

Sensitisation in Paediatric Kidney Transplantation

- A Case Study

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Outline:

- Renal transplantation, paediatrics & sensitisation
- Immunological sensitisation
- Case Study
 - Desensitisation
 - Timeline of Events
 - Issues while waiting for a Transplant
 - Transplant
 - Post Transplantation & Graft function to 1 year
- The Future

Renal Transplantation, Paediatrics & Sensitisation

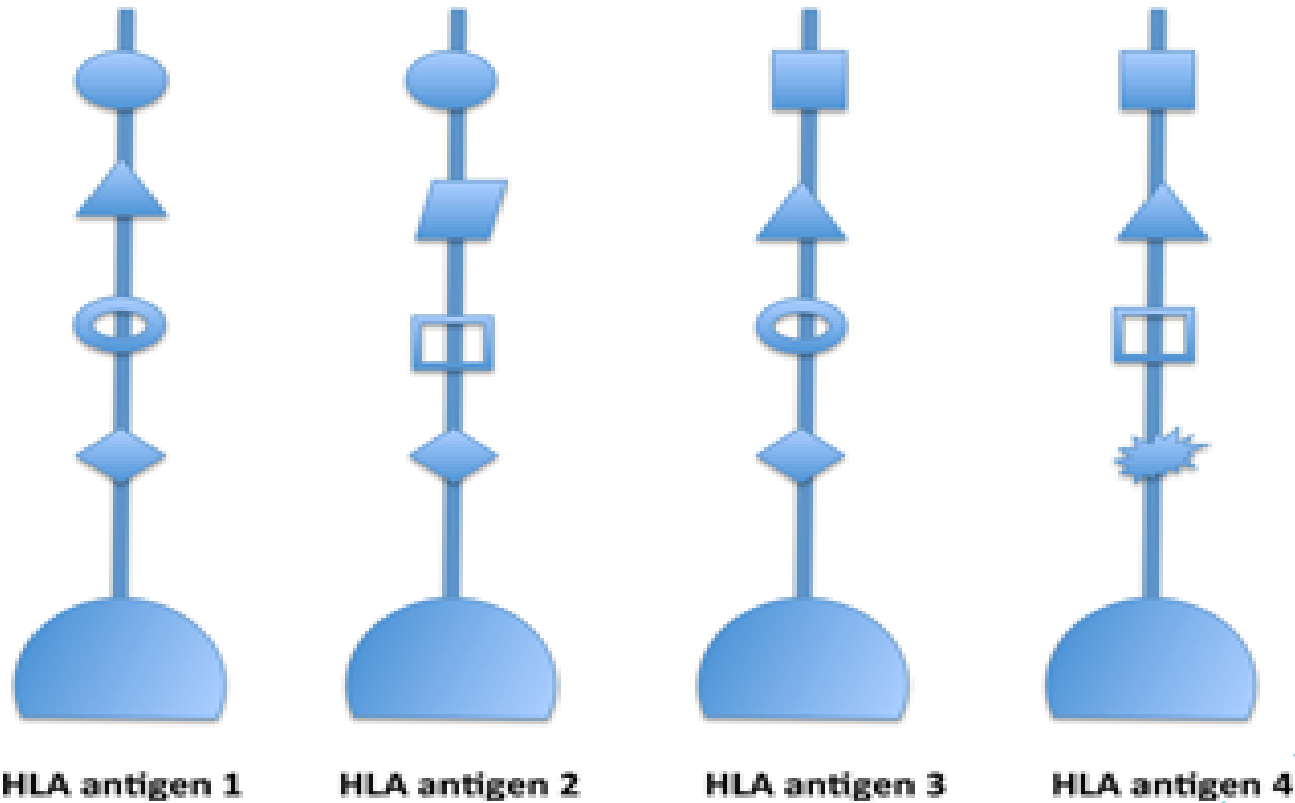
- Kidney transplantation is the ideal treatment for children with End Stage Renal Disease (ESRD)¹
 - Optimises physical & psychosocial growth & well-being²
- Most paediatric renal transplant patients require more than one renal transplant in their lifetime¹
- Development of Donor Specific Antibody (DSA) can lower graft survival³⁻⁶
- Matching for second and subsequent renal transplants is more complex in the presence of DSA^{1,2,7}
 - There is an increased risk of acute rejection^{8,9}
 - The pool of potential donors is reduced¹⁰
 - Longer wait times for an organ^{1,7,8}

Immunological Sensitisation

- Human Leukocyte Antigen (HLA) is a gene complex and each individual inherits a set of HLA (haplotype) from each parent
- Epitope mismatches have been shown to predict the development of DSA ^{9,11}
- Current literature supports the realisation that HLA mismatches lead to higher immunological sensitisation due to eplet mismatches ^{1,2,8-10,11,12}

Immunological Sensitisation

Figure 1: An HLA antigen and expression of unique epitopes ¹³



Case Study - Background

Male Caucasian: Posterior Urethral Valves (PUV)

- 2002 ESRD, age 2 yrs 9 mo
 - Haemodialysis
- 2003 Renal Transplant, age 3 yrs 2 mo
 - Donor: Living Related Donor (LRD)

Figure 2: Summary HLA Typing Recipient & Donor

| | | | | | | | | |
|-----------|--------|--------|-------|-------|-------|-----------------|---------|-------|
| Recipient | A23,32 | B55,57 | Bw4,6 | Cw3,- | DR1,3 | DRB1*0101,*0301 | DRw52,- | DQ1,2 |
| Parent | A1,23 | B8,55 | Bw-,6 | Cw3,7 | DR1,3 | DRB1*0101,*0301 | DRw52,- | DQ1,2 |

Case Study

- 2010: age 11 yrs
 - DSA identified - high A1 (8590) & A2 (6195)
 - Renal biopsy (RBx): Chronic Allograft Nephropathy (CAN)
- 2013: Transplant failed, age 13 yrs 6 mo
 - Graft survival of 10 ½ years
 - Haemodialysis

Issues now included:

- No suitable LRD (no access to paired kidney exchange program)
- Sensitisation high calculated Panel Reactive Antibody (cPRA) at 99% class 1 & 62% class 2

Desensitisation

2014

Reassessed for Transplantation - **Sensitisation high **

2015

2 years and no offer of Deceased Donor (DD) kidney

Desensitisation protocol

July: Rituximab infusion

August: Intravenous Immunoglobulin (IVIg) x 2 treatments

2016

Feb & March: Plasma Exchange (PLEX) - 6 treatments

March: IVIg 1 treatment

No further Rituximab required as B cell depletion persisted

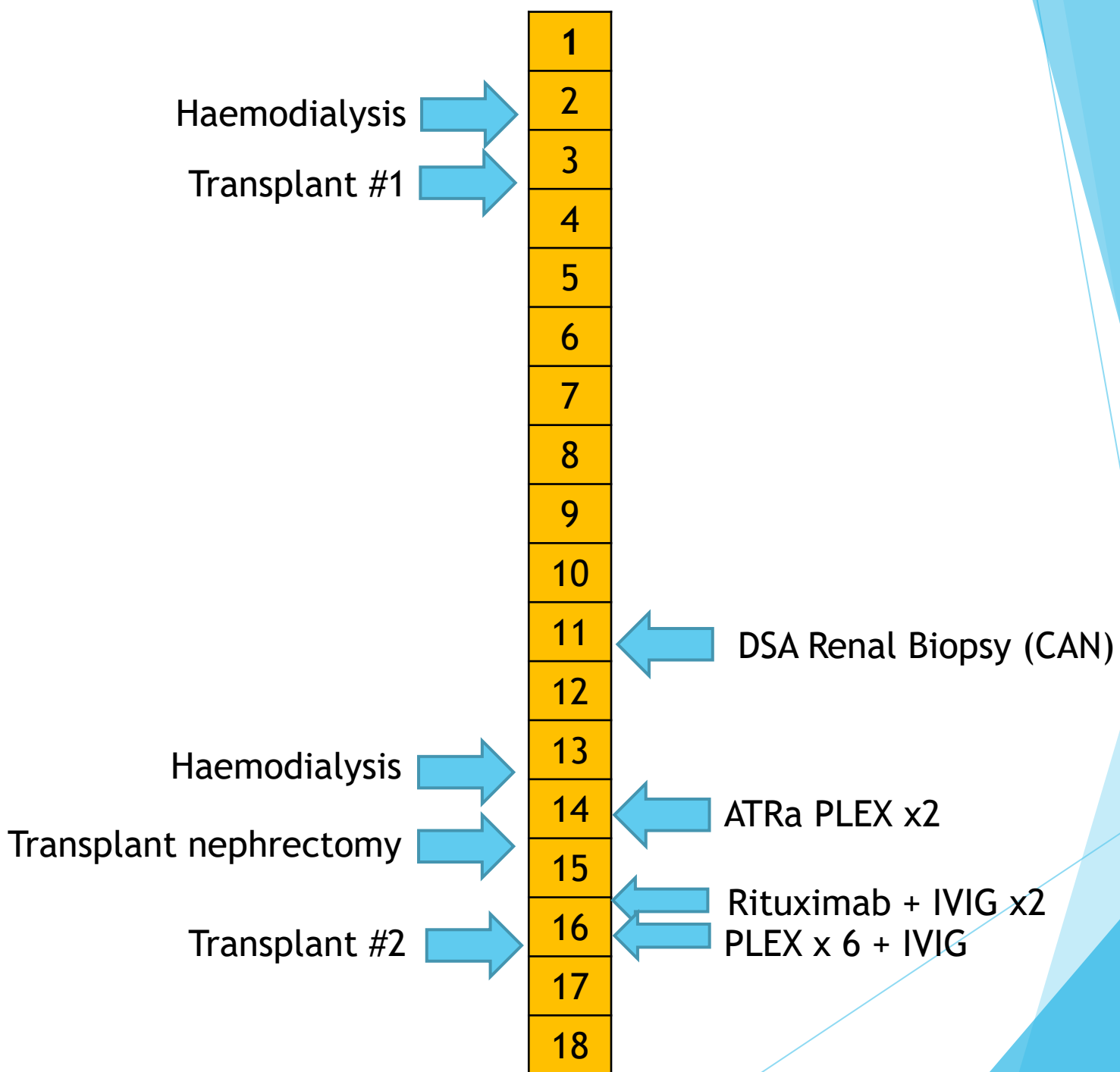
Issues while waiting for a Transplant

Patient

- Failure to gain weight
- Frequent headaches, nausea & aching limbs
- Low mood
- Daily hospital admissions for Dialysis, PLEX & IVIg
- Schooling - poor attendance

Family

- Time off work
- Cost of transport & parking
- Frequently at hospital



Transplant

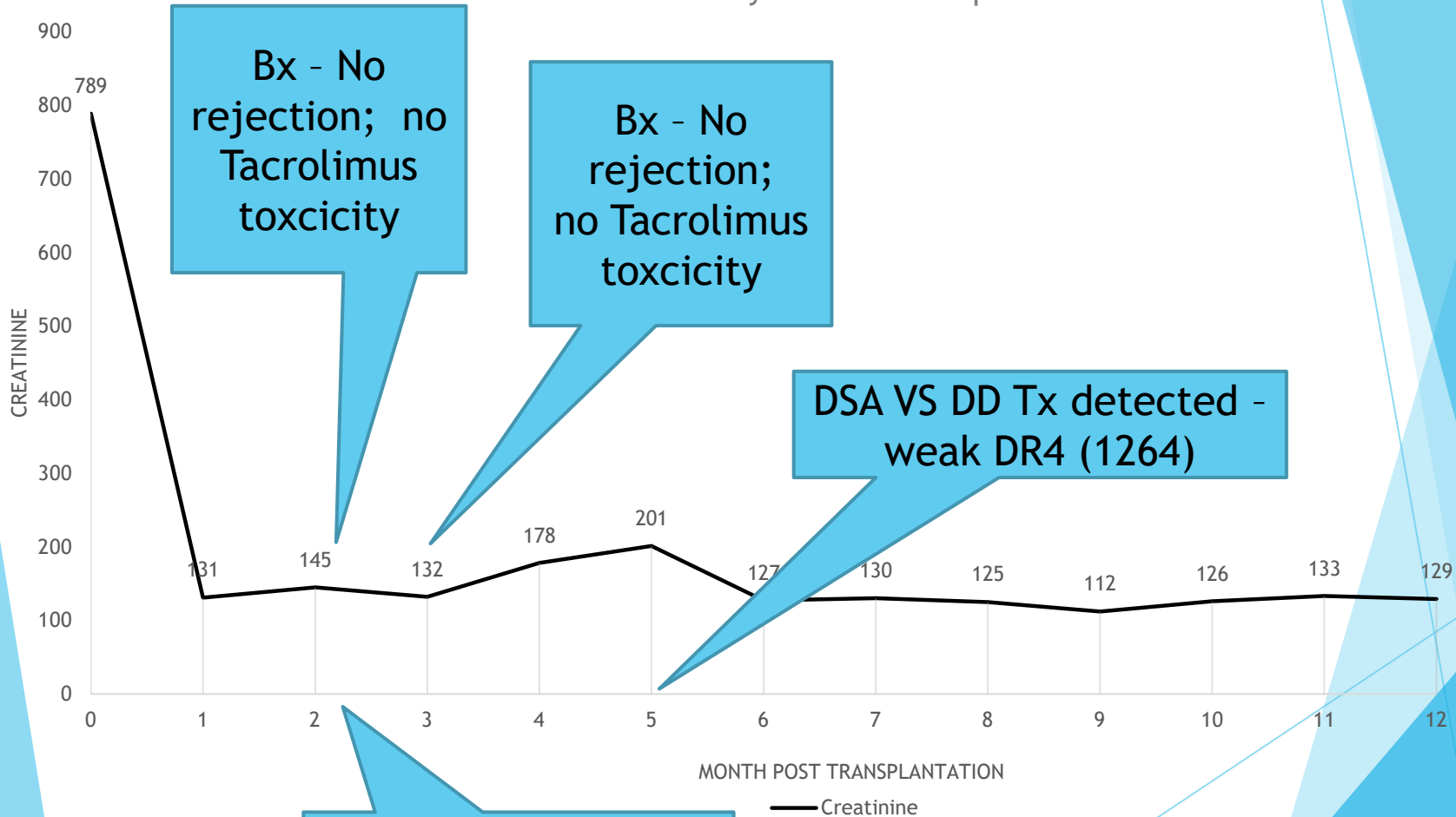
2016 April

2nd Renal Transplant: Age, 16 yrs 8 mo DD

- DSA present, historical sera
- Complement Dependent Cytotoxicity (CDC) crossmatch negative
- Induction - PLEX pre & post
- Anti-thymocyte Globulin (ATG) 10 days - T cell suppression
- Immunosuppression regime:
Tacrolimus / Mycophenolate mofetil (MMF) / Prednisolone
- Delayed graft function

Post Transplantation & Graft Function to 1 year

Creatinine to 1 year Post Transplantation



Bx - No rejection; no Tacrolimus toxicity

Bx - No rejection; no Tacrolimus toxicity

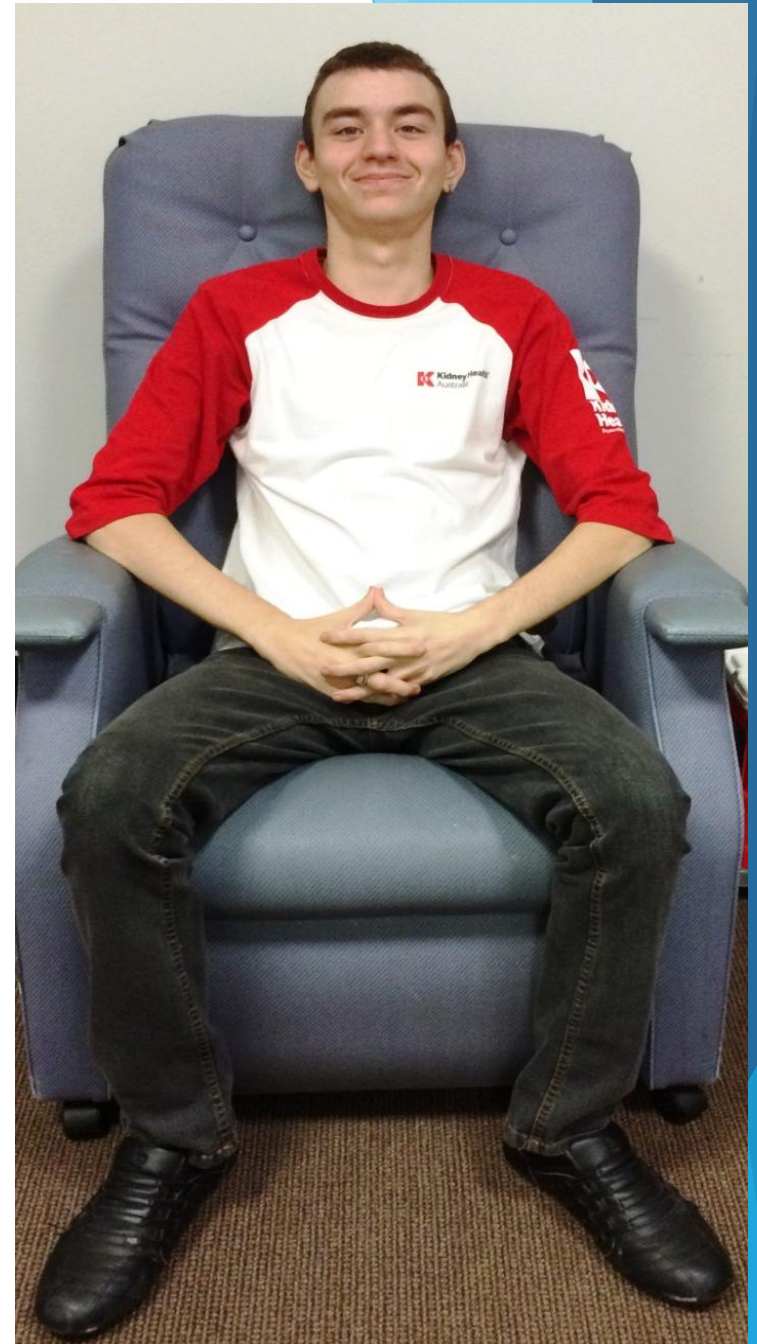
DSA VS DD Tx detected - weak DR4 (1264)

Cytomegaloviraemia

The Future

- It is now known that better haplotype matching can prevent sensitisation
- Selection of kidneys for 1st renal transplant now looks at potential for sensitisation
- Paediatric patients may be listed to receive a kidney from either the deceased donor (DD) or paired kidney exchange (AKX) programs rather than from a LRD if sensitisation a potential issue

The Patient



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Conflict of Interest

The author declares that funding to travel & attend the 46th EDTNA/ERCA conference has been received via successful application for the “Astellas Practice Development Travel Award” in association with the Transplant Nurses’ Association Australia

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Abbreviations

ABO - Blood Group A, B, AB or O

AMR - Antibody Mediated Rejection

ATG - Anti-thymocyte Globulin

AT1R - Angiotensin 1 Receptor

ATRa - Angiotensin Receptor Antibody

RBx - Renal Biopsy

CAN - Chronic Allograft Nephropathy

CDC - Complement Dependent
Cytotoxicity

CM - Cross Match

CMV - Cytomegalovirus

DD - Deceased Donor

DSA - Donor Specific Antibodies

dn DSA - de novo Donor Specific
Antibodies

ESRD - End Stage Renal Disease

LRD - Living Related Donor

MMF - Mycophenolate mofetil

HLA - Human Leukocyte Antigen

IVIg - Intravenous Immunoglobulin

LRD - Living Related Donor

MFI - Median Fluorescence Intensity

MM - Mismatch

PLEX - Plasma Exchange

cPRA - calculated Panel-reactive
Antibodies

PRD - Primary Renal Disease

Tx - Transplant (kidney)