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On the cover this month: Cardiac transplantation has become an exceptionally successful treatment for end-stage heart failure, but it remains plagued by the development of cardiac allograft vasculopathy (CAV), a progressive fibrosing lesion of the coronary arteries that eventually results in ischemic failure of the transplanted heart. In this issue of AJT, Loupy et al (page 111) provide strong evidence that alloantibody formation is a prominent culprit in this disease. This finding, combined with the association between CAV and recipient alloantibodies reported by Starling et al (page 121), underscore the need for controlling humoral immune responses in recipients and screening for alloantibody formation posttransplantation. See also the thoughtful editorial by Margaret Burke on page 9. Cover design by Lauren Halligan, Duke University Department of Surgery.

1–2 The AJT Report

This month, “The AJT Report” talks to several experts about the merits and potential problems associated with allowing marijuana users to be candidates for transplantation. Also this issue, we look at some of the current significant barriers to access to kidney transplantation and ways to minimize them.

3 Literature Watch

A pair of new studies reveals that the composition of the microbiome alters efficacy of immune checkpoint blockade in mouse cancer models.

Editorials

5–6 S Feng

Got It! Let’s Cool It! But What’s Next in Organ Donor Research?

The remarkable reduction of delayed graft function rates after kidney transplantation achieved simply by cooling deceased donor organs to 34–35°C evidences the yet untapped potential to improve not only organ quality but also quantity through innovative and well-designed donor intervention research. See the related article from Rodrigue et al on page 278.

7–8 EM Gibney

Lifetime Insurance Benefit for Living Donors: Is It Necessary and Could It Be Coercive?

This editorial examines potential problems with offering lifelong health insurance benefits to living donors. See the personal viewpoint from Newell et al on page 29.

9–10 MM Burke

Late Cardiac Allograft Failure, Cardiac Allograft Vasculopathy, and Antibody-Mediated Rejection: Untangling Some Knots?

In heart transplantation, semiquantitative scoring schemes of structural and inflammatory components of coronary allograft vasculopathy (CAV) identify a subset of recipients with CAV who also show concurrent or previous subclinical antibody-mediated rejection, of potential importance in CAV pathogenesis. See the article from Loupy et al on page 111.

Comprehensive Review

11–20 CF Bryan, WS Cherikh and DA Sesok-Pizzin

A₂/A₂B to B Renal Transplantation: Past, Present, and Future Directions

In this review, the authors summarize and discuss the experience that led to the inclusion of the A₂/A₂B → B component into the United States’ new kidney allocation system in 2015, describe future directions to further expand A₂/A₂B → B renal and simultaneous liver–kidney transplantation, and emphasize that in order for this allocation component to improve access of blood group B candidates, more B candidates must be made eligible in the UNOS system.

continued.

- 21–28 F Agüero, MA Castel, S Cocchi, A Moreno, CA Mestres, C Cervera, F Pérez-Villa, M Tuset, R Cartaña, C Manzardo, G Guaraldi, JM Gatell and JM Miró

An Update on Heart Transplantation in Human Immunodeficiency Virus–Infected Patients

The authors find that the survival rate of HIV-infected patients undergoing heart transplantation in the highly active antiretroviral therapy (HAART) era is much better than in the pre-HAART era, and they discuss the challenging issues that must be addressed in the pretransplant and posttransplant periods.

Personal Viewpoint

- 29–32 KA Newell, RN Formica and JS Gill

Engaging Living Kidney Donors in a New Paradigm of Postdonation Care

The authors advocate the provision of lifelong health insurance for living donors to create a new program of postdonation care that engages donors in their own health maintenance, facilitates early treatment of new health concerns, and provides an efficient mechanism to collect information to advance our understanding of the long-term health outcomes of living donors. See Gibney's editorial on [page 7](#).

Original Articles

Basic Science

- 33–43 JP Stone, WR Critchley, T Major, G Rajan, I Risnes, H Scott, Q Liao, B Wohlfart, T Sjöberg, N Yonan, S Steen and JE Fildes

Altered Immunogenicity of Donor Lungs via Removal of Passenger Leukocytes Using *Ex Vivo* Lung Perfusion

In a randomized porcine lung transplant study, the authors demonstrate that *ex vivo* lung perfusion reduces passenger leukocyte transfer from the donor to the recipient, which results in impaired recipient T cell recruitment to the lung after transplantation.

- 44–57 H-S Lee, J-G Lee, HJ Yeom, YS Chung, B Kang, S Hurh, B Cho, H Park, JI Hwang, JB Park, C Ahn, SJ Kim and J Yang

The Introduction of Human Heme Oxygenase-1 and Soluble Tumor Necrosis Factor- α Receptor Type I With Human IgG1 Fc in Porcine Islets Prolongs Islet Xenograft Survival in Humanized Mice

In an adult pig islet to humanized mouse transplantation model, overexpression of human HO-1 or sTNF- α R-Fc in porcine islets improves islet xenograft survival by suppressing both early apoptosis of islet cells and inflammation.

- 58–71 IE Dijke, RE Hoepfli, T Ellis, J Pearcey, Q Huang, AN McMurchy, K Boer, AMA Peeters, G Aubert, I Larsen, DB Ross, I Rebeyka, A Campbell, CC Baan, MK Levings and LJ West

Discarded Human Thymus Is a Novel Source of Stable and Long-Lived Therapeutic Regulatory T Cells

Discarded pediatric thymus is a source of therapeutic CD4⁺CD25⁺FOXP3⁺ regulatory T cells that are more potent, stable and long-lived than CD4⁺CD25⁺FOXP3⁺ regulatory T cells isolated from peripheral blood.

- 72–82 P Talayero, E Mancebo, J Calvo-Pulido, S Rodríguez-Muñoz, I Bernardo, R Laguna-Goya, FL Cano-Romero, A García-Sesma, C Loinaz, C Jiménez, I Justo and E Paz-Artal

Innate Lymphoid Cells Groups 1 and 3 in the Epithelial Compartment of Functional Human Intestinal Allografts

In human intestinal allografts, a CD103⁺CD3[−] intraepithelial lymphocyte subset predominates and shows features of NK cells and groups 1 and 3 of innate lymphoid cells.

- 83–98 H Kim, J Zhao, Q Zhang, Y Wang, D Lee, X Bai, L Turrell, M Chen, W Gao, S Keshavjee and M Liu

δ V1-1 Reduces Pulmonary Ischemia Reperfusion-Induced Lung Injury by Inhibiting Necrosis and Mitochondrial Localization of PKC δ and p53

Protein kinase C δ inhibition by δ V1-1 inhibits ischemia-reperfusion-induced inflammation and necrotic cell death after lung transplantation by preventing mitochondrial translocation of protein kinase C δ and p53.

- 99–110 LNL Van Aelst, G Summer, S Li, SK Gupta, W Heggermont, K De Vusser, P Carai, M Naesens, J Van Cleemput, F Van de Werf, J Vanhaecke, T Thum, M Waer, A-P Papageorgiou, B Schroen and S Heymans

RNA Profiling in Human and Murine Transplanted Hearts: Identification and Validation of Therapeutic Targets for Acute Cardiac and Renal Allograft Rejection

The authors identify common mRNA pathways and microRNAs differentially expressed during acute cardiac allograft rejection in mice and humans, and subsequently show that targeting the proinflammatory microRNA-155 attenuates inflammation and prolongs graft survival. See also Starling et al on [page 121](#).

continued.

- 111–120 A Loupy, C Toquet, P Rouvier, T Beuscart, MC Bories, S Varnous, R Guillemain, S Pattier, C Suberbielle, P Leprince, C Lefaucheur, X Jouven, P Bruneval and JP Duong Van Huyen

Late Failing Heart Allografts: Pathology of Cardiac Allograft Vasculopathy and Association With Antibody-Mediated Rejection

This study demonstrates that antibody-mediated rejection operates in a substantial fraction of late chronic failing heart allografts, including unrecognized subclinical antibody-mediated rejection episodes observed years before allograft failure. See Burke's editorial on [page 9](#).

- 121–136 RC Starling, J Stehlik, DA Baran, B Armstrong, JR Stone, D Ikle, Y Morrison, ND Bridges, P Putheti, TB Strom, M Bhasin, I Guleria, A Chandraker, M Sayegh, KP Daly, DM Briscoe, PS Heeger and the CTOT-05 consortium

Multicenter Analysis of Immune Biomarkers and Heart Transplant Outcomes: Results of the Clinical Trials in Organ Transplantation-05 Study

In this observational, multicenter, cohort study of 200 heart transplant recipients, the investigators find that acute rejection and evidence of vasculopathy at 1 year posttransplant correlates with several epidemiological parameters, anti-HLA antibodies and plasma angiogenesis-related factors, but not with a panel of cellular and molecular biomarkers. See also Van Aelst et al on [page 99](#).

- 137–142 KJ Halazun, AK Mathur, AA Rana, AB Massie, S Mohan, RE Patzer, JP Wedd, B Samstein, RM Subramanian, BD Campos and SJ Knechtle

One Size Does Not Fit All—Regional Variation in the Impact of the Share 35 Liver Allocation Policy

This study examines the impact of the Share 35 liver allocation policy, with specific emphasis on regional variability in patient characteristics and posttransplant survival before and after its implementation. See also the brief communication by Fernandez et al on [page 287](#).

- 143–156 J Duclos, P Bhangu, C Salloum, P Andreani, F Saliba, P Ichai, A Elmaleh, D Castaing and D Azoulay

Ad Integrum Functional and Volumetric Recovery in Right Lobe Living Donors: Is It Really Complete 1 Year After Donor Hepatectomy?

Though functional recovery occurs in almost all right lobe liver donors, the authors find that at 1 year post-right lobe donor hepatectomy, only 85% of donors achieve *ad integrum* volumetric recovery.

- 157–170 G-W Song, S-G Lee, S Hwang, K-H Kim, C-S Ahn, D-B Moon, T-Y Ha, D-H Jung, G-C Park, W-J Kim, M-H Sin, Y-I Yoon, W-H Kang, S-H Kim and E-Y Tak

ABO-Incompatible Adult Living Donor Liver Transplantation Under the Desensitization Protocol With Rituximab

This article presents the clinical results of ABO-incompatible adult living donor liver transplantation in a single institution.

- 171–180 N Huang, MC Foster, KL Lentine, AX Garg, ED Poggio, BL Kasiske, LA Inker and AS Levey

Estimated GFR for Living Kidney Donor Evaluation

In this article, the authors evaluate the accuracy of estimated GFR compared to measured GFR for evaluation of candidates for living kidney donation, and provide a website for using creatinine and cystatin C to compute estimated GFR and its accuracy.

- 181–193 MB Allen, E Billig, PP Reese, J Shults, R Hasz, S West and PL Abt

Donor Hemodynamics as a Predictor of Outcomes After Kidney Transplantation From Donors After Cardiac Death

Using novel approaches to characterize donor hemodynamics in donation after cardiac death kidney transplantation, the authors show that data available at the time of organ procurement may predict delayed graft function and graft failure, particularly for recipients of kidneys from older donors.

- 194–203 FG Cosio, M El Ters, LD Cornell, CA Schinstock and MD Stegall

Changing Kidney Allograft Histology Early Posttransplant: Prognostic Implications of 1-Year Protocol Biopsies

This study demonstrates that histologic changes seen at 1 year posttransplant relate to subsequent outcomes and are relevant in determining graft prognosis.

204–212 DO Dahle, A Åsberg, A Hartmann, H Holdaas, M Bachtler, TG Jenssen, M Dionisi and A Pasch

Serum Calcification Propensity Is a Strong and Independent Determinant of Cardiac and All-Cause Mortality in Kidney Transplant Recipients

This study uses a novel blood test to quantify the serum calcification propensity in 1435 kidney transplant recipients and finds a strong independent association with cardiac and all-cause mortality.

213–220 BJ Orandi, N Alachkar, ES Kraus, F Naqvi, BE Lonze, L Lees, KJ Van Arendonk, C Wickliffe, SM Bagnasco, AA Zachary, DL Segev and RA Montgomery

Presentation and Outcomes of C4d-Negative Antibody-Mediated Rejection After Kidney Transplantation

This study shows kidney transplant recipients with c4d-negative antibody-mediated rejection (AMR) are indistinguishable from c4d-positive AMR recipients in terms of baseline demographic and transplant characteristics, but c4d-negative AMR presents significantly later posttransplant and is more likely to be subclinical, and both groups have worse graft survival than AMR-free matched controls.

221–234 JR Leventhal, JM Mathew, DR Salomon, SM Kurian, JJ Friedewald, L Gallon, I Konieczna, AR Tambur, J Charette, J Levitsky, C Jie, YS Kanwar, MM Abecassis and J Miller

Nonchimeric HLA-Identical Renal Transplant Tolerance: Regulatory Immunophenotypic/Genomic Biomarkers

The authors describe a nonchimeric tolerance protocol in HLA-identical renal transplant recipients given multiple infusions of donor immunoselected hematopoietic CD34⁺ stem cells in which associative biomarkers include CD4⁺CD25⁺CD127⁺FOXP3⁺ PBMC measurements and a characteristic gene expression profile.

235–245 F Vendrame, Y-Y Hopfner, S Diamantopoulos, SK Viridi, G Allende, IV Snowwhite, HK Reijonen, L Chen, P Ruiz, G Ciancio, JC Hutton, S Messinger, GW Burke III and A Pugliese

Risk Factors for Type 1 Diabetes Recurrence in Immunosuppressed Recipients of Simultaneous Pancreas–Kidney Transplants

This study demonstrates that recurrence of islet autoimmunity and type 1 diabetes is a significant cause of immune-mediated endocrine pancreas graft function in immunosuppressed recipients of simultaneous pancreas–kidney transplants, and defines risk factors for this condition.

246–253 MF Nijhoff, MA Engelse, J. Dubbeld, AE Braat, J Ringers, DL Roelen, AR van Erkel, HS Spijker, H Bouwsma, PJM van der Boog, JW de Fijter, TJ Rabelink and EJP de Koning

Glycemic Stability Through Islet-After-Kidney Transplantation Using an Alemtuzumab-Based Induction Regimen and Long-Term Triple-Maintenance Immunosuppression

Alemtuzumab induction followed by triple maintenance immunosuppression in islet-after-kidney transplantation appears safe and leads to graft function with resolution of hypoglycemic events in 92% of patients and insulin independence in 42% of patients after 2 years.

254–261 D Ruttens, SE Verleden, E Vandermeulen, H Bellon, BM Vanaudenaerde, J Somers, A Schoonis, V Schaevers, DE Van Raemdonck, A Neyrinck, LJ Dupont, J Yserbyt, GM Verleden and R Vos

Prophylactic Azithromycin Therapy After Lung Transplantation: *Post hoc* Analysis of a Randomized Controlled Trial

This *post hoc* analysis of a randomized controlled trial demonstrates improved chronic lung allograft dysfunction-free survival, pulmonary function, and exercise capacity with prophylactic azithromycin therapy after lung transplantation.

262–270 M Mansh, M Binstock, K Williams, F Hafeez, J Kim, D Glidden, R Boettger, S Hays, J Kukreja, J Golden, MM Asgari, P Chin-Hong, JP Singer and ST Arron

Voriconazole Exposure and Risk of Cutaneous Squamous Cell Carcinoma, *Aspergillus* Colonization, Invasive Aspergillosis and Death in Lung Transplant Recipients

The authors associate voriconazole with an increased risk for squamous cell carcinoma in lung transplant recipients, but a reduction in all-cause mortality in patients colonized with *Aspergillus*.

271–277 PJ Smith, JA Blumenthal, EP Trulock, KE Freedland, RM Carney, RD Davis, BM Hoffman and SM Palmer

Psychosocial Predictors of Mortality Following Lung Transplantation

Lung transplant recipients with elevated levels of depression and psychological distress following transplant exhibit greater long-term mortality rates.

continued.

278–286 JR Rodrigue, S Feng, AC Johansson, AK Glazier and PL Abt

Deceased Donor Intervention Research: A Survey of Transplant Surgeons, Organ Procurement Professionals, and Institutional Review Board Members

Using a case scenario survey approach, the authors find wide variations in the perceptions of transplant surgeons, organ procurement professionals, and institutional review board members about regulatory, legal, and ethical considerations in research with deceased donors. See related editorial by Feng on [page 5](#).

Brief Communications

287–291 H Fernandez, J Weber, K Barnes, L Wright and M Levy

Financial Impact of Liver Sharing and Organ Procurement Organizations' Experience With Share 35: Implications for National Broader Sharing

In a review to analyze cost changes associated with the implementation of the Share 35 organ allocation policy, the authors show an association of the policy change with an increase in imports, exports, and total cost, with a substantial impact on national costs. See article by Halazun et al on [page 137](#).

292–300 R Ahmed, EK Chow, AB Massie, S Anjum, EA King, BJ Orandi, S Bae, LH Nicholas, BE Lonze and DL Segev

Where the Sun Shines: Industry's Payments to Transplant Surgeons

In this study, the authors quantify and characterize all industry payments made to transplant surgeons, now publicly available under the Physician Payment Sunshine Act.

301–309 LA Goldraich, J Stehlik, AY Kucheryavaya, LB Edwards and HJ Ross

Retransplant and Medical Therapy for Cardiac Allograft Vasculopathy: International Society for Heart and Lung Transplantation Registry Analysis

This analysis of the International Society for Heart and Lung Transplantation Registry compares adult heart transplant recipients with cardiac allograft vasculopathy who were retransplanted versus those who were managed medically and found similar survival rates at 9 years, supporting the current consensus recommendation limiting heart retransplant to highly selected patients with the condition.

310–316 P Lovinfosse, L Weekers, C Bonvoisin, C Bovy, S Grosch, J-M Krzesinski, R Hustinx and F Jouret

Fluorodeoxyglucose F¹⁸ Positron Emission Tomography Coupled With Computed Tomography in Suspected Acute Renal Allograft Rejection

¹⁸FDG-PET/CT imaging noninvasively identifies nonrejection in kidney transplant recipients with suspected acute rejection, and may allow selected patients to forgo renal transplant biopsy.

317–324 V Villani, K Yamada, JR Scalea, BC Gillon, JS Arn, M Sekijima, M Tasaki, TA Cormack, SG Moran, R Torabi, A Shimizu and DH Sachs

Adoptive Transfer of Renal Allograft Tolerance in a Large Animal Model

Tolerated renal allografts contain a potent tolerance-inducing and/or -maintaining cell population sufficient for adoptive transfer of tolerance to a naïve recipient.

325–333 G Castellano, A Intini, A Stasi, C Divella, M Gigante, P Pontrelli, R Franzin, M Accetturo, A Zito, M Fiorentino, V Montinaro, G Lucarelli, P Dittono, M Battaglia, A Crovace, F Staffieri, B Oortwijn, E van Amersfoort, G Pertosa, G Grandaliano and L Gesualdo

Complement Modulation of Anti-Aging Factor Klotho in Ischemia/Reperfusion Injury and Delayed Graft Function

The authors demonstrate a direct involvement of complement in regulating the expression of anti-aging factor Klotho in a swine model of ischemia/reperfusion injury, and lower levels of renal and soluble Klotho in patients affected by delayed graft function years after transplantation.

334–341 BT Stocks, AJ Wilhelm, CS Wilson, AF Marshall, NE Putnam, AS Major and DJ Moore

Lupus-Prone Mice Resist Immune Regulation and Transplant Tolerance Induction

The authors establish the lupus-prone B6.SLE123 mouse as a new model to investigate autoimmunity as a barrier to transplantation tolerance that is associated with effector T cell resistance to regulation by CD4 and CD8 Tregs.

342–352 Y Matsuda, X Wang, H Oishi, Z Guan, M Saito, M Liu, S Keshavjee and C-W Chow

Spleen Tyrosine Kinase Modulates Fibrous Airway Obliteration and Associated Lymphoid Neogenesis After Transplantation

Inhibition of spleen tyrosine kinase attenuates fibrous airway obliteration following allograft transplant in a mouse intrapulmonary transplant model of obliterative bronchiolitis.

continued.

Case Reports

- 353–357 CJE Watson, V Kosmoliaptsis, LV Randle, NK Russell, WJH Griffiths, S Davies, H Mergental and AJ Butler

Preimplant Normothermic Liver Perfusion of a Suboptimal Liver Donated After Circulatory Death

The authors report a liver transplant where *ex situ* normothermic machine perfusion was used to reduce cold ischemia and permit functional assessment of a donation after circulatory death liver before implantation.

- 358–363 CE Koval, A Khanna, A Pallotta, M Spinner, AJ Taege, B Eghtesad, M Fujiki, K Hashimoto, B Rodriguez, G Morse, A Bennett and K Abu-Elmagd

En Bloc Multivisceral and Kidney Transplantation in an HIV Patient: First Case Report

The authors present the first case report of multivisceral transplantation in an HIV-positive patient with a comprehensive description of technical, immunologic, and infectious challenges that resulted in an unfavorable outcome.

Reports From the CDC: MMWR

- 364 **Notes From the Field: Multistate Outbreak of Human *Salmonella* Poona Infections Associated With Pet Turtle Exposure — United States, 2014**

Images in Transplantation

- 365–367 S Abu-Gazala, PL Abt and MH Levine

CME Successful Liver Retrieval After Acute Aortic Dissection Involving the Celiac Artery Origin

Letters to the Editor

- 368–369 T Bachelet, P Merville, J Dechanet-Merville and L Couzi

Cytomegalovirus-Induced $\gamma\delta$ T Cells During Rejection: An Ambivalent T Cell

- 370 X-L Shi and J Kwekkeboom

Reply to "Cytomegalovirus-Induced $\gamma\delta$ T Cells During Rejection: An Ambivalent T Cell"

- 371–373 KF Erickson, WC Winkelmayer, S Busque, R Lowsky, JD Scandling and S Strober

A Cost Analysis of Tolerance Induction for Two-Haplotype Match Kidney Transplant Recipients

- 374 H Zhao, J Tsauo and X Li

Percutaneous Retroperitoneal Splenorenal Shunt: An Alternative to Transjugular Intrahepatic Portosystemic Shunt?