

Antibody-Mediated Rejection – an Ounce of Prevention is Worth a Pound of Cure

The presence of pre-formed donor-HLA-specific antibodies is associated with a high risk of hyperacute and acute antibody-mediated rejection (ABMR), and often limits potential recipients' access to willing living donors and deceased donor organs. Over the last decade, however, understanding of ABMR has increased markedly and given rise to many strategies for the transplantation of allosensitised recipients. Renal transplant recipients with a willing but antibody-incompatible living donor have undergone successful antibody desensitisation programmes and others have circumvented the antibody incompatibility altogether through entry into a paired kidney exchange scheme. This symposium will bring together internationally renowned researchers to provide an update of recent advances in the laboratory science of ABMR and review how it can be prevented in clinical practice.

The first presentation will set the scene by outlining current thinking on how antibody-mediated immunity damages an allograft. As well as describing how alloantibodies mediate graft injury through a range of classical antibody-mediated effector pathways, new insights will be provided into how antibody-mediated immunity may influence the development of cellular rejection.

There has been a revolution in the technology available for assessing the antibody-mediated immune response to HLA antigens, best exemplified by the widespread introduction of single HLA antigen beads and Luminex technology. The second presentation will give an update on the newer techniques for detecting, characterising and tracking donor-specific alloantibodies before and following transplantation, and relate these to methods for pre-emptive management of recipients through virtual cross-match techniques.

Many patients with donor-HLA- or ABO-specific antibodies can be sufficiently desensitised to allow transplantation to proceed. There are a number of challenges, however, including the identification of those patients who are readily amenable to desensitisation, selection of an optimal strategy for desensitisation, monitoring the effectiveness of therapy, and understanding the risks and limitations of this relatively aggressive approach. High-dose IVIg and plasmapheresis are the mainstays of many desensitisation strategies, but new immunomodulatory agents are also being tested. These topics will be addressed in the third presentation.

Paired kidney exchange schemes provide sensitised recipients with a way of circumventing HLA antibody and ABO incompatible living donor kidney transplantation with no added immunosuppressive burden to the recipient. However, the chance of finding a matching pair is heavily dependent on blood group and the degree of sensitisation of the recipient. The success of exchange schemes is determined by the size and composition of the pool, and mathematical modelling approaches can be used to determine the chances of a particular recipient/donor pair finding a suitable match. Innovations such as three-way and four-way exchanges, altruistic domino paired kidney donation, and non-simultaneous extended altruistic donor (NEAD) chains all markedly increase the success rate of paired donation schemes, although they also pose logistic challenges. Such schemes may also be used in conjunction with desensitisation in carefully selected recipients. These topics will be discussed in the last talk of this symposium.

As the title of the symposium implies, the risks of combating ABMR are formidable both in terms of risk to the allograft and to the patient. As such, ABMR is an entity best avoided: prevention is better than cure.

We hope this journey through recent developments in the management of allosensitised patients will bring the audience up to date in this fast moving area and stimulate new research in this important field of clinical transplantation.

ROTRF Sunrise Symposium

Vancouver Convention Centre
Vancouver, Canada
Room 220 – 222
Monday, August 16, 2010, 07:00 – 08:15



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Moderators: **J. Andrew Bradley**, *University of Cambridge, Cambridge, UK*
Allan D. Kirk, *Emory University, Atlanta, USA*

7:00 – 7:10

Introduction
J. Andrew Bradley

7:10 – 7:25

**Humoral Immunity: Mechanisms of Graft Injury and
Relationship to Cellular Immunity**
William M. Baldwin III, *Lerner Research Institute, Cleveland, USA*

7:25 – 7:40

**Detection and Identification of Alloantibodies circa 2010:
Myths and Realities**
Howard M. Gebel, *Emory University Hospital, Atlanta, USA*

7:40 – 7:55

The 2 Key Questions for Desensitization: Who and How?
Denis Glotz, *Hôpital Saint Louis, Paris, France*

7:55 – 8:10

**Giving the Incompatible Patient Hope with
Kidney Paired Donation**
Adam W. Bingaman, *Texas Transplant Institute, San Antonio, USA*

8:10 – 8:15

Closing Remarks
Allan D. Kirk

This workshop is CME accredited through the XXIII International Congress of The Transplantation Society. No pre-registration is required for attending this workshop. For further information on the ROTRF and the workshop, please visit our information booth #36 at TTS or www.rotrf.org.

