript levels of MDA5 and RIG-I were significantly increased during CMV ($p<0.03$) and BKV ($p<0.05$) but not during EBV infection. TLR3 protein was detectable in tubuli and in occasional immune cells present in the interstitium and glomeruli, which morphologically resembled macrophages. During viral infection, both tubular TLR3 expression and the number of TLR3 positive immune cells were increased. MDA5, known to be broadly expressed, was present at low levels in all cell types. Yet, high MDA5 expression was predominantly found in proximal tubuli. RIG-I was expressed in tubular epithelium, infiltrating lymphocytes and endothelial cells and expression was enhanced during viral infection.
Conclusion: dsRNA receptor expression in the renal transplant is increased during viral infection. TLR3, MDA5 and RIG-I are expressed by tubular epithelial cells, which enable them to provoke anti-viral immune responses.

Induction of VZV-specific effector memory T-cell response by herpes zoster infection after lung transplantation

N.M. van Besouw[1], P.Th.W. van Hal[3], G.M.G.M. Verjans[2], J.M. Zuijderwijk[1], W. Weimar[1], Depts. of [1]Internal Medicine – Transplantation, [2]Virology, [3]Respiratory Medicine, Erasmus Medical Centre, Rotterdam, The Netherlands

Purpose: Primary infection with VZV causes varicella, and VZV reactivation results in herpes zoster (HZ). Compared to healthy individuals, the incidence and severity of HZ is higher in transplant recipients. We questioned whether VZV-specific T-cell reactivity is impaired in transplant recipients, and whether this reactivity restores after HZ. Methods and materials: Patients and controls had experienced varicella during childhood. $CD3^+$ T-cells and $CD14^+$ monocytes were isolated from PBMC from transplant recipients (n=11) who did not develop HZ, and healthy gender and age matched volunteers (n=13). Additionally, PBMC were sampled from 5 recipients who experienced a HZ infection after lung transplantation. $CD14^+$ were differentiated into mature moDCs and infected with VZV. T-cells were co-cultured with autologous VZV-infected moDCs and subjected to flowcytometric analysis to identify the phenotype (naïve (NA: $CCR7^+CD45RO^-$), central (CM: $CCR7^+CD45RO^+$) and effector memory (EM: $CCR7^-CD45RO^+$) T-cells) and the frequency of VZV-reactive T-cell subsets (i.e. IFN-γ^+). Results: The proportion NA, CM and EM within the CD4 and CD8 cells were comparable. No difference was found in the percentage of VZV-specific CD4 and CD8 NA and CM and CD4 EM T-cells between transplant recipients and controls. Remarkably, fewer transplant patients without HZ (5/11) had circulating VZV-specific CD8 EM T-cells compared to controls (10/13). The percentage VZV-specific CD8 EM cells was significant lower in patients without HZ compared to controls (p=0.05). All lung transplant recipients who experienced HZ had detectable frequencies of VZV-specific CD8 EM, and this percentage was significantly higher compared to transplant recipients without HZ (p=0.003).
Conclusion: The VZV related complications after transplantation may results from an impaired VZV-specific EM T-cell response. Prophylactic VZV vaccination before transplantation might boost the patient's memory T-cell repertoire and thereby reduces the morbidity associated with HZ after transplantation.

ABCB1 expressing memory CD8+ T cells; a new memory CD8+ T cell subset?

S.H.C. Havenith[1,2], S.L. Yong[1,2], B. Piet[2], S.D. Koch[1,2], R.A.W. van Lier[2], R.J.M. ten Berge[1], [1]Renal Transplant Unit, Dept. of Internal Medicine and [2]Dept. of Experimental Immunology, Academic Medical Centre, Amsterdam, The Netherlands

Recently a subset of memory $CD8^+$ T cells resistant to chemotherapy was discovered, able to efflux cytostatic drugs using the multidrug efflux protein ABCB1. Multidrug efflux proteins are highly expressed on stem cells including cancer stem cells, making them less susceptible to xenobiotics. The immunosuppressive drugs cyclosporine, tacrolimus, sirolimus and glucocorticoids are also substrates for the ABCB1 transporter. Therefore, the ABCB1 bearing memory $CD8^+$ T cells might play an important role in rejection of transplanted organs, and in hampering the induction of tolerance. The ABCB1 bearing memory $CD8^+$ T cells can be identified by their high expression of CD161 and IL-18Rα. Here we questioned whether $CD161^{++}$/IL-$18R\alpha^+$, ABCB1 bearing memory $CD8^+$ T cells have different proliferative and homing capacities compared to CD161-/IL-18Rα- "classical" memory $CD8^+$ T cells.
We studied paired peripheral blood and lymph node samples (n=15); paired peripheral blood and lung samples (n=5); bone marrow (n=12); spleen (n=9) and cord blood (n=5). The frequency and phenotype of the $CD161^{++}$/IL-$18R\alpha^+$ memory $CD8^+$ T cells in the different compartments was determined by flow-cytometric analysis. We sort purified $CD161^{++}$/IL-$18R\alpha^+$ memory $CD8^+$ T cells out of peripheral blood mononuclear cells of healthy volunteers and stimulated them in vitro under various different conditions.
$CD161^{++}$/IL-$18R\alpha^+$ $CD8^+$ T cells were found in the circulation of all adult individuals tested (n= 30, mean 6.4% of $CD8^+$T-cells, SEM 1.03) but not in cord blood (p=0.01). Purified $CD161^{++}$/IL-$18R\alpha^+$ memory $CD8^+$ T cells from healthy individuals were not able to proliferate in response to a TCR-stimulus in combination with costimulation (aCD3aCD28). However they did divide after addition of $CD4^+$ T cells and monocytes, or after addition of IL-2 or IL-12 in combination with IL-18. $CD161^{++}$/IL-$18R\alpha^+$ memory $CD8^+$ T cells were found mainly in peripheral blood, spleen and bone marrow and significantly at lower numbers in lymph nodes (p=0.006) and lungs (p=0.05). They expressed the chemokinereceptors CCR5 and CXCR6 but lacked CCR7, suggesting that they can migrate to inflamed tissue but not to non-inflamed lymph nodes.
Thus, $CD161^{++}$/IL-$18R\alpha^+$, ABCB1 bearing memory $CD8^+$ T cells form a distinct memory $CD8^+$ T cell subset with specific proliferative and homing capacities, which may play an important role in the rejection of transplanted organs.

Viability of the human small bowel graft in the scope of intestinal transplantation (ITx)

A.M. Roskott[1], H.G.D. Leuvenink[1], G. Dijkstra[2], R.J. Ploeg[1], H. v. Goor[3], V.B. Nieuwenhuijs[1], Depts. of [1]Surgery, [2]Gastroenterology and Hepatology and [3]Pathology, Groningen University Medical Centre, Groningen, The Netherlands

Introduction: Survival after ITx has improved. Results, however, remain inferior compared with other transplant types. Pre-transplant graft viability is the key factor of outcome. The intestinal graft is extremely sensitive to transplant-related trauma such as brain death (BD) and ischemia-reperfusion-injury. BD has been recognized to induce inflammation causing reduced quality of donor organs. The effects of BD on the intestine and the quality of intestinal grafts from human donors deceased after cardiac death (DCD) are largely unknown. This descriptive study aims to assess intestinal graft viability and explore transplantation-related graft deterioration in different donor types. Methods Medical students were trained to collect patient data, blood and intestinal samples during multi-organ-donation procedures (DBD/DCD) after aortic flush with UW. Histological Park score was assessed. Blood was drawn before start of aortic flush. Control blood was collected from 5 living kidney donors. Serum lipopolysaccharide binding protein (LBP) and CRP was measured. Results: Sixty intestinal tissue samples were recovered from 33 donors (22 DBD, 11 DCD). Mean BD duration was 653 min, mean CS time was 254 min, mean total ischemia time (TIT) was 381 min. Histology: Mean Park score was 3.9 (denuded villi) for jejunum and 2.9 (extensive epithelial lifting) for ileum. A trend was seen for less ileal damage than jejunal damage in the total donor group (2.8 vs. 3.9 p=0,055). When analyzing donor types separately, this difference was significant in DBD (2.4 vs. 3.8 p=0.034). BD duration and ischemia time were unrelated to histological damage. Serum markers: CRP levels were <5 mg/L in all living kidney donors vs higher CRP levels for both DBD/DCD donors (72 mg/L p=0.001, 122 mg/L p=0.003). Serum LBP level was 4 times higher in both DBD/DCD (p=0.002, 0.004) compared to control donors. Conclusion: The intestinal graft endures substantial damage from BD and ischemia causing structural deterioration reflected by Park scores expressing at least extensive epithelial lifting. The jejunal part of the intestinal graft seems more susceptible than the ileum. Along, increased serum CRP/LPB levels indicate systemic inflammation, possibly reflecting functional deterioration. Donor interventions directed towards structure and barrier protection will be a major step towards improvement of ITX. Planned RNA and immunohistochemical analysis of the material will follow to gain insight in the pathophysiological mechanisms of damage.

Adverse effects of mTOR inhibition on liver regeneration

S.M.G. Fouraschen[1], J. de Jonge[1], P.E. de Ruiter[1], G. Kazemier[1], R.W.F. de Bruin[1], H.J. Metselaar[2], J. Kwekkeboom[2], H.W. Tilanus[1] and L.J.W. van der Laan[1], Depts. of [1]Surgery and Laboratory of Experimental Transplantation and Intestinal Surgery and [2]Gastroenterology & Hepatology, Erasmus Medical Centre, University Medical Centre Rotterdam, The Netherlands

Objective: Current immunosuppressive strategies in the first period after liver transplantation mostly involve treatment with steroids in combination with calcineurin-inhibitors or IL-2 receptor antagonists. A combination with the mTOR inhibitor rapamycin, although effective, is rarely used, especially after small-for-size liver transplantation, since rapamycin is known to delay tissue-repair. The exact role of mTOR in liver regeneration, however, is to be defined. In rodents, it is known that IL-6 and HGF are key cytokine/growth factors for stimulating hepatocyte proliferation and that mTOR is involved in their downstream signal transduction. The aim of this study is to investigate the role of mTOR in IL-6 and HGF stimulated liver regeneration.
Methods: C57BL/6 mice were subjected to a 70% partial hepatectomy (PH) and treated every 24 hours, starting at time of PH, with a combination of rapamycin and the steroid dexamethasone (rapa-dex) or with PBS. In the rapa-dex group, part of the animals was additionally treated with IL-6 and HGF. Animals were sacrificed 2 or 3 days after PH and liver and body weight, hepatocyte proliferation (BrdU) and gene expression were determined.
Results: Treatment with rapa-dex caused a lower liver weight at day 3 compared to controls (53% vs 76% of pre-PH weight, p=0.04). This effect could be completely overcome by treatment with IL-6/HGF (75%, p=0.02). The percentage of BrdU-positive hepatocytes was drastically reduced by rapa-dex versus PBS treatment (2% vs 12% at day 2, p=0.0002). Treatment with dex alone had no effect on hepatocyte proliferation, suggesting that rapa is responsible for the inhibition. Treatment with IL-6/HGF did not restore hepatocyte proliferation. Hepatic gene expression showed a significantly increased expression of TNF-α (7.6-fold) and IL-6 (3.9-fold) in the rapa-dex group versus controls. Furthermore, a decreased expression of Cyclin D1 (2.4-fold) and PCNA (6.4-fold) was seen. Combined treatment with IL-6/HGF significantly upregulated Cyclin D1 (3.6-fold) and PCNA (1.7-fold) expression and downregulated TGF-ß expression (2.6-fold) versus rapa-dex treatment alone.
Conclusions: This study shows that mTOR plays an important role in liver regeneration. mTOR inhibition impaired liver weight gain and hepatocyte proliferation. Exogenous IL-6 and HGF can, in part, overcome the adverse effects of rapamycin on liver.

Functional paralysis of CD8 memory T Cells in rATG treated kidney transplant patients

A.P. Bouvy[1], M.M.L Kho[1], M. Klepper[1], J.N.M. IJzermans[2], W. Weimar[1], C.C. Baan[1], Depts. of [1]Internal Medicine and [2]Surgery, Erasmus Medical Centre, University Medical Centre Rotterdam, The Netherlands

Introduction: Rabbit anti-thymocyte globulin (rATG) induction therapy depletes circulating lymphocytes from the peripheral blood. This depletion is followed by repopulation of T cells, skewed to regulatory and memory subsets. While this effect has been extensively studied by FACS analysis, functional studies on these repopulating T cell subsets are lacking. Here we report on their functional capacities in kidney transplant recipients who had received rATG induction therapy. Materials and Methods: Phospho-specific flow cytometry on whole blood was used to study IL2 mediated phosphorylation of signal transducers of activated T cells (P-STAT5) in naïve, regulatory and memory CD4+ and CD8+ T cells, before and 3 months after kidney transplantation. Patients were treated with rATG induction therapy (3 x 2mg/kg/day) in combination with Tacrolimus, MMF and steroids.
Results: At 3 months after rATG therapy an incomplete recovery of the absolute numbers of CD4+ naïve (CD4+CD45RO-, 5% of pre-transplant levels), regulatory (CD4+CD25+CD127-, 11%) and memory (CD4+CD45RO+, 13%) T cells and CD8+ naïve T cells (CD8+CD45RO-CCR7+, 37 %) were measured (all $p<0.01$), while the CD8+ memory T cells (CD8+CD45RO+ and CD8+CD45RO-CCR7-) almost fully recovered (92%).
At the functional level these repopulated CD4+ naïve, regulatory and memory T cells, including effector memory (CD4+CD45RO+CCR7-) and central memory (CD4+CD45RO+CCR7+) populations, responded to IL2 stimulation by effectively phosphorylating STAT5. In contrast, the recovered CD8+ T cell subsets showed impaired responses to IL2. Especially the CD8+ memory population had significantly less STAT5 phosphorylation ($p<0.03$). Within the CD8+ memory population the functional paralysis is found in all memory subsets; effector memory, central memory and EMRA (CD8+CD45RO-CCR7-) ($p=0.02$; $p=0.05$; $p=0.02$; respectively).
Conclusion: After depleting rATG induction therapy CD8+ T cell subsets more rapidly repopulate the peripheral compartments compared to CD4+ T cells. However, while the recovered CD4+ subsets show cytokine driven reactivity, CD8+ subsets remained paralyzed at the functional level.

Dexamethasone increases ROS production and T cell suppressive capacity by anti-inflammatory macrophages

M.D. Kraaij, S.W. van der Kooij, M.E.J. Reinders, K. Koekkoek, A.J. Rabelink, C. van Kooten, K.A. Gelderman, Dept. of Nephrology, Leiden University Medical Centre, The Netherlands

Introduction: Anti-inflammatory macrophages (Mph2) can suppress T cell responses by producing Reactive Oxygen Species (ROS) and by ROS-dependent induction of Treg. Mph2 may thus be instrumental in down-regulating T cell responses against allografts. However they should be able to exert their suppressive function under immunosuppression, since transplanted patients are treated with immunosuppressive drugs. Here we investigated the effect of immunosuppressive drugs on ROS production by Mph2 and the subsequent effects on T cell activation. Methods: Macrophages were differentiated from peripheral blood monocytes with M-CSF or GM-CSF, in presence or absence of cyclosporine A, FK506, dexamethasone, rapamycin, mycophenolic acid or prednisolone and the ROS producing capacity was tested by flowcytometry. T cell suppressive capacity was tested in an MLR. The effect of dexamethasone on ROS production and Treg numbers *in vivo* was investigated in rats with normal ROS production (congenic DA.*Ncf1*$^{E3/E3}$) or low ROS production (DA.*Ncf1*$^{DA/DA}$). Results: The ROS producing capacity of fully differentiated Mph was highest in anti-inflammatory Mph2 and this was not affected by exposure to the various immunosuppressive drugs. However, when drugs were added during Mph2 differentiation, it was shown that rapamycin decreased the ROS-producing and T cell suppressive capacity. In contrast all other immunosuppressive drugs investigated, with dexamethasone being the most potent, increased the ROS producing capacity of Mph2. In addition, dexamethasone enhanced the T cell suppressive capacity of Mph2 with regard to proliferation, IFN-γ and IL-4 production. Dexamethasone injection in rats resulted in long-lasting upregulation of ROS production by macrophages and induced increased numbers of circulating Treg in a ROS-dependent fashion.
Conclusion: Immunosuppressive drugs do not directly affect the ROS producing capacity of already differentiated Mph. During the differentiation phase, dexamethasone enhances the ROS producing capacity of macrophages in vivo and in vitro, thereby contributing to the macrophage-mediated suppression of T cell responses.

Renovascular resistance of machine perfused DCD kidneys is associated with primary non-function

E.E. de Vries[1], E.R.P. Hoogland[1], B. Winkens[2], M.G. Snoeijs[1], L.W.E. van Heurn[1], [1]Dept. of General Surgery, [2]Department of Methodology and Statistics, Maastricht University Medical Centre, The Netherlands

Background: Donation after cardiac death (DCD) has shown to be a valuable extension of the donor pool despite a higher percentage of primary non-function (PNF) and delayed graft function (DGF). Limiting the incidence of primary non-function is of crucial importance because transplantation of non-viable kidneys results in unnecessary risk of surgery and immuno-suppression, and sensitizes the recipient for future transplants. Moreover, viable donor kidneys should be prevented from being discarded. Renovascular resistance is said to predict graft outcome, however literature is not unambi-guous. Therefore, we studied the association between renovascular resistance during machine perfusion and short-term and long-term graft and patient survival. Methods: All transplanted and contralateral DCD kidneys preserved by machine perfusion in our center between 1993 and 2007 were analyzed (n=440). We used multivariable analyses to determine if renovascular resistance was independently associated with outcome measures. Results: 439 recipients were transplanted with Maastricht category 1 to 4 DCD kidneys. We showed that renovascular resistance at the start (T0) and after 1, 2, and 4 hours of machine perfusion was significantly and independently associated with PNF (T0: OR 2.040, 95% CI 1.362 to 3.056; p=0.001) and DGF (T0: OR 2.345, 95% CI 1.110 to 4.955; p=0.025). Long-term renal function, graft survival and patient survival, were not significantly associated with renovascular resistance, however graft survival of kidneys with a renovascular resistance of >2,5 mmHg/ml/min/100g had a PNF rate of > 58% and a 5-year graft survival of less than 40%, which is unacceptable. Conclusion: Renovascular resistance in DCD kidneys at the start of machine perfusion is an independent risk factor for PNF and must therefore be considered in viability assessment.

Long term postoperative complaints recorded after donation in 509 living kidney donors in a single centre

F. van de Logt[1], H.J. Kloke[1], J.F. Langenhuijsen[2], F.C.H. D'Ancona[2], J.A. van der Vliet[3], Ph.M.M. Dooper[1], A.J. Hoitsma[1], [1]Dept. of Nephrology, [2]Dept. of Urology, [3]Dept. of Surgery, Radboud University Nijmegen Medical Centre, The Netherlands

Introduction: Previously, we reported on early postoperative complications graded by Clavien classification till month 3 after surgery. In this study we describe long term postoperative complaints in living kidney donors between 1968 and December 2009. Methods: Donors were encouraged to meet for yearly control visits in our outpatient clinic. Patients reported freely on diseases and complaints which had occurred during the past year. Complaints were divided in those most probably and those only possibly related to surgery. Complaints regarded as most probably related to surgery were incisional hernia and persistent local pain at the scars. Complaints regarded as only possibly related to surgery were persistent tiredness, depression, belly discomfort and scrotal swelling. Complaints and diseases most probably not related to the donation are not reported here.
Results: In our centre 793 patients donated a kidney till December 2009. A total of 1661 visits of 509 individual patients with at least one yearly follow-up visit after kidney donation were recorded in our NOTR database. In the first follow-up year 398 visits were recorded, numbers gradually declining during the subsequent years. Mean weighted follow-up was 3.7 years (range 1 to 32 years). We recorded 24 complaints (23 patients, 4.5% of patients) probably related to surgery, i.e. 5 complaints of incisional hernias (in 4 surgical correction was done) and 19 times complaints of local pain at the scars. 60% were recorded during the first follow-up year. There were 25 complaints (24 patients, 4.7% of patients) only possibly related to kidney donation, i.e. 12 times persistent tiredness, 6 times depression, 3 times persistent belly discomfort and 5 times complaints of enlarged testes. Again, 60% were recorded during the first follow-up year.
Conclusion: The rate of long term complaints probably or only possibly related to kidney donation was fortunately rather low. Nevertheless, this small group of patients had considerable discomfort. Therefore, potential future living kidney donors should be informed on the chance to develop long term complaints after donation.

Living donor exchange remains the main solution for incompatible couples by its direct and indirect effects

M. de Klerk, for the 8 kidney transplant centers, Dutch Transplant Foundation and National Reference Laboratory for Histocompatibility

Living donor kidney exchange has become an efficient solution for recipients with incompatible donors. Here we describe the fate of all patients that were enrolled in our program. Methods: Data on registration, computerized matching, cross matching, and transplantations within or outside the program were collected. Results: From January 2004 till December 2010 422 pairs were registered. To create new combinations a match procedure was run 28 times with a median input of 14 (7-22) new pairs and a median of 55 (16-92) participating couples. Matching couples were found for 127/185 (69%) X^+ pairs and 91/237 (38%) ABO incompatible pairs. Of 141/218 matched pairs the recipients received a kidney in an exchange procedure. However, for 26/77 match procedures that were discontinued for medical or psychological reasons, an alternative was found. So in total 167 (141 + 26) recipients received a transplant. Of the remaining 51 discontinuations 26 definitely left, for 22 an alternative transplantation was found outside the program and 3 are still waiting. For the 204 unmatched couples, 46 are still in the program while 34 others definitely left, while for 124 recipients an alternative living kidney donor was found outside the exchange program. In total after 7 years 39% of the participants received a kidney within an exchange procedure, 35% of the recipients were transplanted outside the program, 14% of the couples were delisted and 12% is still waiting. The 146 patients who received a kidney outside the program were transplanted with a deceased kidney in 47 cases, 21 found another direct donor, 37 were transplanted across the blood type barrier and 41 received a transplantation in a domino-paired procedure triggered by an unspecified donor.

Conclusion: In the 7 years of our kidney exchange program 313/422 (74%) of the participating recipients became transplanted. Approximately half of them (167/313, 53%) received a kidney within the exchange program, while 47 (15%) received a deceased donor kidney and 99 (32%) were transplanted within other living donation programs. The exchange program proved to be highly successful not only in its direct results but also indirectly by triggering alternative solutions.

Validation of the Donor Risk Index (DRI) in orthotopic liver transplantation within the Eurotransplant region

J.J. Blok[1], J. Ringers[1], R. Adam[2], A.K. Burroughs[3], N.G. Kooreman[1], J. Dubbeld[1], H. Putter[4], A.O. Rahmel[5], R.J. Porte[6], X. Rogiers[7], A.E. Braat[1], [1]Dept. of Surgery, [4]Dept. of Medical Statistics, Leiden University Medical Centre, [2]Centre Hépato-Biliaire, Hôpital Paul Brousse, Villejuif, France, [3]Liver Transplantation and Hepatobiliary Medicine, Royal Free Hospital, London, United Kingdom, [5]Eurotransplant Int. Foundation, Leiden, [6]Dept. of Surgery, University Medical Centre Groningen, [7]Dept. of Surgery, Ghent University Hospital Medical School, Belgium

Introduction: In Eurotransplant over 50% of livers are from extended criteria donors. However, not every extended criteria donor is the same. Outcome after liver transplantation is highly dependent on donor quality and therefore it is important to better define these criteria. A continuous scoring system for analyzing donor risk has been developed within the UNOS region. Liver donors may be quite different in both regions and this Donor Risk Index (DRI) has never been validated within the Eurotransplant region. Objective: Validation of the DRI within the Eurotransplant region. Methods: Database analysis of all 5936 liver transplantations from deceased donors into adult recipients from the 1st of January 2003 until the 31st of December 2007 in Eurotransplant. Data on donor, transplant and recipient variables were analyzed with Kaplan Meier and Cox regression models. Outcome was patient death or graft failure, whatever occurred first. Results: From 5517 patients follow-up data were available with a mean of 2.4 years. The mean DRI in the Eurotransplant region was remarkably higher than in the UNOS region (1.7 vs 1.3), indicating a different donor population. Regardless, we were able to validate the DRI for the Eurotransplant region. Kaplan Meier curves per DRI-category showed a significant correlation between DRI and outcome ($p<0.0001$). Multivariate analysis demonstrated the DRI to be the most significant factor influencing outcome ($p<0.0001$). An interesting finding was that when corrected for DRI outcome between the UNOS and Eurotransplant regions were quite comparable.
Conclusion: The DRI was the strongest predictor for outcome of all donor, transplant and recipient variables and we would strongly advocate its use when looking at outcome data.

This is a study supported by the European Liver and Intestine Transplant Association (ELITA) and Eurotransplant Liver Intestine Advisory Committee (ELIAC)

Living kidney donation among ethnic minorities: a Dutch qualitative study on attitudes, communication and knowledge of kidney patients

S.Y. Ismail[1], L. Claassens[1], E.K. Massey[2], A.E. Luchtenburg[2], W. Weimar[2], J.J. Busschbach[1], Depts. of [1]Medical Psychology and Psychotherapy and [2]Internal Medicine, Erasmus Medical Centre, Rotterdam, The Netherlands

Introduction: Living donor kidney transplantation (LDKT) has proven to be a better treatment alternative compared to deceased donor kidney transplantation, e.g. in terms of waiting time and survival rates. However, we observed a significant inequality in the number of LDKT performed between the non-European and the Dutch patients in our center. It has been suggested that such inequality relates to differences in psychosocial and cultural factors.
We set out to investigate whether attitudes, communication patterns and knowledge relate to inequalities in LDKT rates between Dutch and non-European patients. Methods: Focus group discussions and in-depth interviews were conducted among 50 kidney patients, most of who were being treated with dialysis and were on the deceased donor waiting list. Analysis was conducted according to 'grounded theory' using Atlas.ti. Results: We found nearly all patients to be in favour of LDKT (96%). However, multiple prohibiting and interrelated factors played a role in considering LDKT. We propose a model which addresses these factors as barriers to LDKT in our non-European patients. These barriers are: 1) a perceived gap in information 2) cognitions and emotions 3) social interference 4) and non-communication with family and friends. Additionally, we found that our patients held a welcoming attitude towards tailored education program, for instance a home-based education.
Conclusion: This study has identified modifiable factors that contributed to the ethnic disparity in our LDKT program. As these factors appear modifiable, and because patients are open to education, we argued that a home-based educational intervention suits the complexity of these factors and our patients' personal needs. Our intervention protocol and the results of the first six pilot patients will be presented.

The influence of ethnicity on re-hospitalization and complications after kidney transplantation

L. Maasdam[1], E.K. Massey[1], M.M.L. Kho[1], J.N.M. IJzermans[2], W. Weimar[1], Depts. of [1]Internal Medicine and [2]General Surgery, Erasmus Medical Centre Rotterdam, The Netherlands

Introduction: Cultural and social norms have a large influence on interpretation and understanding of information as well as coping with lifestyle requirements and medication regimes after transplantation. It has been argued that these issues are especially important for non-native Dutch patients with their own cultural lifestyle and potential language barriers. We investigated whether non-native Dutch kidney transplant patients have more complications or re-hospitalizations than native Dutch kidney transplant patients. Methods: Data were collected from our database over 2009. We analyzed graft survival, function and complications for which hospitalization proved necessary. These data were analyzed in SPSS. Results: In 2009 158 patients were transplanted, of which 34 were non-native Dutch. Participation in the living kidney transplant programs was 78% for the native and 62% for the non-native patients (p=0.07). The median hospitalization time immediately after transplantation was comparable for native and non-native patients (14 and 15 days respectively). Re-hospitalization was recorded for 78 (63%) native patients and 18 (53%) non-native patients (p=0.34). The median time between discharge and the first re-hospitalization also did not differ between the two study groups, 46 days for the native and 40 days for the non-native patients. Native patients experienced urological complications (16%) more often than non-native patients (3%, p=0.04). There was no statistically significant difference (p=0.2) between the rate of re-hospitalization for rejection between native (10%) and non-native patients (18%). All over one year survival was 89% for the natives and 91% for the non-native patients (p=0.76). Median serum creatinine was 130 umol/l for the natives and 126 umol/l for the non-native patients.
Conclusions: The re-hospitalization rate was high in both groups. Possible language barriers and other cultural lifestyles among non-native patients do not result in a higher number of re-hospitalizations after kidney transplantation in this study. Nevertheless, it remains important that health care professionals are competent with health literacy. Research into health literacy in both patient groups is recommended.

Psychosociale screening bij partnerniertransplantatie

E.C.M. Berendsen, T. Winkel, A. D. van Zuilen, F. E. van Reekum. Dept. of Nephrology, University Hospital Utrecht, The Netherlands

Inleiding: Het succes van partnerniertransplantatie gaat gepaard met andere (relatie)problemen dan bij andere vormen van levende donatie. Deze problemen worden nog onvoldoende methodisch in kaart gebracht. Het doel van het onderzoek is vast te stellen welke psychosociale screeningsmethode(n) in de fases vóór partnerniertransplantatie kunnen worden uitgevoerd, waardoor (relatie)problemen tijdig worden gesignaleerd. Methoden: Er is een review gedaan van de beschikbare literatuur en er zijn interviews en een vergelijkend onderzoek tussen transplantatiecentra uitgevoerd. De interviews zijn uitgevoerd bij drie categorieën: experts (n=2), koppels die een partnerniertransplantatie hebben ondergaan (n= 18) en collega's in het eigen centrum en in twee andere transplantatiecentra. Resultaten: *Literatuurreview:* Er worden verschillende aandachtspunten bij partnerniertransplantatie gevonden, bijvoorbeeld: de vrij acute rolveranderingen in de nazorgfase, het copinggedrag binnen de relatie en vroegtijdige counseling bij distress. *Collega's en experts:* Er zijn drie kernpunten. 1) Er is behoefte aan standaardisering van de rapportage en evaluatie n.a.v. de psychosociale screening van de donor. 2) Er dient een duidelijke taakafbakening tussen de diverse betrokken disciplines te bestaan. 3) Ook bestaat behoefte aan een methodisch evaluatiesysteem, waarmee de risico- en beschermende factoren worden geïnventariseerd. De resultaten van deze systematische beoordeling kunnen worden gebruikt in de benadering van het koppel voor en na de procedure. *Donoren en ontvangers*: Er zijn drie kernpunten. 1) Zij hebben veel zorgen over elkaar, die veelal niet worden geuit om de ander te sparen. Achteraf blijkt er toch een spanningsveld tussen de wens te doneren/te ontvangen en de angst voor de procedure dat zich in de relatie manifesteert. 2) Koppels blijken vooraf de implicaties van de gelijktijdige opname en postoperatieve periode op somatisch en emotioneel vlak niet goed te kunnen overzien. Nadien bestaat een drempel voor het inroepen van hulp. 3) Zelfs volwassen kinderen behoeven begeleiding in verband met het gelijktijdig opgenomen zijn van beide ouders.
Discussie: In de pretransplantatie screening van partners moet gericht en systematisch aandacht worden besteed aan de impact van de procedure op hun relatie i.p.v. een eenzijdige beoordeling van de geschiktheid van de potentiële donor. Er is behoefte aan een gezamenlijke voorbereiding en afronding van de procedure.

Transitie; zelfmanagement en zelfredzaamheid bij jongeren met een donornier

J.L. Knoll[1], M. van Helden[2], R. Scholten[1], E.A.M. Cornelissen[1], I. Dooper[2], E. Ensink[1], S. van Duin[2], G. Reuhl[1], [1]Dept. of pediatric nephrology, [2]Dept. of nephrology, Radboud University Nijmegen Medical Centre, The Netherlands

Inleiding: Transitie is de doelgerichte, geplande overstap van jong volwassenen met een chronische aandoening van kindgerichte zorg naar het volwassen zorg systeem. Het is een (ingrijpende) gebeurtenis voor jongeren in een levensfase die zich kenmerkt door veranderingen op lichamelijk, psychisch en sociaal gebied. Er bestaat een verhoogde kans op non-compliance, sociaal isolement, onvoldoende tot geen loopbaanbegeleiding/werk enz. Om de jongeren en hun ouders zo goed mogelijk te begeleiden zijn we in 2010 gestart met het project Op Eigen Benen Vooruit! Het is een multidisciplinair verbeter- en implementatieproject gezamenlijk uitgevoerd door de afdelingen kindernefrologie en nefrologie. Patiënten en methoden: Alle jongeren van 12 t/m 18 jaar, die een niertransplantatie hebben ondergaan en in ons centrum onder controle zijn, nemen deel aan het project. Er wordt een Individueel TransitiePlan (ITP) opgesteld voor deze jongeren en hun ouders. Hierdoor wordt begeleiding op maat geleverd. De jongeren van 16 t/m 20 jaar worden bovendien besproken in een multidisciplinair overleg waarbij alle disciplines vanuit zowel de kindernefrologie als de volwassenen nefrologie aanwezig zijn. Rond de leeftijd van 18 jaar vind de werkelijke transitie plaats. Nurse practitioners en maatschappelijk werkenden spelen een centrale rol in de begeleiding van de jongeren en ouders. Er worden o.a. groepsbijeenkomsten georganiseerd voor zowel jongeren als hun ouders (separaat) met onderwerpen als leefstijl, seksualiteit, omgaan met ziekte en medicijnen, loslaten. Resultaten: ITP's worden opgesteld. Alle zorggerelateerde onderwerpen komen aan bod zodra het kind er aan toe is en op het niveau van het kind. Jongeren voelen zich serieus genomen en worden meer en meer regisseur van hun eigen leven. Ouders voelen zich gesteund en zijn zich meer bewust van het feit dat ze hun kind meer verantwoordelijkheden moeten geven.
Conclusies: Transitie is een continu proces. Wat gestart is als een project wordt nu ingebed in de dagelijkse zorg.

Development of new onset diabetes after lung transplantation in patients with cystic fibrosis compared with patients suffering from other lung diseases

G. van Meerkerk[1,2], E.A. van de Graaf[1], J.W.J. Lammers[1], D.H. Biesma[2], H.W. de Valk[2], Depts. of [1]Respiratory Medicine and [2]Internal Medicine, University Medical Centre Utrecht, The Netherlands

Objective: New onset diabetes after transplantation (NODAT) becomes more prominent due to increased survival. As approximately 50% of the lung transplant (LTx) recipients have Cystic Fibrosis (CF) we postulate that cystic fibrosis related diabetes may decrease survival after transplantation. Aim of our study was to create an incidence curve of NODAT for lung transplantation recipients with and without cystic fibrosis and to determine the moment of NODAT after LTx. Methods: All patients transplanted in August 2001-December 2009 in our centre were included. Using the guideline of the American Diabetes Association the diagnosis diabetes was made in case of a) glucose lowering drugs *or* b) fasting glucose ≥7.0 or 2h glucose ≥11.1mmol/l during an OGTT *or* c) on ≥2 separate days fasting ≥7.0 or random glucose ≥11.1mmol/l. Diagnosis could only be determined in a period without infection, with stable use of corticosteroids and before or ≥3 months after LTx.
Results: 40 CF (28 male) and 35 non-CF patients (14 male) were included. CF patients were significantly younger (mean age CF: 31; non-CF 54 years old) and had a lower BMI (mean BMI CF 19.4; non-CF 23.4 kg/m2, p<0.001. Before LTx 62% of CF and 6% of non-CF patients had developed diabetes (p<0.001, adjusted for age, sex, BMI). In both groups the same number of patients developed diabetes after LTx (p=0.9, CF: 62%, 8 of 13 patients at risk and non-CF 67%, 18/27 patients). NODAT developed mainly in the first year after LTx.
Survival analysis within the CF group showed a significantly better survival after LTx for patients without diabetes before LTx (Kaplan Meier; p=0.015). These groups were similar for age, BMI, high urgency indication and severity of CF mutation.
Conclusions: Before LTx more CF patients than non CF patients had diabetes. After LTx the number of patients in both groups developing NODAT was similar (≈65%). CF patients without diabetes before LTx had significantly longer survival than those with diabetes.

Dysbalance of angiopoietins and a decrease in pericytes in a rat model of renal ischemia reperfusion injury

M. Khairoun[1], P. van der Pol[1], E. Lievers[1], N. Schlagwein[1], H.C. de Boer[1], D.K. de Vries[3], A. J. van Zonneveld[1,2], T.J. Rabelink[1,2], C. van Kooten[1], M.E.J. Reinders[1], [1]Dept. of Nephrology, [2]Einthoven Laboratory for Experimental Vascular Research, [3]Dept. of Surgery, Leiden University Medical Centre, The Netherlands

In the context of transplantation microvascular endothelial cells (ECs) are very susceptible to injury, including ischemia/reperfusion injury (IRI). Alterations in the integrity and function of the endothelial monolayer have important implycations for organ function and it is assumed that effective early mico-vas-cular repair will sustain graft function. Rejection induced microvascular injury results in peritubular capillary loss, graft dysfunction and ultimately leads to graft loss. Pericytes play a critical role in the stabilization and proliferation of peritubular capillaries via interaction with ECs. This process is mediated by several angioregulatory factors, including the anti-inflammatory factor Angio-poietin-1 (Ang-1) produced by pericytes and the proinflammatory factor Angiopoietin-2 (Ang-2) produced by ECs. Since pericytes and angiopoietins are considered as important hallmarks for microvascular integrity, we investigated the impact of IRI on pericyte function and angiopoietin expression. Male Lewis rats (n=6 per group) were subjected to 45 minutes of unilateral renal ischemia followed by removal of the contralateral kidney during ischemia. Leukocyte infiltration (CD45), EC integrity (RECA-1), pericytes (NG2) and angiopoietins (Ang-1 and Ang-2) were measured and quantified in sham operated controls (72 hr) and at 2, 5, 24, 48 and 72 hr after IRI. Immunohistochemical studies revealed a significant increase in infiltrating leukocytes as early as 48 hr with a peak at 72 hr after reperfusion in both the cortex and medulla ($p< 0.05$). We did not find a loss of ECs early after IRI, which is consistent with previous studies of rat renal IRI, where an alteration of microvascular density has been observed to occur only several weeks after the inciting event. However, Ang-1 protein was markedly decreased after 24 hr and remained decreased up to 72 hr ($p< 0.001$). In contrast, Ang-2 increased after 24 hr ($p< 0.01$) and remained elevated up to 48 hr ($p< 0.05$) after IRI. Interestingly, the pericyte marker NG2, which was expressed in glomerular and peritubular capillaries, demonstrated a reduction at 5 hr, reaching significance at 48 hr and 72 hr after IRI ($p< 0.05$). Our results suggest that loss of peritubular capillaries may be preceded by an early loss of peritubular pericytes and a switch in the Ang-1/ Ang-2 balance to a condition of destabilization. This might have important effects for vascular maintenance and survival in the kidney following ischemic injury.

High Throughput Sequencing of hCMV-pp65 reactive CD8-clones formed during primary infection and subsequent reactivation

E.B.M. Remmerswaal[1,2], P.L. Klarenbeek[3], S. Koch[1,2], M.E. Doorenspleet[3], B.D.C. van Schaik[4], K. van Donselaar[2], F. Bemelman[2], R.E.E. Esveldt[3], A.H. van Kampen[4], F. Baas[5], A. ten Brinke[6], R.A.W. van Lier[1], N. de Vries[3], I.J.M. ten Berge[2], [1]Dept. of Exp Immunology, [2]Renal Transplant Unit, Dept. of Nephrology, Div of Int Medicine, [3]Dept. of Clin Immunology and Rheumatology, [4]Dept. of Clin Epidemiology, Biostatistics and Bioinformatics, [5]Dept. of Genome Analysis, [6]Sanquin Research, Dept. of Immuno-pathology, Academic Medical Centre, Amsterdam, The Netherlands

Infection with human cytomegalovirus (hCMV) remains a puzzling example of a persisting infection despite strong and chronic anti-viral T-cell responses of the immune system. Little is known on the T-cell receptor (TCR) repertoire of the responding CD8 clones during the acute and chronic phase of the infection. We overcame current technical limitations by using a new 'next-generation' sequencing technique to identify individual clones during the acute and chronic phase of primary CMV infection in two kidney-transplant recipients. The second patient also experienced CMV reactivation. CMV pp65-tetramer$^+$CD8$^+$ T cells and total CD8$^+$ T cells from both the acute and chronic phase (1 year and 3 – 5 years) of infection were sorted to very high purity. Clones were identified by sequencing their TCR β-chain CDR3 region. Over 15000 TCR-β-chains were sequenced per time point. Clones found in the CMV pp65-tetramer$^+$CD8$^+$ T cells were traced back in the total CD8$^+$ T cell population.
A surprisingly broad repertoire of TCR-Vβ usage against just one dominant HLA-peptide complex appeared to be generated during the primary response against the virus. Most high frequency hCMV-specific CD8$^+$ T cell clones generated during the primary hCMV infection became virtually undetectable after several years. Reactivation of hCMV resulted in the recuitment of a vast amount of new T cell clones into the hCMV-specific CD8$^+$ T cell pool.

Who benefits from Alternative living kidney donation programs?

J.I. Roodnat, J. Wetering, J.A. Kal van Gestel, M. de Klerk, W. Zuidema, J.N.M. IJzermans, M. van Agteren, W. Weimar, Dept. of Internal Medicine and General Surgery, Erasmus Medical Centre, Rotterdam, The Netherlands

Background: 1 in 6 couples that present for living donor renal transplantation is blood type ABO incompatible or has a positive cross-match. We compared recipients of a direct vs alternative program transplantation concerning donor relation, ABO blood type and panel reactive activity (PRA). Methods: Between 2000 and 2010 1292 renal transplantations were performed, 501 deceased donor, 618 direct living, and 173 alternative living donor transplantations. Alternative programs in our centre are: kidney-exchange (37), domino-paired (41) in combination with altruistic donation (58) and ABO-incompatible donation (37). The October 2010 Rotterdam waiting list (444 patients) was used for comparison. Results: There were significantly more partner donors in the recipient population of alternative compared to the direct donation program (55 versus 26%, $p<0.001$). In recipients of a direct donor, blood type O was underrepresented compared to the waiting list population (37.5% vs 46%, $p<0.001$). This was also true for recipients via the kidney-exchange (32%, ns) and domino-paired program (15%, $p<0.001$). But the prevalence of blood type O was higher in altruistic (50%, ns) and ABO-incompatible programs (76%, $p=0.012$). 7% of waiting list patients was highly sensitized (PRA>80%); significantly more than in the population of recipients of a direct donor (0.6%, $p<0.001$) and in recipients via ABO-incompatible program (0%, ns). In the altruistic and domino-paired programs the proportion of highly sensitized patients was 1% ($p=0.026$) resp. 7.3% (ns). In the population transplanted via the donor exchange program there were no highly sensitised patients but the percentage of intermediately sensitised patients was higher ($p<0.001$). For comparison: in the population of recipients of a deceased donor kidney 41.1% had blood type O ($p=0.01$ compared to waiting list) and 13.8% was highly sensitised ($p<0.001$ compared to waiting list).
Conclusion: Partners is the main population participating in alternative donation programs. In direct living donation significantly less blood type O recipients and less highly sensitised patients are transplanted than expected based on the waiting list. Donor-exchange and domino donations primarily serve low-sensitized blood type non-O patients. Obviously blood type O recipients profit from the ABO-incompatible program, while both highly sensitized and blood type O patients benefit from altruistic donations.

Adenosine and renal dendritic cells; integration of tissue integrity, danger signals and immune regulatory processes

C. van Kooten, S. Kamerling, M. Reinders, Dept. of Nephrology, Leiden University Medical Centre, The Netherlands

CD39 and CD73, two enzymes involved in the conversion from ATP to adenosine, have been identified as markers of regulatory T cells. This has generated an increasing interest in adenosine as a local coordinator of immune regulation and as one of the key mediators of an immunosuppressive milieu. However, histological analysis of the kidney has shown a much broader distribution of these enzymes, including interstitial fibroblasts. Dendritic cells (DC) are an intrinsic part of the interstitial cellular network and are central players in immune regulation. In the current study we explored the role of DC in adenosine metabolism and responsiveness.

Monocytes, DC and tolerogenic Dex-DC were isolated from peripheral blood and generated using specific growth factors. Quantitative PCR was developed for CD39, CD73 as well as for the 4 specific adenosine receptors A1R, A2aR, A2bR and A3R. DC were stimulated with varying doses (10E-5 – 10E-7 M) of NECA (a stable analogue of adenosine) and/or LPS. Cytokine production and T cell stimulatory capacity were used as a specific read out for DC function.

Dendritic cells showed a low expression of CD39 and CD73. However, upon combined stimulation with LPS and NECA a strong synergistic induction of CD73 expression was induced, suggesting a contribution to the local generation of adenosine. Therefore we investigated the distribution of the 4 adenosine receptors on DC. We observed that compared to monocytes, immDC show an increased expression of A1R. Upon LPS-induced maturation, especially expression of the A2aR was increased. Interestingly, when we investigated the distribution on tolerogenic Dex-DC, we found a specific and unique upregulation (100-1000 fold) of the A3 receptor. To investigate the biological response, DC were exposed to NECA, or generated in the presence of NECA. We found no consistent direct effects of NECA on LPS-induced cytokine production. However, generation of DC in the presence of NECA resulted in cells with a reduced capacity to produce IL-12 or activate allogeneic T cells.

In conclusion, we have shown that DC might not only be an important target of adenosine but also contribute to local generation. Receptor expression on DC is tightly regulated and varies strongly between tolerogenic, immature and mature DC. Adenosine specifically dampens the IL-12 response of immunogenic DC. The biological consequence of adenosine signaling via the A3R in tolerogenic DC is presently under investigation.

Anatomical suitability of the iliac fossa for implantation of living donor kidneys with a short renal vein

J. Hellegering[1], R. van Es[2], H.J. Kloke[3], F.C.H. D'Ancona[4], A.J. Hoitsma[3], J.A. van der Vliet[1], L.J. Schultze Kool[2], M.C. Warlé[1], [1]Dept. of Surgery, Division of Vascular- and Transplant Surgery, [2]Dept. of Radiology, [3]Dept. of Nephrology, [4]Dept. of Urology, Radboud University Nijmegen Medical Centre, The Netherlands

Background: In general, left living donor kidneys are technically easier to implant due to their longer renal veins. Nevertheless, transplant centers preferring left living donor kidneys, also select right kidneys on a regular basis for a variety of reasons. To our knowledge, no attempts have been made so far to study the anatomical suitability of the iliac fossa for kidney transplantation. We hypothesize that anatomical mapping of the iliac fossa may identify patients who are less suitable to receive right living donor kidneys with a short renal vein (<2 cm). Methods: Pre-transplant computed tomography (CT) scans of 50 patients who consecutively underwent living donor nephrectomy between February and September 2010 at our hospital were used to assess anatomical features of the kidneys and iliac fossa. The Aquarius Workstation (TeraRecon), designed to reconstruct images acquired from multi-slice CT scans, was used to perform 3-D center lumen line measurements of both renal veins. The length of the right renal vein was also measured in a 2-D single slice, coronal plane. The depth of the iliac vein in relation to the ventral border of the psoas major muscle was measured in transverse, single slices using the sacroiliac joint as reference. Results: Using the center lumen line reconstruction, the mean length of the left and right renal vein was 76.5 (± 11.3) mm and 29.6 (± 8.7) mm, respectively. Single slice measurement of the right renal vein showed a mean length of 29.9 (± 8.4) mm. The correlation coefficient between the two methods of measuring the right renal vein length was 0.925 (p<0,001). The mean depth of the left and right iliac vein (at the mid-sacroiliac level) was 22.5 (range 5 - 42) mm and 20.4 (range 8 - 36) mm, respectively. Based on these data, right donor kidneys with a short renal vein (< 2 cm) have an a priori chance of 13% to be transplanted in a patient with an iliac vein depth above 3 cm (length-depth mismatch > 1 cm).
Conclusions: Our results show that measurement of the right renal vein length in a single slice is a valid alternative for the 3-D measurement using center lumen line reconstruction. By anatomical mapping of the iliac fossa, patients with a large distance between the ventral border of the psoas major muscle and iliac vein can be identified. Although we presume that anatomical features of the iliac fossa of healthy donors can be extrapolated to kidney transplant recipients, further research is required to confirm this.

Case report: successful lung transplantation with a positive cross match due to HLA class II antibodies

B.G. Hepkema[1], I. Bouwman[1], T. Jongsma[1], C. Roozendaal[1], L. Bungener[1], G. Nossent[2], E. Verschuuren[2], W. van der Bij[2], M. Erasmus[3], S.P.M. Lems[1], [1]Transplantation Immunology, Dept. of Laboratory Medicine, [2]Lung transplantation, Dept. of Internal medicine, [3]Dept. of Cardiothoracic Surgery, University Medical Centre Groningen, The Netherlands

A positive cross match by a complement dependent cytotoxicity assay (CDC) due to HLA specific antibodies is considered a contraindication for all solid organ transplantations, except for liver transplantation. We report a successful lung transplantation across a positive cross match.
A 22 year old female patient with cystic fibrosis received a liver transplant 7 years ago and was entered on the waiting list for a lung transplantation. During routine screening for the presence of HLA antibodies by CDC, class II specific antibodies with a PRA of 75% were detected. The antibodies were mainly specific for DQ and to a minor extent to DR7, as determined by single antigen beads (LSA) and Luminex technology. Using the Matchmaker algorithm the 18S eplet of DQA1 was identified as a possible specificity, present on all DQA1 alleles, except DQA1*01, which is the DQA1 typing of the patient herself. The antibodies were directed to the mismatches of the still well-functioning transplanted liver. At listing we required a (virtual) cross match negative donor profile, excluding all non-DQ1 donors. After 1 year of waiting time the risk due to the critical clinical situation outbalanced the risk due to the uncertain consequences of these antibodies (with decreasing strength in CDC) and made our transplant team decide to request an HU status and to ignore the HLA antibodies. The patient received a bilateral lung transplant and had an uneventful procedure. The cross match with a current serum was negative by CDC, but positive with historical sera. All pre-transplant sera as well as post transplant sera (drawn daily for the first week, weekly thereafter up to 4 weeks post-transplant) were analysed by LSA. The specificity and the strength of the antibodies was identical in all sera, with fluorescence intensities around 20.000.
In conclusion: A successful lung transplantation was performed across a positive cross match due to HLA class II antibodies with specificity for HLA mismatches of the functioning liver transplant. Several questions remain to be answered: Do we have to reconsider the contra indication with regard to class II antibodies? Is this also possible for other solid organ transplants? What is the role of the transplanted liver? Or is this an example of immunological enhancement?

Long term follow-up of overweight and obese living kidney donors

H. Tent[1], M. Rook[1], H.S. Hofker[2], R.J. Ploeg [2], G.J. Navis[1], J.J. Homan van der Heide[1], Depts. of [1]Internal Medicine Division of Nephrology and [2]Surgery, University Medical Centre Groningen, The Netherlands

Due to donor organ shortage, living kidney donor selection has become more liberal with acceptation of overweight and obese donors. We found that early after donation overweight donors have a higher risk for impaired GFR and lower renal reserve. Whether this results in a worse long term outcome is unknown. We evaluated short term and 5 year outcome in 75 donors who donated at our center. All had GFR (^{125}I-iothalamate) and ERPF (^{131}I-hippuran) measured 4 months prior, and 2 months and 5.4 ± 1.1 year after donation. Delta GFR from 'single kidney status' was calculated as [GFR long term -(pre-donation GFR/2)]. For analysis, donors were divided according a pre-donation Body Mass Index (BMI) ≤ 25 or > 25 kg/m^2. Of the 75 included donors, 45 had a BMI>25 kg/m^2. Overweight donors were older, 51±8 *vs.* 44±12 years, and had higher pre-donation MAP: 93±8 *vs.* 87±9 mmHG (both p<0.02). Pre-donation GFR and FF were similar between overweight and lean donors: 114±15 and 115±20 ml/min, and 26±3 and 27±4% respectively. Early post-donation, the difference in MAP was lost while at long term overweight donors had higher MAP again: 94±8 *vs.* 92±10 and 96±8 *vs.* 92±9 mmHg (p<0.05) respectively. At both time points, GFR was similar: 74±11 *vs.* 75±11 early post-donation and 82±13 *vs.* 80±15 ml/min long term post-donation; as was FF: 26±2 *vs.* 26±3 and 24±8 *vs.* 23±11% respectively. There was no difference in urinary protein excretion long term post-donation: 0.1[0.0-0.2] *vs.* 0.0[0.0-0.2] g/24hour. ΔGFR to short and long term were similar between overweight and lean donors: 17±7 and 17±8 to short term and 24±8 and 23±11 ml/min to long term. On regression analysis ΔGFR to long term was associated negatively with pre-donation age (R^2 0.18, p<0.01), but not with BMI. Long term blood pressure was positively related to age and BMI (R^2 0.14 and 0.05, p<0.05).
In conclusion, in this small population overweight donors have higher blood pressure prior and long term post-donation. However, long term course of renal function is equal to lean donors and not determined by BMI. We want to emphasize that although these overweight donors perform well, close long term monitoring and adequate blood pressure treatment remains necessary.

The natural course of donor chimerism including the NK-cell fraction after liver transplantation: a prospective study

R.C. Verdonk[1], E.B. Haagsma[1], T. Jongsma [2], R.J. Porte[3], C. Roozendaal[2], A.P. v.d. Berg[1], B.G. Hepkema[2], [1]Dept. of Gastroenterology and Hepatology, [2]Dept. of Laboratory Medicine, [3]Dept. of Surgery, Section of Hepatobiliary Surgery and Liver Transplantation, University Medical Centre Groningen, The Netherlands

Background: After solid organ transplantation hematological cells of donor origin can be found in the circulation of the recipients. This phenomenon is called donor chimerism. Donor chimerism can be of clinical relevance because of a presumed important role for donor cells in the development of graft-versus-host disease and tolerance after solid organ transplantation. Aim: To prospectively determine the presence of donor chimerism in whole blood as well as in isolated T-cells and Natural Killer (NK-) cells during the first 3 months after liver transplantation. Materials and Methods: During a period of six months 21 adult patients were transplanted in our centre. Demographic data were collected. Chimerism was determined in whole blood and T-cells and NK-cells every week during admission and during every outpatient visit after discharge during a 3 month follow up. Percentage of donor-DNA was calculated using short tandem repeat markers. Measured chimerism was correlated to potential predictive factors for chimerism and clinical outcome.
Results: 137 samples were analyzed in 21 patients. 15 patients (71%) showed chimerism at least once during follow up. Donor DNA was most prominently present in the first month after transplantation and decreased quickly thereafter. Chimerism was present in whole blood, T-cells and NK-cells. The highest percentage of donor-DNA was found in the NK-cell fraction. We did not observe any episodes of rejection of graft-versus-host disease in the study population. No relationship between clinical outcome and chimerism could be found.
Conclusion: A low percentage of chimerism is a frequent event after transplantation, occurring in up to 71% of our patients, mostly in the first month after transplantation. Chimerism is most prominently seen in the NK-cell fraction. There was no correlation between donor chimerism and clinical outcome.

Adiponectin paradox in renal transplant recipients

L.V. de Vries, J.J. Homan van der Heide, W.J. van Son, R.T. Gansevoort, G.J. Navis, R.O.B. Gans, S.J.L. Bakker, Dept. of Internal Medicine, University Medical Centre Groningen, The Netherlands

Background: Cardiovascular (CV) disease after kidney transplantation limits long-term patient survival. Adiponectin is an adipocyte-derived cytokine and has been suggested to have a protective role in the development of CV disease. Low adiponectin levels are found in obesity, insulin resistance, and diabetes. However, in dialysis patients and patients with heart failure, high adiponectin levels have been found to be associated with increased rather than decreased CV mortality. The role of adiponectin therefore remains controversial. We aimed to investigate the associations of adiponectin with CV risk factors and mortality in renal transplant recipients (RTR). Methods: Baseline measurements were performed between 2001 and 2003 in outpatient RTR with a functioning graft >1 yr. Follow-up was recorded until 19 May 2009. CV mortality was defined as deaths in which the principal cause of death was CV in nature, using ICD-9 codes 410–447. Plasma adiponectin concentration was measured by enzyme-linked immunosorbent assay. Results: A total of 606 RTR (age 51±12 yrs, 55% men) were studied at a median [IQR] of 6.0 [2.6-11.4] years post-transplant. During follow-up for 7.0 [6.2-7.5] years, 71 (12%) RTR died from CV cause. Median [IQR] plasma adiponectin concentration was 19.4 [14.6-27.9] mg/l. Adiponectin was positively associated with HDL cholesterol (β=0.40, P<0.001), whereas it was inversely associated with insulin (β=-0.32, P<0.001), glucose (β=-0.15, P<0.001), BMI (β=-0.19, P<0.001), and waist-to-hip ratio (β=-0.34, P<0.001). No significant associations with CRP or blood pressure were found. In univariate Cox-regression analysis, adiponectin was positively associated with CV mortality (HR=1.65 [95%CI 1.03-2.63], P=0.04). This association became stronger after adjustment for age, sex, CV risk factors, and immunosuppression (HR=2.36 [95% CI 1.31-4.25], P=0.004).
Conclusions: In this prospective cohort study in RTR, we found that high adiponectin is associated with a higher risk for CV mortality. This association became stronger after adjustment for age, sex, CV risk factors, and immuno-suppression. High adiponectin might reflect a compensatory mechanism to attenuate endothelial and vascular damage during CV disease. The adiponectin paradox could also be analogous to the obesity paradox, encompassing a survival advantage rather than disadvantage of dialysis and heart failure patients with higher BMI over patients with lower BMI.

Improvement of microvascular tortuosity after combined kidney-pancreas transplantation

M. Khairoun[1], R.N. de Boer[1], J.I. Rotmans[1], B.M van den Berg[1], D.K. de Vries[2], H.C. de Boer[1], E. Lievers[1], A.J. van Zonneveld[1,3], E.J. de Koning[1], J.W. de Fijter[1], T.J. Rabelink[1,3], M.E.J. Reinders[1], [1]Dept. of Nephrology, [2]Dept. of Surgery, [3]Einthoven Laboratory for Experimental Vascular Research, Leiden University Medical Centre, The Netherlands

Introduction: Diabetic nephropathy (DN) is currently one of the most serious complications of long standing diabetes. Combined kidney and pancreas transplantation (KPTx) is an effective treatment option for DN aiming at long-term normoglycemia and amelioration of secondary complications. Endothelial cell (EC) dysfunction due to hyperglycaemia is a critical part of the pathogenesis of microvascular and macrovascular complications. Sidestream dark-field (SDF) imaging has recently emerged as a non invasive tool to visualize the human microcirculation. SDF used in patients with essential hypertension, diabetes mellitus and autoimmune rheumatic diseases demonstrated microvascular capillary loss and morphological changes. This study sought to assess the effect of KPTx in DN patients on microvascular alterations using SDF and to correlate this effect with markers for endothelial dysfunction, including Ang-1, Ang-2 and thrombomodulin (TM). Methods: Mean capillary density and microvascular morphology were visualized and compared among patients with DN (N=10), KPTx patients (N=10; mean 5, 5 years after KPTx) and healthy controls (N=10) using SDF. Furthermore serum Ang-1, Ang-2 and TM were measured using ELISA in patients with DN (N=30), KPTx patients (N=35) and healthy controls (N=15). We calculated the Ang-2/ Ang-1 ratio, since this is considered to better reflect the loss of microvascular integrity than individual angiopoietin levels. Results: Quantitative analysis of capillaroscopic images showed no significant differences in capillary density between the 3 different groups ($p>0.05$). However, we found more capillary tortuosity in the DN group and an improvement after KPTx ($p<0.05$). In line with these findings, markers of endothelial destabilization including Ang-2 and TM, were significantly increased in DN patients as compared to the KPTx recipients and controls ($p<0.05$). The Ang-2/Ang-1 ratio was significantly lower after KPTx (mean 0.025 ± SD 0.010; $p<0.05$) than in the DN group (mean 0.059 ± SD 0.029), suggesting a reversal of endothelial destabilization. Conclusion: The microcirculation, as assessed by SDF, was disturbed in patients with DN in comparison to controls. Interestingly, KPTx showed an improvement in microvascular tortuosity and EC function compared to DN patients. Our study demonstrates that SDF is an excellent tool to monitor microvascular alterations before and after KPTx.

Risk of infectious complications after renal transplantation; awareness and attitude of renal transplant recipients

G.H. Struijk[1], R. Brinkman[1], M. van Vugt[2], I.J.M. ten Berge[1], F.J. Bemelman[1], [1]Renal Transplant Unit, Dept. of Nephrology, Div. of Internal Medicine, [2]Dept. of Infectious Diseases, Tropical Medicine & AIDS, Academic Medical Centre, Amsterdam, The Netherlands

Background: The number of infectious complications after renal transplantation is increasing due to the use of more potent immunosuppressive drugs. Reactivation of latent infections frequently occurs and a growing number of renal transplant recipients (RTR) travel internationally, hereby increasing the incidence of travel-related diseases. The awareness and attitude of RTR regarding their risk of infectious complications is not fully known.
Methods: Between October 2010 and December 2010, a cross-sectional survey was performed at a Dutch renal transplant outpatient clinic department to investigate the awareness and behaviour of RTR regarding their risk on infectious complications. Results: 248 RTR completed the questionnaire yielding a response rate of 71%. The mean age was 51 years and 53% was male. Sixty-five percent of respondents indicated that their risk on becoming ill is higher compared to someone without a renal transplant and 55% thought that the course of their illness would be more serious for RTR than for someone who has not undergone a renal transplant. Yet 50% of respondents indicated to visit ill relatives and friends. Moreover, 32/66 (48%) respondents who travelled outside West-Europe and North-America did not ask for travel advice. Overall, vaccination rates after transplantation for tetanus, influenza, pneumococci and hepatitis A were 15%, 60%, 2% and 11% respectively.
Conclusion: These preliminary results indicate that the majority of Dutch RTR is aware of their increased risk of infectious complications and the seriousness of infectious diseases after renal transplantation. However, their behaviour does not match their awareness. This suggests an important role for nephrologists in providing adequate counselling.

Islet-after-kidney transplantation using alemtuzumab induction therapy

E.J.P. de Koning[1,2], M.A. Engelse[1], J. Oostendorp[3], J.J. Zwaginga[4], C. Loomans[1], H.J. Guchelaar[3], H. Van Bockel[5], A. Baranski[5], S. Schaapherder[5], J.A. Romijn[2], W. Fibbe[4], O. Korsgren[6], T. Lundquist[7], R. Ploeg[8], P.J.M. van der Boog[1], H.J. de Fijter[1], J. Ringers[5], T.J. Rabelink[1], Depts. of [1]Nephrology, [2]Endocrinology, [3]Clinical Pharmacy & Toxicology, [4]IHB, [5]Surgery, Leiden University Medical Centre, [6]Dept. of Clinical Immunology, Uppsala University, [7]Dept. of Surgery, Karolinska Hospital, Stockholm, Sweden, [8]Dept. of Surgery, University Medical Centre Groningen, The Netherlands

Beta-cell replacement is the only therapy that normalizes glucose control without an increased risk of hypoglycemia. Islet transplantation is a relatively new form of beta-cell replacement therapy with a low risk of procedure-related complications. However, long-term islet function declines which may be related to immunosuppressive drugs that have an adverse effect on beta cells. We studied the effect of a novel immunosuppressive regimen on islet graft function using the T-cell depleting agent alemtuzumab as induction therapy and low dose tacrolimus, prednisone and MMF as maintenance therapy. After screening patients with type 1 diabetes, previous kidney transplantation and unstable glycemic control were put on the islet transplantation waiting list. Transplantation was performed by transhepatic catheterization of a portal vein branch under local anesthesia and infusion of the islets in the portal vein during 20 minutes. Immunosuppressive protocols included induction with alemtuzumab (15 mg s.c. on 2 occasions) and low dose prednisone (5 mg)/low dose tacrolimus/MMF maintenance therapy. For subsequent islet infusions Il-2 receptor blockade was used as induction. Mixed meal (Boost®) tests were performed at 3 months and yearly after the last islet transplantation. C-peptide and glucose concentrations were measured at t=0, 15, 30, 45, 60, 90 and 120 minutes during the test. Eight patients (M/F 5/3, age 52.0±9.7 yrs (mean±SD)) received a total of 12 islet infusions. T-cells were depleted shown by a decrease in CD3+ cells from 1362±671x10^6/l to 68±36x10^6/l within 3 months. In all patients restoration of hypoglycemia awareness and improvement in occurrence of hypoglycemic episodes was achieved within 3 months. During this time period HbA1c improved from 7.6±1.1 % to 6.0±0.7 %. Three out of four patients with more than 1 year follow-up after the last islet transplantation were insulin-independent. At one year after the last transplantation C-peptide increased from 0.7±0.4 nmol/l at baseline to a maximum of 3.1±2.1 nmol/l, with glucose values of 6.2±0.9 at baseline to 8.2±1.0 at 2 hours during a mixed meal test in these 4 patients. Beneficial effects of islet transplantation on hypoglycemic episodes and glycemic control can be achieved using an immunosuppressive regimen including alemtuzumab induction. Insulin indepen-dency is possible but longer follow up is necessary to determine whether this regimen is superior in preserving long-term islet function.

Slow graft function in living donor kidney transplantation: an issue to be addressed

J. Hellegering[1], J. Visser[1], H.J. Kloke[2], F.C.H.D'Ancona[3], A.J. Hoitsma[2], J.A. van der Vliet[1], M.C. Warlé[1], [1]Dept. of Surgery, Division of Vascular- and Transplant Surgery, [2]Dept. of Nephrology, [3]Dept. of Urology, Radboud University Nijmegen Medical Centre, The Netherlands

Background: Slow graft function (SGF) after living donor kidney transplantation is associated with more rejection episodes. However its influence on long-term graft survival remains inconclusive. Methods: Data were collected retrospectively on 468 consecutive living donor kidney transplantations per-formed in our hospital between July 1996 and February 2010 to evaluate the occurrence of SGF and its influence on long-term graft survival. SGF was defined as a serum creatinine $\geq$ 265 µmol/L 5 days after transplantation without dialysis. Results: The incidence of SGF and delayed graft function (DGF) was 9,4% and 4,3%, respectively. Logistic regression analysis revealed recipient BMI, pre-transplant dialysis and anastomotic time as risk factors for the occurrence of SGF. Acute rejection free survival rates at 3 months were 83.4% for recipients with immediate graft function (IGF), 45.5% and 35% for recipients with SGF and DGF, respectively ($p<0.001$). Five year graft survival rates for recipients with IGF, SGF and DGF were 91.6%, 79.1% and 73.7%, respectively ($p<0.001$).
Conclusions: Both, five year graft survival and 3-month rejection free survival are significantly lower in patients with SGF as compared to patients with immediate graft function. These results underline the clinical relevance of SGF as phenomenon after living donor kidney transplantation. Therefore, further research should focus on new strategies to reduce the incidence of slow graft function.

Patient survival after the diagnosis of cancer in renal transplant recipients: a nested case control study

J. van de Wetering[1], J.I. Roodnat[1], A.C. Hemke[2], A.J. Hoitsma[2], W. Weimar[1,2], [1]Internal Medicine and Transplantation, Erasmus University Medical Centre Rotterdam, [2]Dutch Transplant Foundation, Leiden, The Netherlands

Introduction: Malignancy is a well-known complication after renal transplantation. We studied the influence of cancer on patient survival in the Dutch renal transplant population in a nested case controlled analysis. Methods: Between March 1966 and May 2008 15,227 renal transplantations in 12,805 recipients were registered in the Netherlands Organ Transplant Registry (NOTR) database. Total follow-up was 89,651 person years. We performed an analysis of patient and graft survival both from the day of transplantation and the diagnosis of cancer in recipients with invasive cancer. Recipients without invasive cancer, matched for gender, age and year of transplantation, served as a control group. For the survival analysis after the diagnosis of cancer, the matched control group consisted of patients with a functioning graft at the moment the index patient was diagnosed with cancer.
Results: Cancer had been registered in 908 (7.1%) patients, 630 (69%) of them died with functioning kidney, 510 (81%) due to their malignancy (at 8.2 years after transplantation, median). The median patient survival after transplantation was 11.9 versus 16.8 years in the study and control group respectively ($p < 0.001$). The median patient and graft survival, *after the diagnosis of cancer* was 2.1 versus 8.3 ($p<0.001$) and 25 versus 22.4 ($p<0.001$) years in the study and control group respectively.
Conclusion: Mortality due to cancer is observed at a significantly later time after transplantation compared to mortality due to the other main lethal complications. It significantly affects life expectancy and carries a poor prognosis with a limited survival after diagnosis.

mTOR inhibition enhances the procoagulant state of renal transplant recipients

M.C. Baas[1], V.E.A. Gerdes[2, 3], I.J.M. ten Berge[1], J.C.M. Meijers[2], F.J. Bemelman[1], [1]Renal Transplant Unit, Dept. of Nephrology, Div of Internal Medicine, [2]Dept. of Vascular Medicine, Academic Medical Centre, Amsterdam, [3]Dept. of Internal Medicine, Sloter-vaartziekenhuis, Amsterdam, The Netherlands

Background: Renal transplant recipients are at increased risk of venous thrombo-embolic events, which is in part caused by their treatment with maintenance immunosuppressive drugs. Because we observed an increased incidence of venous thrombo-embolic events in renal transplant recipients treated with a mTOR inhibitor (mTORi) (6.3%) versus those treated with either a calcineurin-inhibitor (0%) or mycophenolate sodium (1.1%), we aimed to identify possible prothrombotic mechanisms of this immunosuppressive drug. Methods: In a single center study, nested in a multi-center randomized controlled trial, we measured parameters of endothelial activation, coagulation and fibrinolysis in renal transplant recipients who received the mTORi everolimus (n=16, mTOR group) and compared them to a similar patient group, treated with a calcineurin inhibitor and/or mycophenolate sodium (n=20, non-mTOR group). All patients were at least 6 months following transplantation with a stable transplant function. Results: The use of a mTORi was associated with significantly higher levels of von Willebrand factor, prothrombin fragment 1+2, thrombin-activatable fibrinolysis inhibitor and plasminogen activator inhibitor-1 as compared to a non-mTOR based immuno-suppressive regimen. We found no correlation with C-reactive protein.
Conclusion: Treatment with mTORi leads to increased endothelial activation, thrombin formation and impaired fibrinolysis posing patients at an increased risk of thrombo-embolic complications. Larger studies with clinically relevant end-points are required to establish the final risk.

The impact of donor age in living and deceased donor kidney transplantation

M. Laging[1], J.A. Kal-van Gestel[1], J. van de Wetering[1], J.N.M. IJzermans[2], W. Weimar[1], J.I. Roodnat[1], Depts. of [1]Internal Medicine and [2]General Surgery, Erasmus Medical Centre Rotterdam, The Netherlands

Background: In deceased donor kidney transplantation donor age is known to influence graft survival. We wondered about the influence of living donor age on graft survival. Methods: All 1821 transplants performed in our center between 1990 and 2009 were included in the analysis. 941 patients received a deceased donor kidney and 880 a living donor kidney. Kaplan Meier analysis was performed, including donor age and type (living vs. deceased). Univariate and multivariate Cox proportional hazard analyses were performed, including year of transplantation, number of previous transplantations, pre-treatment, total number of mismatches, number of DR mismatches, maximum PRA, current PRA, recipient gender and age, and donor type, gender and age.
Results: In Kaplan Meier analysis, the influence of donor age was significant in deceased donation, but not in living donation. Graft survival censored for death after living donor transplantation was better than after deceased donor transplantation for any age donor. In multivariate Cox analysis, donor type, total number of mismatches, current PRA, and recipient age were found to have a significant influence on graft failure, censored for death. Donor age had a quadratic influence on graft failure, which means that the influence was U-shaped. The risk was highest for the youngest (children) and eldest donors. The interaction term between donor type and donor age was not significant ($p=0.064$), but for all ages the risk for graft failure in recipients of a deceased donor kidney was more than twice that of recipients of a living donor kidney.
Conclusion: In Kaplan Meier analysis living donor age appears not to have a significant influence on graft survival. However, in Cox analysis donor age has a significant influence on graft failure independent on donor type. The risk for graft failure in recipients of a kidney transplantation increases with increasing donor age according to a quadratic equation. However, the risk in deceased donor transplantation is more than twice that in living donor transplantation so that the graft failure risk for a recipient of a 65-year old living donor kidney is the same as that of a recipient of a 25-year old deceased donor kidney.

A functional polymorphism in Ficolin-2 in the donor kidney is associated with improved renal transplant outcome

M. Eikmans[1], I. de Canck[2], P. van der Pol[3], C.C. Baan[4], G.W. Haasnoot[1], M.J.K. Mallat[3], M. Bryson-Vergunst[1], E. de Meester[2], J.I. Roodnat[4], J.D.H. Anholts[1], M. van Thielen[2], I.I.N. Doxiadis[1], J.W. de Fijter[3], P.J.E. van der Linden[1], E. van Beelen[1], C. van Kooten[3], J. Kal-van Gestel[4], A.M.A. Peeters[4], W. Weimar[4], D.L. Roelen[1], R. Rossau[2], F.H.J. Claas[1], [1]Dept. of Immunohematology, Leiden University Medical Centre, [2]Dept. of Innogenetics, Belgium, [3]Dept. of Nephrology, Leiden University Medical Centre, [4]Dept. of internal Medicine, Erasmus University Medical Center, Rotterdam, The Netherlands

Innate immunity plays a critical role in controlling adaptive immune responses. Here we investigated the clinical relevance of single nucleotide polymorphisms (SNPs) in innate immunity genes for the outcome of renal transplantation.
In a dual-center study of 520 transplant recipients and cadaveric donors 81 SNPs were studied. These were located in genes encoding for secreted pattern recognition receptors (Mannose binding lectin, Ficolins, MASPs, C1qR) and signaling pattern recognition receptors (Toll-like receptors 1-10, CD14, LBP, Sigirr, CARD15). Association with rejection incidence was tested in a definition set (random, one-third of the group). Significant associations were verified in a validation set (remaining two-third).
Both in the definition and the validation set an amino acid substituting polymorphism in exon 8 (Ala258Ser, frequency of 20%) of the Ficolin-2 gene in the donor was associated with lower incidence of severe rejection (GT: 9%, GG: 22% incidence, $P<0.05$). The donor GT variant was associated with improved 10-year graft survival (80%) compared to the donor GG variant (58%) (Log rank=5.8, P=0.016). The donor Ficolin-2 GG genotype was a predictor of severe rejection (OR=3.1, P=0.026) and graft survival (HR=2.0, P=0.046), independently of clinical variables. Ficolin-2 levels in either patient or donor serum (n=105) did not significantly differ between genotypes. Ficolin-2 mRNA was detected with qPCR in pre-transplant biopsies (n=77), but the level was not affected by genotype. However, the GT variant of Ficolin-2 shows increased binding capacity to its natural ligand GlcNAc compared to the GG variant. Ficolin-2 was found to bind to late apoptotic and necrotic cells. Ficolin-2 protein was demonstrated in pre-transplant kidneys between tubules in a passenger leukocyte-like pattern.
The Ficolin-2 Ala258Ser polymorphism in the donor is associated with significantly improved graft outcome for the patient. We propose that this SNP in Ficolin-2, expressed by phagocytosing cells in the engrafted kidney, enables a more efficient handling of injured cells. This may lead to decreased intragraft exposure to danger signals and a dampened alloimmune response.

In vitro skewing of the human KIR repertoire leads to enhanced NK cell alloreactivity

D.N. Eissens[1], F.W.M.B. Preijers[2], B. van Cranenbroek[1], K. van Houwelingen[1], A. van der Meer[1], I. Joosten[1], [1]Dept. of Laboratory Medicine - Laboratory of Medical Immunology, [2]Dept. of Laboratory Medicine - Laboratory of Hematology, Radboud University Nijmegen Medical Centre, The Netherlands

In allogeneic stem cell transplantation (SCT), NK cells are able to perform graft-versus-leukemia (GVL) responses without the induction of graft-versus-host disease (GVHD), a feature that can be exploited for cellular immunotherapy. NK cell alloreactivity is induced when inhibitory killer immunoglobulin-like receptors (KIR) fail to recognize HLA molecules on potential target cells. In this study, we examined the plasticity of the KIR repertoire and the cytolytic response of mature human peripheral blood NK cells in the presence of specific KIR receptor-ligand (i.e. HLA-C) mismatches. We show that the introduction of specific KIR-ligand mismatches (KIR vs. HLA-C) *in vitro* favors the outgrowth of KIR^+ NK cells lacking their cognate ligand leading to an increased frequency of alloreactive KIR^+ NK cells within the whole NK cell population. Furthermore, after culture, these KIR^+ NK cells are more cytolytic on a per cell basis towards KIR-ligand mismatched K562 target cells and primary leukemic target cells. This study demonstrates that HLA class I can skew the mature NK cell phenotype and enrich the alloreactive NK cell population towards leukemic target cells, which may be important for future clinical applications of NK cell-based immunotherapies in transplantation settings.

Oxygenated In Situ Cold Perfusion of DCD Kidneys in Pigs

H.G.D. Leuvenink, C. Krikke, S. Hofker, V. Nieuwenhuijs, H. ten Cate Hoedemaker, R. Ploeg, Dept. of Surgery, University Medical Centre Groningen, The Netherlands

Kidneys retrieved from Deceased Cardiac Death (DCD) donors are subjected to extended periods of warm ischemia (WI). Primary Non Function and Delayed Graft Function are common in these kidneys. To improve outcome after DCD donation we examined the effect of cold oxygenated in situ perfusion (ISP) in large pigs (~70kg) compared to standard flush pocedure.
Methods: Pigs were anesthetized and ventilated before induction of cardiac arrest by means of a ventilator switch off procedure. After cardiac arrest, animals were untouched for 20 minutes. In the control group (n=7) a rapid laparotomy was performed and an abdominal systemic gravity-based flush-out with 4 liters of UW solution through the aorta was performed. In the ISP group (n=8) flush-out was performed by pulsatile perfusion of oxygenated UW at 25 mmHg through the aorta using the ECOPS device (Organ Assist BV). After the abdominal flush-out with 4 liters of UW, an isolated renal circulation was created by clamping the aorta proximal and distal from the renal arteries as well as redirecting the caval drain to the circuit. In both groups, aortic and renal flow as well as renal temperature was measured. Kidneys were retrieved 90 minutes after start of flush-out and cold stored for 20 hrs in UW. Kidneys were then transplanted into recipient pigs with removal of the native kidneys. During the 14 day follow up period renal function was measured. After 14 days animals were sacrificed and kidneys retrieved for further evaluation.
Results: Donation: During the organ procurement procedure renal temperature during flush-out decreased to 25 ±3°C in the control group and 23 ±3°C after 15 minutes. Flow-rate of UW in the aorta was higher in the control group compared to the ISP group (221±12 ml/min vs. 147±24 ml/min), however renal artery flow did not differ due to large variation in the control group. After 90 minutes, renal temperature in the ISP group (19±2°C) was significantly lower than the control group (25±2°C). Post transplant function: In the control group 2 animals suffered from PNF in contrast to none in the ISP group. At day 1and 2 after tx urine production was higher in the ISP group and a better GFR was observed. After 2 days no differences in renal function could be detected anymore.
Summarizing, the use of ISP is a potentially interesting method to reduce WI. Likely further reduction in temperature should be achieved before introduction into clinical practice.

The antioxidant dogma in human ischemia-reperfusion injury: no evidence for free radical mediated damage

D.K. de Vries[1], K.A. Kortekaas[2], D. Tsikas[3], R.J.M. Klautz[2], A.F.M. Schaapherder[1] and J.H.N. Lindeman[1], Depts. of [1]Surgery and [2]Cardiothoracic Surgery, Leiden University Medical Centre, The Netherlands, [3]Institute of Clinical Pharmacology, Hannover Medical School, Germany

Background: Oxidative stress has traditionally been considered the primary initiator of ischemia-reperfusion (I/R) injury. Remarkably, while antioxidant therapy has been highly effective in animal studies, patient trials fail to show a clinically relevant benefit of antioxidant therapy. This challenges the role of reactive oxygen species (ROS) as a major contributor to human I/R injury.
Methods and results: Using an unique method of clinical arteriovenous measurements, various markers of oxidative damage were measured during planned reperfusion in human kidney transplantation and cardiac surgery. Arterial and venous samples were compared in their concentration of oxidative stress markers (i.e. malondialdehyde (MDA) and 15(*S*)-8-*iso*-prostaglandin F2α (15(*S*)-8-*iso*-PGF2α)) and markers of nitrosative stress (i.e. nitrite, nitrate and nitrotyrosine) during the early reperfusion phase. None of the markers of oxidative and nitrosative stress were released upon reperfusion, with the exception of a small, transient release of 15(*S*)-8-*iso*-PGF2α. Urinary measurements during kidney transplantation were in conformance with plasma findings, showing no release of oxidative or nitrosative stress markers.
Conclusions: Results of this study show no evidence for damage caused by oxidative or nitrosative stress in early clinical I/R injury in humans. This finding suggest that endogenous antioxidant systems are sufficiently equipped to handle the excess ROS load during reperfusion; thus preventing damage.

Activated tubular epithelial cells produce chemokines that attrack Th1-, but not Th17 cells

M.W.H.J. Demmers, C.C. Baan, W. Weimar, A.T. Rowshani, Dept. of Internal Medicine, Division of Renal Transplantation, Erasmus University Medical Centre Rotterdam, The Netherlands

Introduction: Renal tubular epithelial cells (TECs) play a central role in inflammatory processes during ischemia-reperfusion injury and allograft rejection. Tubulitis is the hallmark of cellular rejection leading to structural graft damage. We hypothesize that TECs modulate the outcome of the inflammatory process by the production of distinct cytokines/chemokines that may determine the attraction, activation, differentiation and function of different T-cell subsets. Here, we studied whether TECs after stimulation by IFN-γ and TNF-α have the potential to attract T_h1 and T_h17 T-cell subsets.
Materials and Methods: TEC cell lines (N=10) were cultured from cortex tissue of human donor kidneys obtained at the time of transplantation and stimulated by IFN-γ and TNF-α *in vitro* in a dose and time dependent manner. Cell surface expression of CD40 and HLA-II were analyzed by 8 colour flow cytometry, and cytokine/chemokines produced by activated TECs in the supernatant were measured using Luminex and/or ELISA.
Results: The combined stimulation with IFN-γ (50ng/ml) and TNF-α (20ng/ml) resulted in increased expression levels of the costimulatory molecule CD40 (3 fold increase) and HLA-II (2 fold increase) as compared to non-stimulated state. CD80/CD86 molecules were not detectable on TECs in resting or in activated state. This was observed after 24h stimulation and remained present for at least 72h. The cytokine activated TECs abundantly secreted the pro-inflammatory cytokines IL-6 and IL-8 (5-7 fold increase), while IL-1β and IL-12p70 were not detectable. Moreover, IFN-γ and TNF-α stimulation significantly upregulated the production of the T_h1 ligands RANTES, IP-10 and MIG after 72 hours ($p<0.001$) and not the T_h17 ligand MIP-3α. The T_h17 associated cytokine IL-23 was also not measurable.
Conclusion: Our data show that the proinflammatory cytokines IFN-γ and TNF-α stimulate TECs to produce the chemokines necessary to specifically attract T_h1-, but not T_h17 cells.

Factors secreted by liver-derived mesenchymal stem cells promote liver regeneration after partial hepatectomy

S.M.G. Fouraschen[1], J. de Jonge[1], Q. Pan[2], G. Kazemier[1], J. Kwekkeboom[2], H.J. Metselaar[2], H.W. Tilanus[1], L.J.W. van der Laan[1], Depts. of [1]Surgery and Laboratory of Experimental Transplantation and Intestinal Surgery and [2]Gastroenterology & Hepatology, Erasmus University Medical Centre, Rotterdam, The Netherlands

Objectives: Rapid liver regeneration is required after living-donor liver transplantation to warrant sufficient liver function and prevent small-for-size syndrome. Mesenchymal stem cells (MSC) and their secreted factors could represent a new therapeutic strategy to stimulate liver regeneration and thereby reduce morbidity and mortality after major liver resections. In this study we investigated the effect of factors secreted by liver-derived MSC in a 70% partial hepatectomy (PH) model in mice.
Methods: C57BL/6 mice were subjected to a 70% PH and treated with concentrated conditioned culture medium of liver-derived MSC (MSC-CM) or with PBS as vehicle control, starting 4 hours prior to (t=-4) or at time of PH (t=0), and in both cases 24 hours after PH. Animals were sacrificed after 2 days and their livers were analyzed for hepatocyte proliferation and relevant gene expression. Effects of MSC-CM on gene expression in hepatocytes were investigated *in vitro* using Huh7 cells and genome-wide Affymetrix array.
Results: Hepatocyte proliferation was statistically significantly increased in animals treated at t=0 with MSC-CM compared to controls (20.0% vs 12.1%) and showed a similar trend in animals treated at t=-4 (19.3% vs 14.7%). A significant increased gene expression was observed in the MSC-CM group for PCNA (4.8-fold), TNF-α (2.6-fold), TGF-ß (2.1-fold) and HGF (1.9-fold) versus PBS controls. Also genes relevant for angiogenesis, VEGF-A (1.9-fold), Ang-1 (1.8-fold), VEGF-R2 (1.5-fold) and VEGF-R1 (1.4-fold) and the anti-inflammatory cytokines IL-1Ra (3.3-fold) and IL-10 (2.8-fold) were significantly upregulated in the MSC-CM group. Genome-wide gene expression profiling in Huh7 cells showed that MSC-CM significantly altered levels of approximately 3000 genes. Pathway analysis using Ingenuity software showed that MSC-CM strongly affects gene networks associated with protein synthesis, cell survival and cell proliferation.
Conclusion: This study shows that liver regeneration was significantly stimulated by MSC-derived factors as shown by an increase in hepatocyte proliferation and gene expression of relevant cytokines and growth factors. MSC-derived factors represent a promising strategy to expand options in living-donor liver transplantation.

Phosphospecific flow cytometry to monitor P38 MAP kinase activity in T lymphocytes of renal transplant patients

R. Vafadari, M.M. Kho, M. Wabbijn, W. Weimar, C.C. Baan, Dept. of Internal Medicine, Erasmus Medical Centre Rotterdam, The Netherlands

Introduction: Transplant patients frequently suffer from lack of efficacy by immunosuppressive medication or from toxicity, which can be attributed to inter-individual variation in drug sensitivity. This problem can be overcome by pharmacodynamic monitoring, which focuses on measuring the biological effects of drugs. We used phosphospecific flow cytometry to study the effect of tacrolimus (TAC) on P38 MAP kinase (MAPK), the activator of NFAT (nuclear factor of activated T cells), in T cells. Materials & Methods: Freshly obtained whole blood samples were stimulated with PMA/Ionomycin, and P38 MAPK phosphorylation was measured by flow cytometry. Results: In vitro TAC inhibited P38 MAPK in a dose dependent manner: the IC_{50} in T cells was 37 ng/mL (95% CI 32 to 44 ng/ml). Mycophenolic acid and prednisolone had no inhibitory effect on T lymphocytes. In healthy volunteers (N = 4), 2 hours after an oral dose of 10 mg TAC, the P38 MAPK activation was inhibited by 35.3 % (median, range 16.4 - 60.3 %) and gradually recovered to baseline after 24 hours. In patients, one week and one month after renal transplantation, P38 MAPK activation did not decrease 2 hours after intake of TAC. Nevertheless, one week after Tx the P38 MAPK activation in T lymphocytes had significantly decreased in 22 out of 25 patients compared to pre-transplantation ($p < 0.001$). Three patients had elevated P38 MAPK activity and at the same time, a biopsy proven cellular rejection.
Conclusion: In vitro and in healthy subjects TAC inhibits P38 MAPK. After transplantation P38 MAPK reflects an overall immunosuppressed state, which is not only the result of TAC alone. Elevated P38 MAPK activation might be a useful marker for cellular rejection.

Adipose Tissue Derived Mesenchymal Stem Cells Are Not Affected by End Stage Renal Disease

M. van Rhijn[1], M.E.J.Reinders[3], S.S. Korevaar[1], F.J.M.F. Dor[2], J.N.M. IJzermans[2], C.C. Baan[1], W. Weimar[1], M.J. Hoogduijn[1], Depts. of [1]Internal Medicine and [2]General Surgery, Erasmus University Medical Centre Rotterdam, [3]Dept. of Nephrology, Leiden University Medical Centre, The Netherlands

Background Mesenchymal stem cells (MSC) are multipotent cells with regenerative and immunomodulatory capacities. These features make them of interest as a therapeutic agent for a variety of conditions including end-stage renal disease (ESRD) and kidney transplantation. In kidney transplantation, the use of autologous cells is to be preferred in order to avoid induction of anti-HLA reactivity. However, the influence of ESRD on the functionality and genetic stability of MSC is unknown. Therefore, we isolated and expanded MSC from ESRD patients and compared them with those obtained from healthy controls and investigated the in vitro influence of uremic conditions on patient derived MSC. Methods We isolated MSC from adipose tissue of healthy controls (MSC-HC) and ESRD patients (MSC-RD). The cells were characterized and compared for morphology, expansion potential, immunophenotype, apoptosis and immunomodulatory and differentiation capacity. Subsequently, MSC from ESRD patients were tested for genetic stability in culture by whole genome SNP analysis. Finally, their characteristics were investigated under uremic culture conditions. Results MSC-HC and MSC-RD showed comparable spindle shaped morphology and osteogenic and adipogenic differentiation capacity. MSC-HC and MSC-RD were both over 90% positive for CD73, CD105 and CD166 and negative for CD31 and CD45. MSC obtained from both healthy controls and renal disease patients showed comparable population doubling times (2.7 versus 2.6 days) and apoptosis rates (4.1% versus 3.7%) and were capable of inhibiting allo-antigen and anti-CD3/CD28 activated PBMC at a similar capacity. MSC-HC and MSC-RD expressed pro- inflammatory (Il-6, Il-1β) and anti-inflammatory cytokines (TGF-β) at comparable levels. MSC-RD were genetically stable after 1000-fold expansion in culture. In addition, culturing of MSC-RD in human uremic serum did not compromise functionality of MSC-RD. Conclusions In conclusion, in this study we show that MSC of End Stage Renal Disease patients have the same characteristics and functionality as those obtained from healthy controls and are not affected by uremia in vitro. These results indicate the feasibility of isolation, expansion and use of these cells for autologous cell therapy.

Optimizing alloantigen presentation as a tool to monitor indirect alloantigen presentation in renal transplant recipients

E. Breman[1], M.H. Heemskerk[2], F.H. Claas[3], C. van Kooten[1], Depts. of [1]Nephrology, [2]Hematology, [3]Immunohematology and Blood Transfusion, Leiden University Medical Centre, The Netherlands

Upon transplantation recipient T-cells may recognize donor HLA molecules in two different manners: Recognition of intact HLA on donor antigen presenting cells (APC, direct pathway) associated with acute rejection. And recognition of donor-derived HLA peptides restricted by self-HLA on recipient APC (indirect pathway). The latter is mainly associated with chronic rejection and the occurrence of activated T-helper cells with properties of B cell help. Current strategies for the monitoring of alloreactive T-cells (MLR and CTLp) are restricted to cells with direct specificity; there are no consistent assays for the monitoring of indirect presentation. We have used a model system to investigate indirect allo-presentation.
HLA-DR1$^+$/HLA-A2$^-$ monocytes or monocyte derived dendritic cells (moDC) were incubated with different concentrations of HLA-A2 monomer/peptide for different time periods. A CD4$^+$ T-cell clone that specifically recognizes a HLA-A2 derived peptide in the context of HLA-DR1 was used as readout for HLA-A2 presentation. Supernatants were collected and IFN-γ was measured at different time points, as a marker for T-cell activation. The HLA-A2 monomer was furthermore coupled to monoclonal antibodies (mAb) directed against the Mannose Receptor (MR), to improve HLA-A2 processing and presentation by APC. Addition of intact HLA-A2 monomer to HLA-DR1$^+$/HLA-A2$^-$ moDC resulted in specific antigen presentation and a dose dependent increase of IFN-γ secretion by the T-cell clone. T-cell recognition occurred only when HLA-A2 was presented in the context of HLA-DR1 (peptide/monomer) indicating a high specificity. A concentration of 25µg/ml HLA-A2 monomer gave the highest IFN-γ response. DC had to be incubated for at least 4h with the monomer to allow sufficient uptake, processing and presentation. The HLA-A2 peptide was presented in the context of HLA-DR1 for 24h, longer incubation showed a sharp decrease in T-cell activation. Similar characteristics were found when monocytes were used. In an attempt to improve specificity and efficiency of uptake, the HLA-A2 monomer was coupled to mAb targeted against MR. Preliminary data indicate that depending on the ratio (monomer/mAb) improved presentation could be achieved. We have shown that an intact HLA-A2 monomer can be used as a specific tool to allow indirect antigen presen-tation by dendritic cells and monocytes. This is instrumental for develop-ment of a clinically applicable assay to monitor indirectly activated T-cells.

Exosomes can mediate transmission of Hepatitis C virus in the presence of neutralizing antibodies: relevance for Hepatitis C recurrence?

V. Ramakrishnaiah[1], P.E. de Ruiter[1], R. Willemsen[2], J. Demmers[2], D. Diederick[2], G. Jenster[2], J. de Jonge[1], G. Kazmier[1], J. Kwekkeboom[3], H.J. Metselaar[3], H.W. Tilanus[1], L.J.W van der Laan[1], [1]Dept. of Surgery and Laboratory of Experimental Transplantation and Intestinal Surgery, [2]Dept. of Cell Biology and Genetics and [3]Dept. of Gastroenterology & Hepatology, Erasmus University Medical Centre, Rotterdam, The Netherlands

Introduction: Management and treatment of recurrent hepatitis C virus (HCV) infection after liver transplantation remains a major clinical challenge. Unlike for HBV, treatment with neutralizing antibodies (nAbs) does not prevent HCV re-infection. The exact mechanism of this immune deviation remains largely unknown. Recent evidence suggests that small vesicles/-exosomes can transfer mRNA and microRNA between cells. Therefore, the aim of our study is to investigate whether exosomes can shuttle HCV and contribute to the nAb-independent transmission of viral infection.
Method: Huh7 cells harbouring JFH-1 derived infectious HCV virus and naive Huh7 cells were used. Exosomes were isolated by density gradient ultra-centrifugation and analysed for HCV content by primary and secondary infectivity assays, real-time RT-PCR, mass spectrometry and immunostaining electron-microscopy. Cellular uptake of labelled exosomes was visualized by real-time confocal microscopy. Results: Purified exosomes from JFH-1 infected Huh7 cells, but not from naive Huh7 cells, contained HCV genomic RNA as detected by quantitative RT-PCR. Electron-microscopy showed the presence of virus-like particles within exosomes from HCV infected cells and was confirmed by immuno-gold staining. Mass-spectrometry analysis confirmed the presence of HCV viral proteins. Exosomes, labelled with rhodamine, are rapidly taken up by Huh7 cells. Moreover, exosomes can transfer HCV to naive Huh7 cells and establish a productive infection. Treatment with nAbs had a minor effect on exosome-mediated infection, in contrast to the almost complete inhibition of HCV infection by free viral particles.
Conclusion: Hepatocyte-derived exosomes can transfer HCV to naive cells establish a productive infection. Exosome-mediated transfer of HCV is largely resistant to nAbs and therefore may represent an immune evasion strategy of the virus. This may shed new light on the ineffectiveness of prophylactic nAbs to prevent HCV recurrence.

Lysis of Mesenchymal Stem Cells by NK Cells can not be Prevented by Immunosuppressive Drugs

M.J. Hoogduijn, S.S. Korevaar, A. Grohnert, M. van Rhijn, W. Weimar, C.C. Baan, Dept. of Internal Medicine, Erasmus Medical Centre Rotterdam, The Netherlands

Introduction: Mesenchymal stem cells (MSC) have potential for application in organ transplantation as an immunomodulatory and regenerative agent. The survival of MSC after infusion is however not clear and evidence suggests that MSC disappear within days after infusion. This may be associated to the capability of NK cells to lyse MSC. In the present study we examined whether NK cell mediated lysis of MSC could be inhibited by immunosuppressive drugs.
Methods: Human MSC were isolated from adipose tissue and expanded in culture. PBMC were activated by IL-2 (200U/ml) and IL-15 (10ng/ml) for 7 days. $CD3^{-}CD16^{+}CD56^{+}$ NK cells were then separated by FACS and added to Europium-labeled MSC for 4h in the presence or absence of immunosuppressive drugs. Alternatively, NK cells were incubated with the drugs for 24h prior to exposure to MSC. Lysis of MSC was determined by spectrophotometric measurement of Europium release.
Results: Non-activated NK cells were not capable of lysing MSC. NK cells activated by IL-2 and IL-15 showed upregulated levels of granzyme B and perforin and efficiently lysed allogeneic and autologous MSC. Tacrolimus (10ng/ml), Rapamycin (10ng/ml) or Sotrastaurin (50ng/ml) did not inhibit the lysis of MSC. Pre-incubation (24h) of activated NK cells with the immunosuppressive drugs had no effect on MSC lysis. These results indicate that an intrinsic property of MSC, which may include high expression of activating NK cell receptor ligands and low expression of granzyme B inhibitory molecules and inhibitory NK cell receptor ligands, triggers lysis by activated NK cells that can not be modulated by immunosuppressive drugs.
Conclusions: In conclusion, the immunosuppressive drugs Tacrolimus, Rapamycin and Sotrastaurin are not capable of inhibiting the lysis of allogeneic and autologous MSC by activated NK cells. Other approaches of controlling lysis of MSC should be investigated as controlling lysis would provide tools for controlling MSC therapy.

Cardiac allograft vasculopathy: a quantitative analysis of changes in coronary artery wall architecture after heart transplantation

M.M.H. Huibers[1], J. Kaldeway[1], A. Huisman[1], H.F.J. Dullens[1], M.E.I. Schipper[1], N. de Jonge[2], R.A. de Weger[1], Depts. of [1]Pathology, and [2]Cardiology, University Medical Centre Utrecht, The Netherlands

Background: Long time survival after heart transplantation (HTx) is hampered by chronic rejection. A critical step in this process is the immune reaction directed to the donor coronary arteries, leading to Cardiac Allograft Vasculopathy (CAV). Part of the underlying pathophysiological process is a mononuclear cell (MNC) infiltration in the neo-intima of the vessel. This leads to progressive neo-intimal thickening and luminal narrowing. Aim: Quantitatively investigate the relation between artery wall architecture and duration of survival after HTx. Methods: Three or more arterial cross sections were available after autopsy of thirty HTx patients. The surface area of the different vessel layers was measured microscopically using Aperio ImageScope. To distinguish the layers in the arterial wall, sections were stained with Haematoxilin eosin, Elastica von Gieson and Smooth muscle cell (smc) actin. Results: Survival after HTX did not exceed ten years in all but one patient. From two weeks upward infiltration of MNC was detected. Up to three years after HTx neo-intimal proliferation and luminal narrowing was observed ($p = 0.0048$ and $p = 0.0014$, respectively). In the ten year period these relations were not detected and only thinning of the media was observed ($p = 0.0005$). Arteries can be classified in four stages: Stage 1 is a normal coronary artery with smc neointima (NI-SMC) between the lamina elastica interna and the endothelium. During stages 2-4 CAV developed an additional layer between the endothelium and NI-SMC layer. In stage 2 this layer consists of loose connective tissue, whereas in stage 4 a dense collagen layer was observed. Stage 3 is an intermediate stage. Some cases showed total luminal occlusion, which can be observed at all CAV stages.
Conclusions: CAV is an ongoing process with increasing fibrosis of the neo-intima. In the first few years after transplantation mnc infiltration, neo-intimal proliferation and luminal narrowing is found. Unexpectedly these relations disappear in the ten year survival period. The media progressively gets thinner, but the neo-intima does not increase, nor does the lumen reduce. The neo-intima seems to solidify into solid fibrous tissue with presumably loss of contractility and elasticity, but the diameter of the lumen remains uncompromised.

Microwell scaffolds for extrahepatic islets of Langerhans transplantation in type I diabetes

M. Buitinga[1], E.J.P. de Koning[2], M.A. Engelse[2], C.J.M. Loomans[2], R. Truckenmüller[1], L. Moroni[1], C.A. van Blitterswijk[1], A.A. van Apeldoorn[1], M.Karperien[1], [1]Dept. of Tissue Regeneration, University of Twente, [2]Dept. of Nephrology, University Medical Centre Leiden, The Netherlands

Background: The conventional therapy for type I diabetes is insulin administration, but despite this, some patients are poorly controlled and suffer from hypoglycemic events and long-term complications. For these patients, allogeneic islet transplantation into the liver via islet infusion into the portal vein has become an alternative therapy. Patients benefit from this therapy due to near normalization of blood glucose levels without an increased risk of hypoglycemia. However, islet graft function in the liver tends to decline over years indicating that the liver is not an optimal transplantation site. In order to develop alternative islet transplantation sites with better long-term outcome, we have developed a new microwell scaffold platform. Methods: Both dense and porous scaffolds containing microwells with a diameter of ~330µm, were fabricated from 4000PEOT30PBT70 block-copolymer (PolyActive™) using microthermoforming. Wettability of the polymer surface was assessed by contact angle measurements. For the dense microwell scaffolds ~50µm thick polymer films were prepared by solution casting. Microporous scaffolds were fabricated from ~150µm thick electrospun membranes. Fiber diameter and scaffold topology were assessed by scanning electron microscopy (SEM). Furthermore, the constructs were characterized for their permeability for the nutrient glucose. To determine their applicability for islet transplantation, human islets were seeded into the scaffolds and cultured for 10 days. Morphology of the islets was studied by SEM and histological analysis.
Results and discussion: We were able to fabricate reproducible polymer films and porous membranes with a fiber-diameter of 1.71± 0.42µm. SEM analysis showed well formed microwells. Diffusion tests revealed that the electrospun scaffolds were permeable for glucose. The polymer films were hydrophilic, but human islets did not attach to the microwell scaffolds and they retained their rounded morphology. Based on SEM and histological analysis there were no indications for islet spreading or outgrowth of islet stromal cells. Preliminary function tests revealed that human islets remained responsive to glucose challenge in the constructs.
Conclusion: In this study we report on the development of a novel microwell scaffold platform for extrahepatic islet of Langerhans transplantation. Alternative transplantation sites using biomaterial scaffolds may improve islet transplantation outcome.

Preservation Solution and Method Affect Organ Temperature during Procurement

E. Buiter[1],C. Billault[1,2], B. Barrou[2], R.J. Ploeg[1], H.G.D. Leuvenink[1], [1]Dept. of Surgery, University Medical Centre Groningen, The Netherlands, [2]Dept. of Service d'Urologie et de Transplantation Rénale, Hôpital de la Pitié Salpêtrière, Paris, France.

Rapid cooling during procurement by intravascular administration of preservation fluids combined with topical cooling is common practice to reduce metabolic rate (MR) and reduce warm ischemia. The true reduction in MR depends on the efficacy of cooling. At 4 °C MR is reduced with 90% while at 25 °C a reduction of ~50% will be reached. Recent clinical assessment during procurement in our retrieval areas revealed renal temperatures at the end of procurement of 19.9 ±0.8 °C (Groningen) and 19.2± 4.2°C (Paris) after flush-out with 4-6 L UW. To get more insight in the efficacy of cooling we compared in a pig model two commonly used preservation solutions UW and HTK. In addition, we studied if cold continuous in situ perfusion (ISP) would result in lower temperatures. Four regimen were studied: Gravity flush with UW (Ctrl-UW) or HTK (Ctrl-HTK) and ISP with UW (ISP-UW) or HTK (ISP-HTK) Exp. Methods: Pigs were anesthetized and ventilated followed by induction of cardiac arrest due to the ventilator switch-off procedure. In the Ctrl groups a rapid laparotomy was performed followed by an abdominal systemic gravity-based flush-out with 5 L UW or 9 L HTK. In the ISP groups flush-out was performed by pulsatile perfusion of oxygenated preservation solution at 25 mmHg. After the abdominal flush-out with 4 L UW or 8 L HTK, an isolated renal circulation (1 L solution) was created by redirecting the caval drainage to the circuit. In all groups renal temperatures were measured.
Flush-out with UW resulted in lower temperatures compared to HTK (15 vs 24 °C). Despite topical cooling in the Ctrl groups renal temperature increased after flush-out was completed to 24 °C. Compared to Ctrl in both ISP groups temperatures decreased further reaching a difference of ~10 °C .
It can be concluded that during clinical and experimental procurement renal temperatures are much higher than the desired 4 °C and depend on the type of solution used. ISP could be a valuable tool to decrease metabolic rate during procurement reducing warm ischemia and subsequent post transplant DGF.

The emotional response to the receipt of an organ in liver transplant recipients

J.H. Annema[1], P.F. Roodbol[1], R.J. Porte[2], A.V. Ranchor[3], [1]Wenckebach Institute, School of Nursing & Health, [2]Dept. of Surgery, [3]Dept. of Health Psychology, University Medical Centre Groningen, The Netherlands

Introduction: Little is known about how transplant recipients respond emotionally to the receipt of an organ. The Transplant Effects Questionnaire (TxEQ) was developed to measure this response. The TxEQ comprises five subscales regarding topics important to transplant recipients: worries about the transplant, feelings of quilt, disclosure about the transplant, behaviour regarding medication adherence, and perceived responsibility. In this study we investigated the emotional response to organ transplantation in liver transplant recipients. Methods: Data on the TxEQ were collected as part of a cross-sectional study on the psychological impact of organ transplantation among 374 liver transplant recipients transplanted in our centre. Inclusion criteria were: age at transplant ≥18 years, transplant at least six months ago, currently receiving post transplant care at our centre, and able to fill in a Dutch questionnaire. Results: The response rate to the questionnaire was 75% (281/374). A majority of the respondents (58%) developed a feeling of responsibility for the received organ, especially towards the transplant team. Worries about the transplanted organ were reported by 22% of the respondents, mainly regarding the vulnerability and longevity. Only a minority reported feeling of guilt towards the donor (1.4%), problems in disclosing their transplant to others (1.8%), or difficulties in complying with the medication regimen (4.7%). Recently transplanted respondents (1-5 years) showed higher scores on 'feelings of responsibility' and 'worry about the transplant' than respondents who were transplanted more than 5 years ago. Also, they reported more difficulty in talking about their transplant. Recipients who were transplanted more than 15 years ago reported a higher level of feelings of quilt and had a lower adherence score than respondent transplanted 1-5 years or 5-10 years ago. However, none of these differences were significant.
Conclusion: In general, few liver transplant recipients report emotional difficulty in dealing with the transplantation. The majority responded to the receipt of an organ with a feeling of responsibility and good health behaviour regarding medication adherence. Only a minority have conscious feelings of guilt and shame. Time since transplantation seems to be of little influence on the TxEQ subscale scores. The TxEQ seems to be a useful screening instrument to detect patients with problematic emotional responses to organ transplantation.

Donation after cardiac death in liver transplantation: a calculated risk

J.J. Blok[1], J. Ringers[1], R. Adam[2], A.K. Burroughs[3], N.G. Kooreman[1], J. Dubbeld[1], H. Putter[4], A.O. Rahmel[5], R.J. Porte[6], X. Rogiers[7], A.E. Braat[1], [1]Dept. of Surgery, Leiden University Medical Centre, [2]Centre Hépato-Biliaire, Hôpital Paul Brousse, Villejuif, France, [3]Liver Transplantation and Hepatobiliary Medicine, Royal Free Hospital, London, United Kingdom, [4]Dept. of Medical Statistics, Leiden University Medical Centre, [5]Eurotransplant Int. Foundation, Leiden, [6]Dept. of Surgery, University Medical Centre Groningen, [7]Dept. of Surgery, Ghent University Hospital Medical School, Belgium

Introduction: The donation-after-cardiac-death (DCD) procedure increases warm ischemia time and is potentially harmful to the liver. Only donors with little other risk factors are being evaluated and stricter criteria for donation are used compared to donation-after-brain-death (DBD) donors. This study analyzes risk factors associated with outcome and how they vary in both groups. Objective: Analysis of DCD as a risk factor for liver transplantation and how this is corrected for by other risk factors. Methods: Database analysis of all 5946 liver transplantations from deceased donors into adult recipients from 1-1-03 to 12-31-07 in Eurotransplant. All data were gathered from Eurotransplant and ELTR databases. Outcome was patient death or graft failure, whatever occurred first. Results: There were 5819 DBD vs 127 DCD donors. DCD procedures were only performed in Belgium and The Netherlands. Significantly different donor factors ($p<0.001$) between both groups were: mean age (DCD 41 vs DBD 48), cause of death (more CVA in DBD), no split livers in DCD, allocation (DCD mainly local and regional), and shorter cold ischemia time (DCD 7.6 vs DBD 9.8). Recipients for DCD livers seemed better, regarding lower recipients age ($p=0.016$) and fewer high urgency status ($p=0.001$). Donor risk index (DRI) was clearly higher in the DCD group (2.0 vs 1.7). When DCD itself was not taken into account, DRI was much better in the DCD group (1.3 vs 1.7). Multivariate analysis showed DCD as significant factor influencing outcome ($p=0.009$), with a hazard ratio of 1.54 (95% CI 1.11 - 2.14). Because of fewer other risk factors in DCD procedures, outcome was equally good in both groups with similar Kaplan-Meier curves ($p=0.83$). 3-months, 1-year and 3-years outcome was 80%,72% and 65% respectively for DBD donors vs 80%, 74% and 63% for DCD donors.
Conclusion: DCD is a significant factor influencing outcome, with a hazard ratio of 1.54. Selection of donors and recipients with fewer associated risk factors for these DCD procedures results in equally good outcome after liver transplantation for DCD and DBD donors.

This is a study supported by the European Liver and Intestine Transplant Association (ELITA) and Eurotransplant Liver Intestine Advisory Committee (ELIAC)

Unspecified and specified living kidney donation to unrelated recipients

W. Zuidema, J. van de Wetering, F. Dor, J. Roodnat, E. Massey, J. IJzermans, W. Weimar, Depts. of Internal Medicine and General Surgery, Erasmus Medical Centre Rotterdam, The Netherlands

Background: In unspecified living kidney donation, formerly known as Good Samaritan, altruistic or anonymous donation to a stranger, the recipient is not specified by the donor. There is no emotional relationship between them and there is no material benefit for the donor.
Methods: Over the last 10 years we have been approached by 168 individuals with the intention to donate a kidney to an emotionally and genetically unrelated patient.
Results: A minority 16/168 did specify a recipient and 12 donated either directly to their intended recipient (n=10) or in kidney exchange procedures (n=2). The vast majority, 152/168 were potential unspecified living kidney donors. 57 of them have donated thus far (see table): 19 directly to the wait list and 38 in domino-paired procedures in which 46 incompatible couples participated. This has in total resulted in 103 kidney transplants: 57 in patients on the wait list and 46 in recipients of incompatible couples.

Performed	**N**	**Total TXP**	**Unspecified donor**	**Inc Couple**		**Waitlist recipient**
Doublet	31	62	31	31		31
Triplet	6	18	6	12		6
Quartet	1	4	1	3		1
TOTAL	**38**	**84**	**38**	**46**		**38**
Single	19	19	19	0		19
TOTAL	**57**	**103**	**57**	**46**		**57**

Conclusion: We conclude that most altruistic donors to emotionally and genetically unrelated patients do not specify an intended recipient. Both wait list patients and recipients of incompatible couples profit from unspecified living kidney donation.

Overgewicht voor en na nierdonatie bij leven

E.C.M. Berendsen, A.G.E. Vink, A. Moazenni, F.E. van Reekum, P.F. Vos, A.D. van Zuilen, Dept. of Nephrology, University Medical Centre Utrecht, The Netherlands

Inleiding: Overgewicht (BMI1[1] ≥ 25 kg/m2) en obesitas (BMI ≥ 30 kg/m2) bij (potentiële) nierdonoren komt frequent voor. Overgewicht is een bekende cardiovasculaire risicofactor en wordt ook geassocieerd met een versnelde achteruitgang van de nierfunctie. Bij patiënten met obesitas is het peri-operatieve risico op complicaties verhoogd. Om die reden worden alle patiënten met overgewicht in ons centrum gemotiveerd af te vallen. Voor obese donoren is dit een voorwaarde om te doneren.
De indruk bestond dat velen na donatie weer aankwamen. Het was onbekend hoeveel en met welke gewichtsverandering. Het doel van ons onderzoek was te inventariseren welke gewichtsveranderingen optraden bij donoren voorafgaande aan donatie en in het eerste jaar daarna. Methoden: Retrospectief zijn gegevens verzameld van 63 nierdonoren bij leven uit 2008 en 2009. Gewicht bij aanvang screening, bij opname voor nefrectomie en 1 jaar na donatie zijn gedocumenteerd naast creatinine en albumine-creatinine ratio.
Resultaten: Van de 63 donoren hadden bij screening 24 een BMI<25, 29 een BMI tussen 25 en 30 en 10 een BMI boven de 30. Gemiddelde leeftijd was respectievelijk 56,5, 58,4 en 55,1 jaar en het percentage mannen respectievelijk 25%, 52% en 60% (p=0.06). 48% van de donoren valt af voor donatie, 73% komt aan na donatie, waarvan 11% meer dan 5 kg en 51% weegt meer na dan voor donatie. Van de 10 die moesten afvallen om te doneren kwam 80% aan, waarvan 20% meer dan 5 kg en 40% weegt meer dan voor donatie. 1 jaar na donatie hebben van de 63 donoren nog 15 een BMI<25, 36 een BMI tussen 25 en 30 en 12 een BMI boven 30.
Conclusies: Een substantieel aantal potentiële nierdonoren met overgewicht of obesitas valt af vóór nierdonatie. In het jaar na donatie neemt het gewicht in een groter percentage toe. 76% heeft dan een ongezond hoog BMI.
Donoren kunnen afvallen voor donatie. Velen houden dit gunstige effect niet vast na de donatie.
Artsen en verpleegkundigen beoordelen de actuele gezondheid van potentiële nierdonoren en de gezondheidsprognose op de langere termijn. In het jaar na donatie verslechtert de gezondheidstoestand van een substantieel aantal donoren door gewichtstoename, resulterend in een toename van cardio-vasculaire risico's en mogelijk snellere achteruitgang van de nierfunctie. Gewichts-behoud na donatie lijkt een belangrijk aandachtspunt in de begeleiding van levende donoren. Aanvullende onderzoeken naar de optimale strategie dit te realiseren zijn noodzakelijk.

Zelfstandig Uitname Team,1 jaar operationeel

J. Dubbeld[1], E. Luijer[1], S. Hamelinck[2], Y.M.L. Verwer[2], J.Ringers[1]. [1]Afdeling Heelkunde, Leids Universitair Medisch Centrum, [2]Afdeling Operatie Kamer, Leids Universitair Medisch Centrum, Nederland

Inleiding: In juni 2008 heeft de Coördinatiegroep Orgaandonatie een advies uitgebracht aan de minister van VWS. Dit advies "Masterplan Orgaandonatie, de vrijblijvendheid voorbij" is een rapport waarin adviezen en aanbevelingen worden gegeven om te komen tot een afname van het schrijnend tekort aan organen voor transplantatie. In onze regio is in augustus 2008 door de Begeleidingscommissie Domein Ziekenhuis gevraagd om samen met regio Groningen als eerste het Masterplan Orgaandonatie uit te rollen in onze twee regio's. In november 2008 is gestart met de uitvoering hiervan. In het plan van onze regio is hierbij de nadruk gelegd op verdere kwaliteitsverbetering van de uitname procedures en maximale service aan de ziekenhuizen waar een donorprocedure plaatsvindt. Op het advies van de Begeleidingscommissie hebben wij specifiek één punt uitgewerkt: Implementatie Zelfstandig Uitname Team (ZUT). Het project is in oktober 2009 van start gegaan. Doel: Door een zelfstandig uitname team zal er een toename worden gerealiseerd van het aantal te transplanteren organen. Daarnaast verwachten we een kwaliteitsverbetering van de organen, verminderde belasting van de donorziekenhuizen, en snellere en efficiënte uitname procedure met als gevolg minder lange wachttijden. Methode: Het ZUT is een volledig zelfstandig functionerend uitname team, dit houdt in dat een orgaandonatie procedure in elk donor-ziekenhuis kan worden verricht met alleen het gebruik van een lokale operatiekamer. Het team bestaat uit 2 chirurgen, 2 operatiekamer assistenten en 1 anesthesioloog.
Tijdens de periode van het project is de bestaande situatie met een regionaal uitname team (RUT) vergeleken met het ZUT. Om de week is gewerkt met het RUT of het ZUT. De uitgangssituatie voor start van het project is weergegeven met een T0 meting. Resultaat na 1 jaar is weergegeven met een T1 meting. De analyse van deze metingen is verricht door de NTS als onafhankelijk deskundige, deze resultaten worden gepresenteerd (zijn op het moment van insturen dit abstract nog niet bekend). De volgende parameters zijn geanalyseerd: totale duur van de orgaandonatie procedure, wachttijden op IC/OK, duur van operatie, aantal procedures/uitgenomen organen, afgekeurde organen, belasting/tevredenheid donorziekenhuizen
Conclusie: De invoering van het ZUT is succesvol verlopen. Definitieve analyse zal de meerwaarde van het ZUT ten opzichte van RUT moeten aantonen.

A preoperative protein deficient diet protects against renal and hepatic ischemia and reperfusion injury

T.C Saat[1], T.M van Ginhoven[1], M. Verweij[1], J.N.M. IJzermans[1], J.H.J. Hoeijmakers[2], R.W.F. de Bruin[1], Depts. of [1]Surgery and [2]Genetics, Erasmus University Medical Centre, Rotterdam, The Netherlands

Background: Ischemia/reperfusion (I/R) injury is a serious and common complication of organ transplantation. We showed previously that two weeks of 30% dietary restriction (DR) and three days of preoperative fasting protect against renal and hepatic I/R injury. In the present study, we investigated whether the protective effect was induced by a reduction in calories, or a specific food component. Materials and methods: Male C57BL/6 mice (n= 4-6/group, 8-12 weeks old) had ad libitum access to diets deficient in protein, fat, carbohydrate, methionine, tryptophan or leucine for 14 or 3 days before induction of renal I/R injury. Renal I/R injury was induced by clamping the renal artery and vein of both kidneys for 37 minutes. Renal I/R injury was assessed by serum urea levels and signs of animal discomfort consistent with renal dysfunction. Partial hepatic I/R injury (75 minutes) was induced in mice with preoperative ad libitum access to diets deficient in protein or leucine for three days. Hepatic I/R injury was determined by serum ALAT and LDH levels and amount of hemorrhagic necrosis. Mice fed ad libitum control diets and mice pair-fed (PF) a control diet for the deficient diets were used as controls.
Results: A 14 day protein-, methionine-, tryptophan- or leucine-deficient diet protected against renal I/R injury, whereas fat- and carbohydrate-free diets did not. PF controls revealed that mice on modified diets restricted their calorie intake by approximately 30%. Therefore, the effect of individual dietary components could not be separated from the effect of DR. Since three days of DR does not induce protection against I/R injury, we repeated these experiments using a 3 day preoperative diet. Only a protein-deficient diet protected against renal I/R injury. In the liver, a 3 day protein- or leucine-deficient diet both protected against I/R injury.
Conclusion: Three days of preoperative protein-deficient diet protects against renal and hepatic I/R injury. These data show that proteins are responsible for the protection induced by DR.

Clinical and experimental monitoring of temperature during cold static preservation of kidney grafts with a new organ preservation container

C. Billault[1,2] , H.G.D. Leuvenink[1], R.J. Ploeg[1], B. Barrou[2], [1]Dept. of Surgery, University Medical Centre Groningen, The Netherlands, [2]Service d'Urologie et de Transplantation Rénale, Hôpital de la Pitié Salpêtrière, Paris, France

Organs for transplantation are commonly preserved in cold storage at 4°C. This ensures a low metabolism compatible with hypoxic conditions during cold storage. However, whether the actual preservation conditions match the theoretical ones is not known. A new organ preservation container BIOTAINER® was tested as an alternative for the styrofoam container routinely used. The BIOTAINER is composed of a plastic container for placing the kidney in preservation solution, two plastic bags to surround it, and a main enclosure for ice, set inside a transport bag with added compartments for donor samples and documents. The optimal placement of the thermal probes for temperature measurements was established using pig kidneys. The kidneys were cold stored in UW solution for 96 hours, temperatures were monitored every 10 minutes. Kidneys were stored either in the BIOTAINER or in the styrofoam container. Temperatures measured were the same whether the probe was placed inside a sliced-open kidney, in the solution, between the plastic container and the first bag or between the two bags. With both systems temperatures decreased in a few minutes. With the styrofoam container, the lowest temperature reached was 1.5°C, for a maximum of 80 minutes; temperatures rose above 5°C after 10 hours and 40 minutes. With the BIOTAINER, the lowest temperature reached was 0.5°C for a maximum of 15 hours; temperatures rose above 5°C after 57 hours. For the human study, thermal probes were routinely placed along all kidney grafts retrieved from deceased, heart-beating donors at our institution from August 2007 to May 2008. Thermal probes were conditioned in a sterile way and placed between the two plastic bags surrounding the plastic container where the kidney was stored. Thermal probes were retrieved at transplantation and data analyzed with the dedicated ThermoTrack software. Only 9 of 30 thermal probes could be recovered from transplantation centers all over France. The mean cold ischemia time was 20 hours. During cold storage, the mean temperature was 0.83°C (0-1.5°C).
In conclusion, the BIOTAINER container ensures stable preservation temperatures below 5°C for more than 48 hours, where as the styrofoam container was clearly inappropriate for long term preservation. Observations from the human practice matches the data from the animal study.

Gaseous hydrogen sulfide (H2S) is protective during cardiac ischemia/reperfusion

P.M. Snijder[1,2], R.A. de Boer[3], E.M. Bos[1,2], J.C. van den Born[1,2], W.T. Ruifrok[3], I. Vreeswijk-Baudoin[3], M.C.R.F. van Dijk[1], H.G.D. Leuvenink[2], H. van Goor[1], [1]Dept. of Pathology and Medical Biology, [2]Dept.of Surgery, [3]Dept. of Cardiology, University Medical Centre Groningen, The Netherlands

H2S has drawn considerable attention for its recently discovered role in various physiological processes. H2S can reversibly induce a hypometabolic state in mice, and also has anti-apoptotic, anti-inflammatory and ROS scavenging properties. In the kidney, H2S is highly protective against ischemia/-reperfusion injury (IRI). Here, we investigated whether gaseous administration of H2S is protective in cardiac IRI and whether a state of hypometabolism is required for a beneficial effect. Male C57BL/6 mice were intubated, mechanically ventilated with 100% O2 and assigned to one of three different treatment regimens receiving a 0 (control), 10 ppm, or 100 ppm H2S-nitrogen mixture starting 30 minutes prior to ischemia until 5 min pre-reperfusion. IRI was inflicted by temporary ligation of the left coronary artery for 30 min. Core body temperature was maintained at 37 °C. Mice were sacrificed after 1 and 7 days. High-resolution respirometry equipment was used to assess CO2-production during H2S treatment. Cardiac damage and fibrosis was determined in haematoxylin-eosin (1 day) and Masson (7 days) stained sections. To investigate granulocyte influx sections were stained for Ly-6G. CO2-production of mice treated with 100 ppm H2S rapidly declined to ~60% of basal levels, while treatment with 10 ppm had no effect on CO2-production. IRI caused significant damage in controls compared to sham-operated animals after 1 and 7 days ($p<0.01$). Histological analysis at 1 day of reperfusion showed no effects of 10 ppm H2S on relative infarct size, while treatment with 100 ppm H2S reduced infarct size by 62% ($p<0.05$). At 7 days of reperfusion, both 10 ppm and 100 ppm H2S showed a reduction in fibrosis compared to control animals (relative fibrotic area: sham 2.0%; control 17.2% ($p<0.001$ vs sham); 10 ppm 7.0%; 100 ppm 7.4% (both $p<0.01$ vs control)). The influx of Ly-6G+ granulocytes was reduced by 46% after treatment with 100 ppm H2S ($p<0.05$) but was not affected by 10 ppm H2S. We conclude that gaseous administration of H2S is a promising treatment for reducing cardiac IRI when administered during an ischemic insult. Since IRI is a frequent and important cause of myocardial damage during percutaneous coronary intervention and cardiac transplantation, H2S may be used in these settings to salvage myocardial function.

Quantification of demethylated FOXP3 DNA demonstrates a lower proportion of natural regulatory T cells 1 year after kidney transplantation

K. Boer, A.M.A. Peeters, W. Weimar, C.C. Baan, Dept. of Internal Medicine, Erasmus Medical Centre Rotterdam, The Netherlands

Introduction: FOXP3+ regulatory T cells (Treg) are important for the induction and maintenance of tolerance after organ transplantation. Circulating FOXP3+ Treg are not a uniform population and can be subdivided into those developed in the thymus (natural Treg; nTreg) and those induced in the periphery (iTreg). Since specific markers for either Treg population were lacking until now, their relative importance in alloreactivity remains unknown. Based on the recent identification of nTreg-specific DNA demethylation of the *FOXP3* gene, we established a quantitative PCR assay to identify the DNA methylation status of *FOXP3*. Using demethylated *FOXP3* DNA as a marker for nTreg, the proportion of nTreg of total PBMC was studied in 15 patients before and 1 year after kidney transplantation. Methods: Isolated DNA was treated with bisulfite to introduce methylation dependent changes in the DNA sequence. These changes were quantified with methylation- and demethylation-specific primers and probes in real-time PCR. Results: FACS sorted $CD4^{+}CD25^{bright}CD127^{low}$ cells (nTreg pool; demethylated at *FOXP3*) and $CD14^{+}$ cells (highly methylated at *FOXP3*) from a healthy male donor demonstrated the expected discrimination between methylated and demethylated DNA with a proportion of demethylated *FOXP3* DNA of 96% and 0.03% respectively. The detection limit was 0.06% demethylated *FOXP3* DNA. In kidney transplantation patients, the proportion of nTreg of total PBMC before transplantation was similar to the proportion of nTreg in age and gender matched donors. One year after kidney transplantation, the proportion of nTreg (4.2%) significantly decreased ($p=0.002$) compared to the proportion of nTreg before trans-plantation (2.8%). This decrease was more prominent in the tacro-limus/ mycophenolate mofetil treated patients than the tacrolimus/ rapamycin treated patients ($p=0.007$ versus $p=0.13$, respectively).
Conclusion: Using *FOXP3* DNA demethylation as a marker of nTreg, a lower proportion of nTreg is present 1 year after kidney transplantation depending on their immunosuppressive regimen. Quantification of demethylated *FOXP3* DNA is the first specific marker for nTreg and will be used to study their relative contribution in alloreactivity.

Donor serum angiopoietin 2 is an independent predictor of kidney transplant outcome

L.G. Koudstaal[1,2] ,C. Moers[1], J.G.M. Burgerhof[3], H. van Goor[2], A.O.Rahmel[4], A. Paul[5], J. Treckmann[5], D. Monbaliu[6], J. Pirenne[6], R.J. Ploeg[1] and H.G.D. Leuvenink[1], Depts. of [1]Surgery, [2]Pathology and [3]Epidemiology, University Medical Centre Groningen, [4]Eurotransplant Foundation, Leiden, The Netherlands, [5]Abdominal Transplant Surgery, University Hospital Essen, Germany, [6]Abdominal Transplant Surgery, University Hospital Leuven, Belgium

Donor-derived biomarkers that have predictive value for posttransplant outcome are useful to prevent unnecessary discard of donor organs and to fine-tune post-operative treatment of the recipient. Recently, we found that serum angiopoietin levels are elevated in brain dead donors. Angiopoietin-2 is a prognostic survival marker in critically ill patients. In this study we investigated whether donor angiopoietins have a predictive value in renal transplantation. From 297 deceased kidney donors included in an international prospective randomized controlled trial, serum was analyzed for angiopoietin-1 and angiopoietin-2. Using multivariate models we tested whether donor serum angiopoietins were independently associated with delayed graft function (DGF), primary non-function (PNF) and graft survival (GS) in the recipient. Serum angiopoietin-2 concentration was significantly associated with GS: higher values in donor serum were predictive of a lower risk of graft failure (HR=0.91, p=0.027). For angiopoietin-1 no association with GS could be found. Donor angiopoietin levels had no predictive value for DGF and PNF. In conclusion, the present study shows that angiopoietin-2 measured in donor serum prior to donation is an independent predictor of kidney graft survival.

Transplantation of right living donor kidneys in obese recipients correlates with a decreased graft survival

J. Hellegering[1], J. Visser[1], F.C.H. D'Ancona[2], J.F. Langenhuijsen[2], A.J. Hoitsma[3], J.A. van der Vliet[1], M.C. Warlé[1], [1]Dept. of Surgery, Division of Vascular- and Transplant Surgery, [2]Dept. of Urology, [3]Dept. of Nephrology, Radboud University Nijmegen Medical Centre, The Netherlands

Background: During surgery in general, exposure of the operating area is compromised in obese patients. It is also known that vascular anastomosis of right kidneys is technically more demanding as compared to left kidneys due to a shorter renal vein. We hypothesize that transplantation of right kidneys into obese recipients affects outcome after living donor kidney transplantation.
Methods: Data were collected retrospectively on 447 consecutive adult living donor kidney transplantations performed in our hospital between July 1996 and February 2010. Slow graft function (SGF) was defined as serum creatinine > 265 µmol/L at day 5 after transplantation. To allow a statistical analysis with a balanced number of cases over the subgroups, 'obese' patients were defined using a BMI cut off level of 27. Results: Multivariable linear regression analysis revealed recipient BMI (0.55 ± 0.16 minutes per BMI point) and right donor kidney (3.9 ± 1.4 minutes) as major determinants of vascular anastomosis time. Logistic regression analysis showed a significant correlation between anastomosis time and the occurrence of SGF (p=0.02). Obese recipients of right kidneys showed a decreased 5-year graft survival rate (70.8%) as compared to all other recipients (91.0%, p=0.016).
Conclusions: Obese recipients of right living donor kidneys are at risk of a prolonged vascular anastomosis time, which correlates with the occurrence of slow graft function. We also found that transplantation of right living donor kidneys in obese recipients affected graft survival. Our data indicate that the selection of right living donor kidneys, especially those kidneys with short renal veins, should be avoided in obese recipients.

Effects of rituximab-treated B cells on T cell proliferation and cytokine production in vitro

E.G. Kamburova[1], H.J. Koenen[1], L.B. Hilbrands[2], I. Joosten[1], [1]Dept. of Laboratory Medicine, Laboratory of Medical Immunology, [2]Dept. of Nephrology, Radboud University Nijmegen Medical Centre, The Netherlands

Background: Rituximab is a chimeric anti-CD20 monoclonal antibody used in various autoimmune disorders and transplantation to reduce auto- or alloreactive antibody levels. Although rituximab treatment results in full B cell depletion in peripheral blood, there remains a residual B cell population in secondary lymphoid tissues. We have previously shown that rituximab modulates B cell differentiation with potential effects on B-T-cell interactions.
Objective: To investigate the *in vitro* effects of rituximab on antigen presentation and cytokine production by B cells. Methods: $CD19^+$ B cells isolated from peripheral blood of healthy donors were stimulated with soluble anti-CD40 and IL-21 in the presence or absence of rituximab. On day 6 the cells were harvested and added to CFSE labelled $CD4^+CD25^-$ conventional T cells (T_{conv}). Intracellular cytokine production and proliferation of T_{conv} were measured after an additional 6 days of culture by flow cytometry.
Results: While anti-CD40/IL-21 pre-stimulated B cells induced weak T_{conv} proliferation, rituximab-treated pre-stimulated B cells in comparison, induced enhanced proliferation of T_{conv}. Of note, after stimulation with rituximab-treated B cells, the production of Th1 cytokines, such as TNFα and IFNγ, by the proliferating T_{conv} was similar to that induced by untreated pre-stimulated B cells.
Conclusion: The modulation of B cell differentiation and maturation by rituximab, results in maintained APC function and ability to induce substantial T_{conv} proliferation and associated cytokine production.

Hepatocyte-derived MicroRNAs in Human Serum are Sensitive Markers for Hepatic Injury in Liver Transplantation

W.R.R. Farid[1], Q. Pan[2], A.J.P. van der Meer[2], P.E. de Ruiter[1], V.Ramakrishnaiah[1], J. de Jonge[1], J. Kwekkeboom[2], H.L.A. Janssen[2], H.J. Metselaar[2], H.W. Tilanus[1], G. Kazemier[1] and L.J.W. van der Laan[1] [1]Department of Surgery and Laboratory of Experimental Transplantation and Intestinal Surgery and [2]Department of Gastro-enterology & Hepatology, Erasmus MC - University Medical Center, Rotterdam, The Netherlands

Background: MicroRNAs (miRNA), a class of small non-coding RNAs, are key regulators of many cellular functions by post-transcriptional suppression of gene expression. MiRNAs are emerging biomarkers for cancer and recent studies in animal models have highlighted the potential of hepatocyte-derived miRNAs (HDmirs) in serum as early and sensitive biomarker for liver injury. However, whether HDmirs are useful markers in humans remains unknown. The aim of this study is to investigate the utility of serum HDmirs in the setting of liver transplantation. Methods: Liver graft biopsies (n = 50) and serum samples from healthy controls (n = 12) and liver transplant recipients (n = 70) were analyzed. Hepatocyte-derived miRNAs, miR-122 and 148a, and control miRNAs, miR-133a and miR-191, were quantified by RT-PCR. Results: We found the expression of miR-122 and miR-148a in liver tissue showed a significant reverse correlation with the duration of the grafts warm ischemia time (R = -0.31 and R = -0.40 respectively, $P < 0.05$). In patients, levels of serum HDmirs significantly correlated with transaminases (AST and ALT, $R > 0.75$, $P < 0.001$) and were significantly elevated as compared to healthy controls. Even in patients with serum transaminases below 50 IU/L, a significant increase of HDmirs was found (> 8-fold, $P < 0.01$), while control miRNAs remained unchanged. In patients experiencing an episode of acute rejection, serum HDmirs were 9-fold higher as compared to levels six months after rejection was resolved (n = 10, $P < 0.005$). Interestingly, longitudinal analysis in three patients showed the peak of serum miRNAs preceded the elevation of transaminases, suggesting HDmirs are early markers for liver injury. Additional testing showed that repeated freezing and thawing of serum samples did not cause degradation of HDmirs.
In conclusion: This study demonstrates the potential application of miRNAs in serum as biomarkers in the setting of liver transplantation. Our results show that HDmirs represent novel candidates for stable, specific and sensitive biomarkers for liver injury in humans.

Aanmeldingsformulier lidmaatschap

naam en voorletters			m / v
voornaam			geb. datum:
titel			
specialisme / functie			
doctoraal examen	neen / ja d.d.	zo ja, studierichting:	
arts examen	n.v.t. / ja d.d.		
inschrijving MSRC	neen / ja d.d.	BIG registratie nr.	
huisadres			
postcode en plaats			
telefoonnummer			
werkinstelling			
afdeling			
adres			
postcode en plaats			
telefoonnummer			
e-mail adres			
Toezending verenigingspost aan huis- / werkadres			

Wenst tevens lid te worden van onderstaande sectie:

☐ Landelijke Werkgroep Transplantatie Verpleegkunde

Datum: Handtekening:

_____

☐ Hierbij machtig ik de penningmeester van de Nederlandse Transplantatie Vereniging om de verschuldigde contributie ad € 35,-- per jaar (voor 2011) tot wederopzegging automatisch van mijn bank-/girorekening af te laten schrijven.

Bank- / girorekening: Datum en handtekening:

Aanvullende informatie:
- Het lidmaatschap loopt per kalenderjaar. Opzeggen dient vóór 1 december plaats te vinden.
- Indien u geen machtiging tot incasso geeft ontvangt u automatisch een acceptgiro, hiervoor geldt een toeslag van € 2,50 administratiekosten.

Sturen naar: Secretariaat NTV, Postbus 6235, 2001 HE Haarlem

Colofon

Vormgeving en druk:
Secretariaat NTV / Drukkerij Bijto, Enkhuizen

Inlichtingen:
Secretariaat Nederlandse Transplantatie Vereniging
Mevr. M.J. van Gijtenbeek
Postbus 6235
2001 HE Haarlem
Telefoon (023) 551 3016
Fax (023) 551 3087
e-mail: secretariaat@transplantatievereniging.nl
www.transplantatievereniging.nl