

# Sensitised (cardiothoracic) Patients

All patients referred to in this presentation have given consent for their cases to be shared

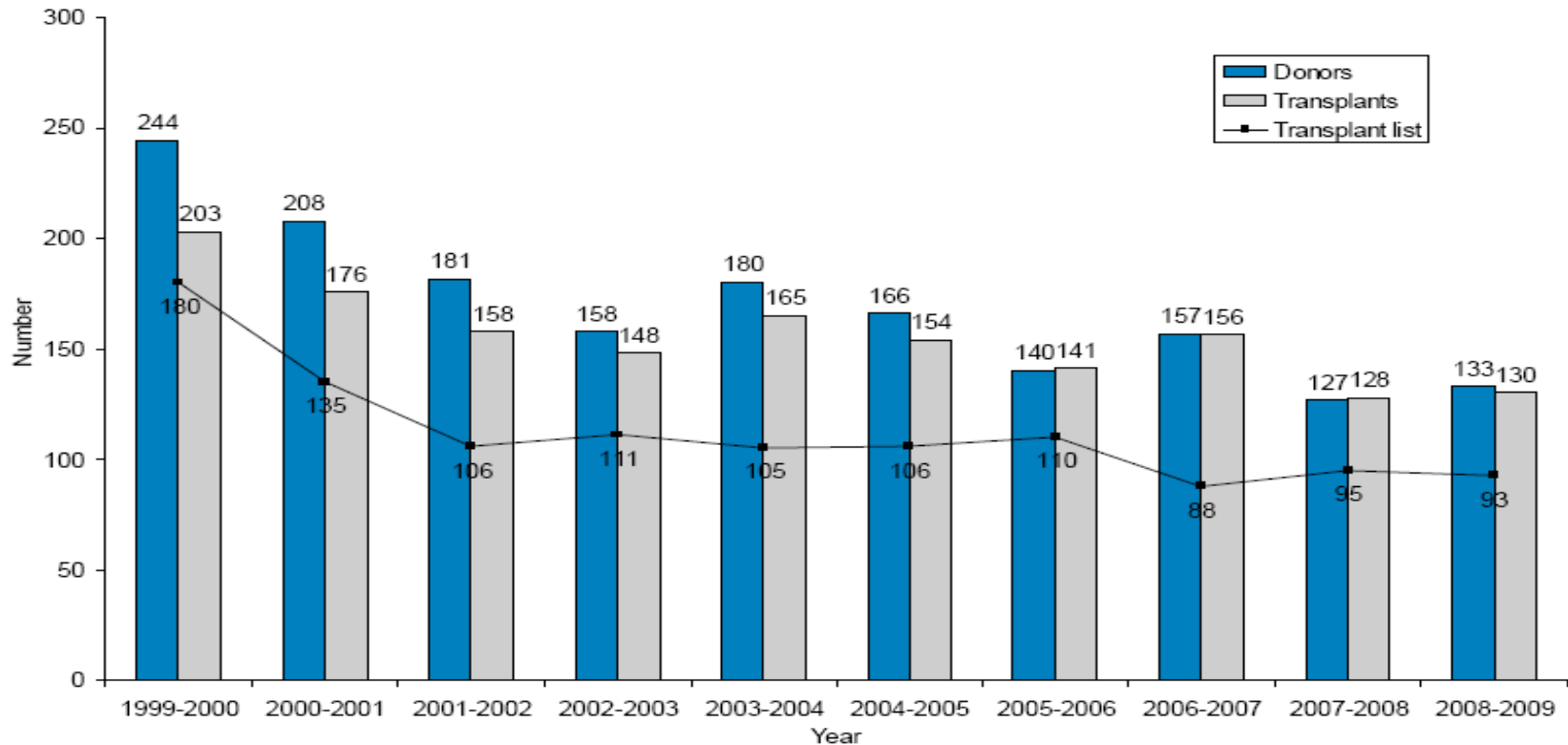
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# Cardiothoracic vs Renal Patients

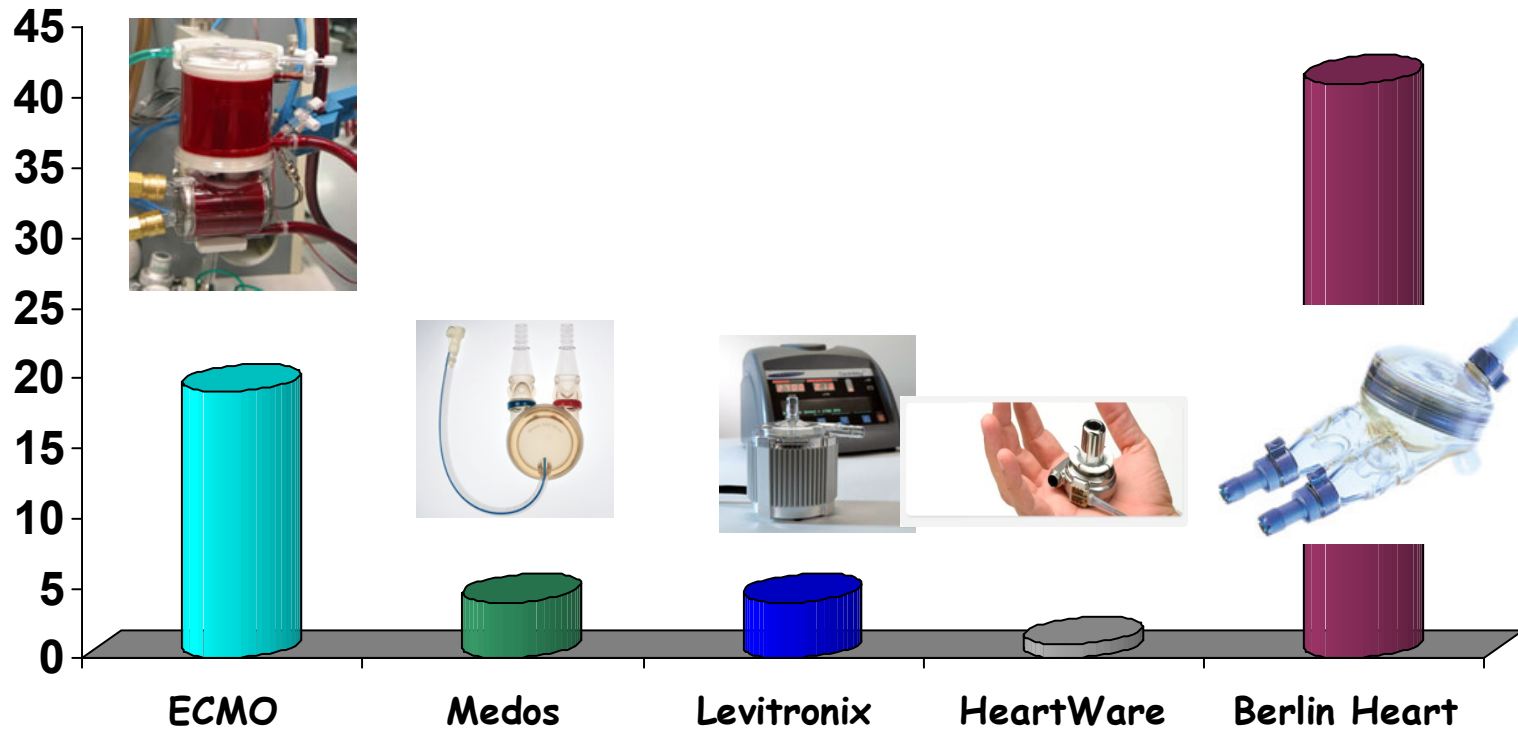
	<b>Cardiothoracic</b>	<b>Kidney</b>
<b>Life threatening</b>	Usually	Sometimes
<b>Replacement therapy</b>	Short term/No	Long term
<b>Optimal Cold Ischaemia</b>	< 4 Hour (heart) 6 hour (lung)	< 18 hour (shorter preferred)
<b>Live donor availability</b>	Not usually	yes
<b>Average life expectancy</b>	6-8 Months	6-10 years
<b>Quality of life</b>	Very poor	Poor
<b>HLA antibody Screening</b>	Crucial	Moderate
<b>Pre transplant Crossmatch</b>	Not usually	Available

# Different Challenges

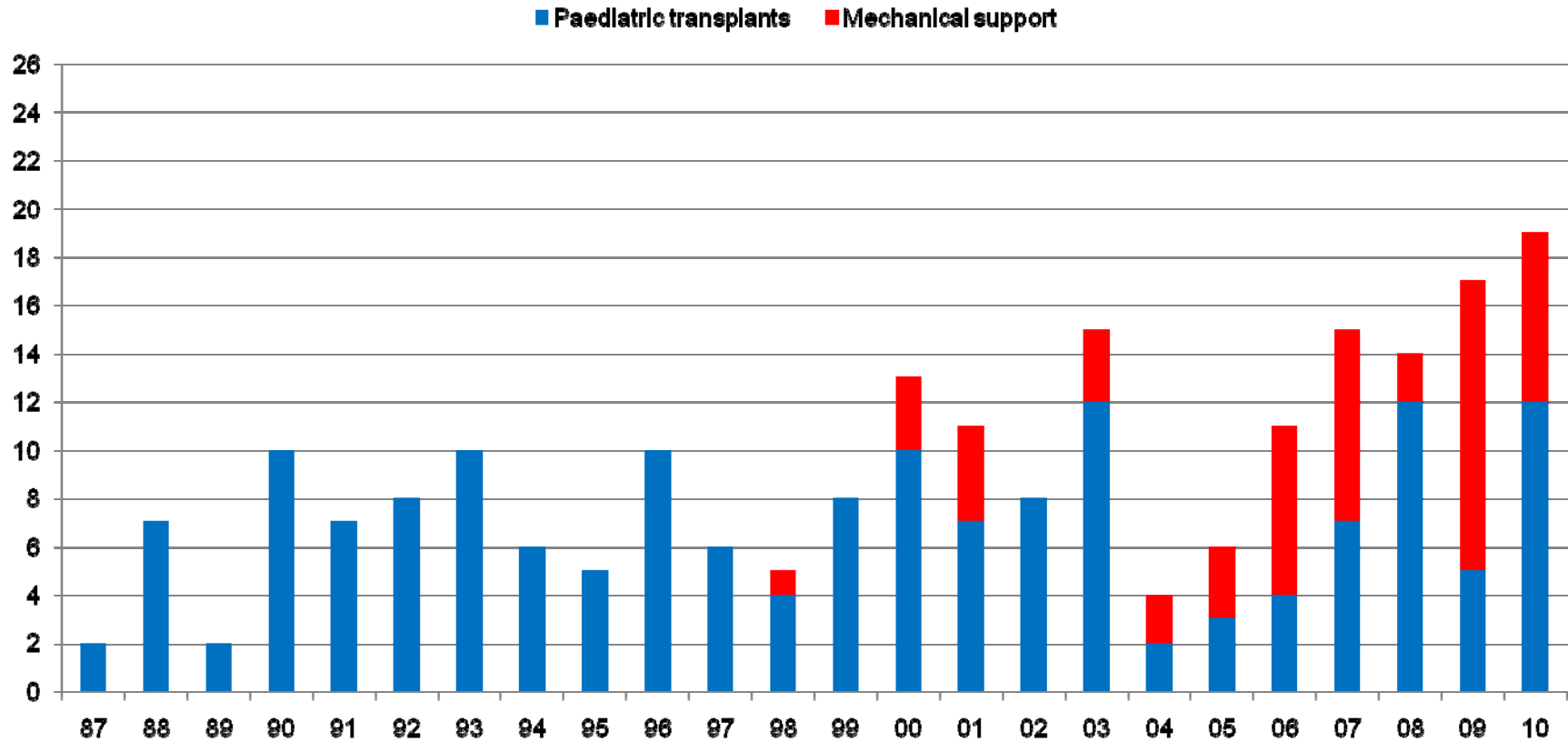
**Figure 5.1 Deceased donor heart programme in the UK, 1 April 1999 - 31 March 2009**  
**Number of donors, transplants and patients on the active transplant list at 31 March**



# Mechanical Support

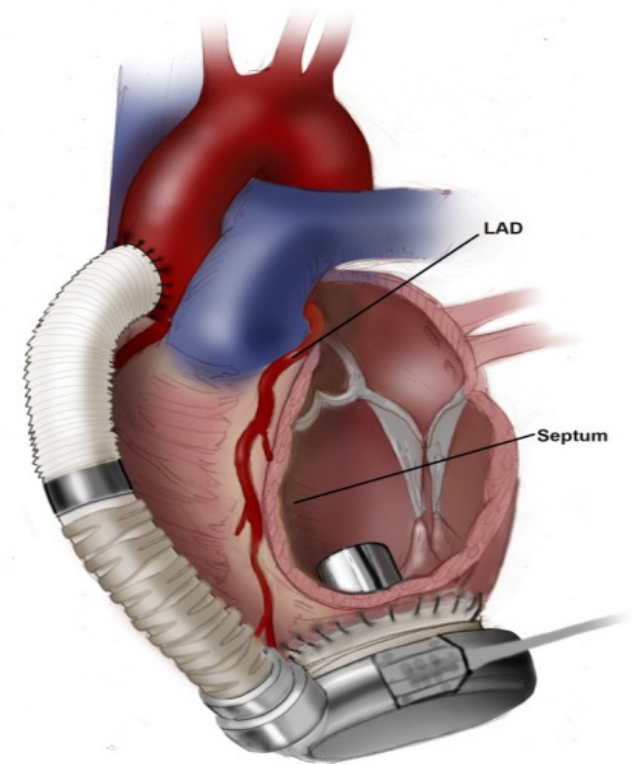


# Transplants and mechanical support



# Berlin Heart

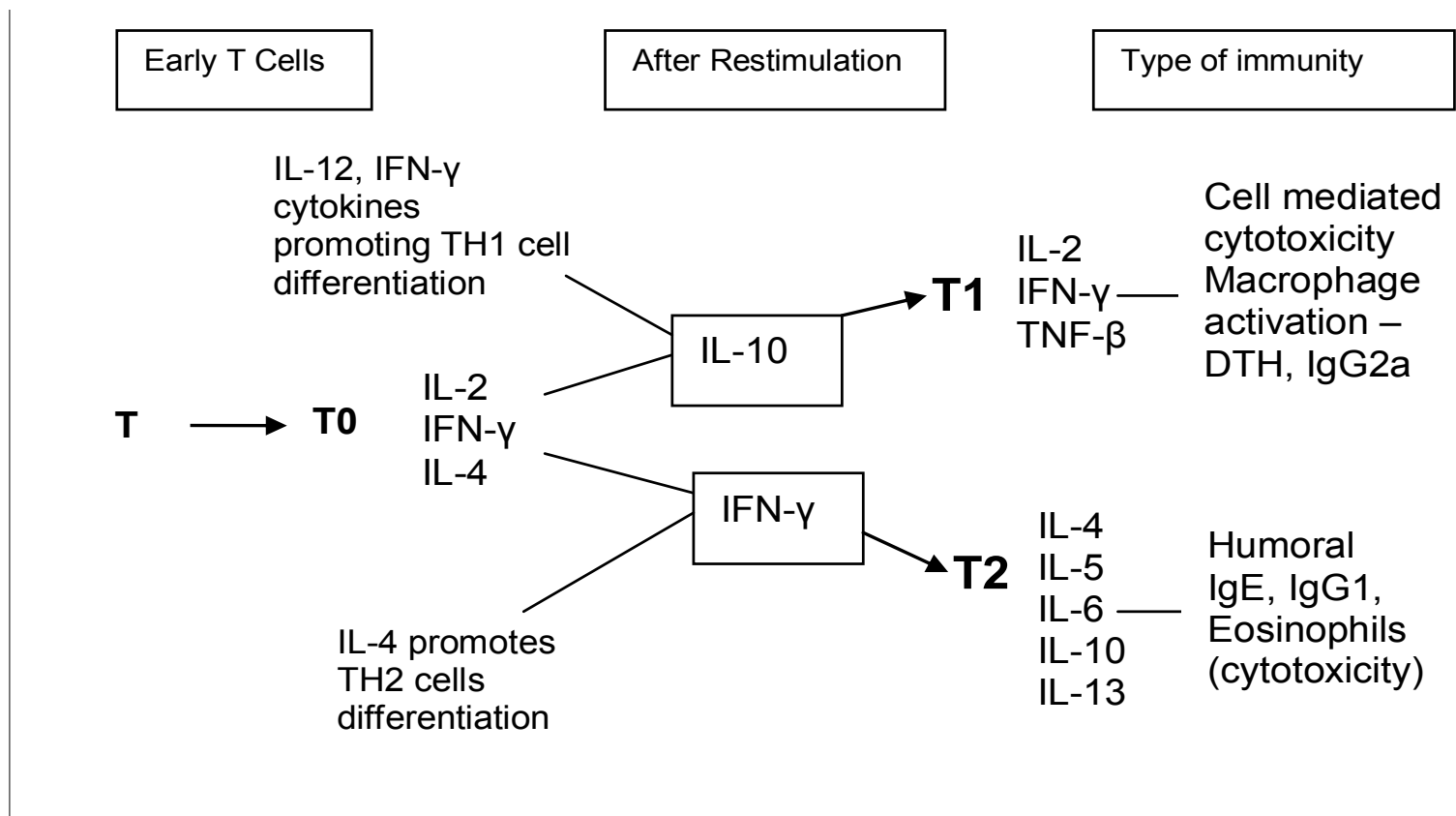
# Heartware



# Mechanical support - issues

- Surgery
- Blood transfusion
- Thrombosis
- Altered immunity
- HLA antibodies – DP, DQA, Allele specific
- At front of queue

# Normal arms of the Immune response



# Ventricular Assist Devices

- Are not allogeneic
- Do not cause de-novo sensitisation
- Are related to potential bleeding, infections and thrombo-embolic events
- Require surgery and blood transfusion
- Are associated with increased HLA sensitisation

# Shift of balance

- Interactions of the device with the recipient immune system
- Up-regulation of CD95 (FAS) on Th1 cells (found on VAD surfaces)
- Loss of Th1 cytokine producing T cells through activation-induced cell death and apoptosis
- Impaired Th1 responses
- Vulnerable to infections (particularly fungal)

# Th2 > Th1

- Unopposed activation of Th2 cytokine producing T-cells leading to B-cell hyper-reactivity
- Polyclonal expansion of B-cell clones (normally controlled by Th1 cells)
- Heightened CD40-CD154 interactions.
- Resultant increase in Ig
- Introduction of Allogeneic material increases risk of HLA sensitisation

# Sensitisation issues

- HLA – What is safe to transplant? Very limited offers
- Cw, DR, DQA, DPB1, DPA1..... Expression
- Regular transfusion – when to test?
- Failing controls, Live lymphocyte assays
- Ethical issues –optimal organ useage
- Patient-specific protocols

Presented in lab Nov 2008.

**Gabby** — A POS HLA-A3,68;  
B7,60; CW7,10 DR13,16;DQ5,6

HLA antibody profile – IgG antibodies  
detected against A2,A69, B8  
B17,B35,B44,B51,B53,  
DR1,DR10,DR53,DQ7

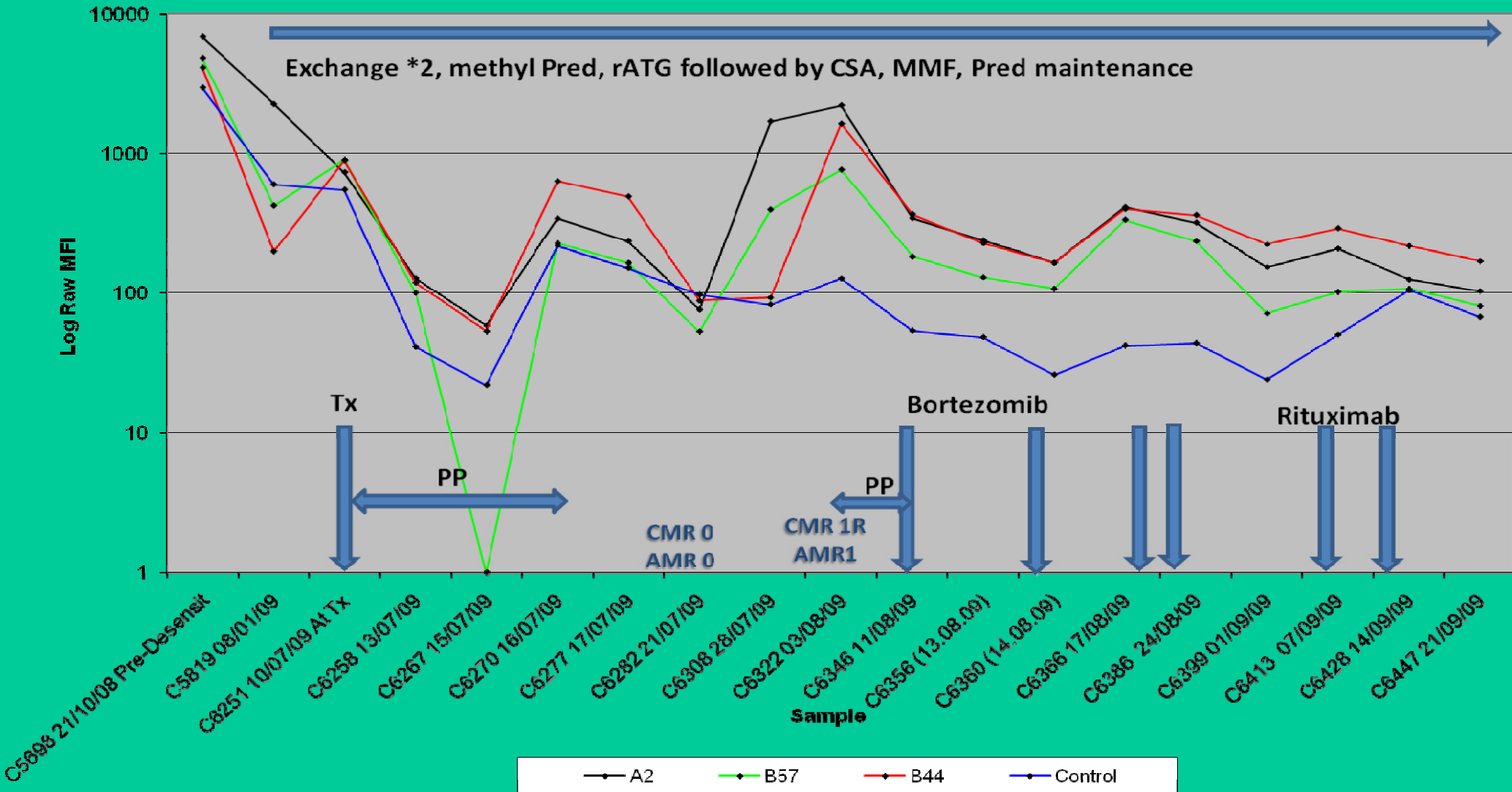
Desensitisation in January 2009 with  
Rituximab MMF and IvIg with moderate  
success

**Transplanted 10/07/09**

**Donor** — **B POS** HLA- **A2,24**;  
**B44,57**; CW5,6 DR**4,7**; DQ**7,9**.  
X/M- CDC T POS DTT NEG B INVALID.  
FLOW T POS B INVALID

# Desensitisation

GF summary all samples tested Class I



## 2 years later

Good function- no signs of graft damage

Current antibody profile – HLA antibodies present but no Donor Specific antibodies. A29,A31,B67, Cw16 with reasonable MFI.

??Immature immune system or desensitisation success

# HLA antibodies in adults

- Problems with DP antibodies and Typing ??  
Expression level. Also now finding DQA antibodies.
- Limits transplants or deal with differently
- Offer prospective XM – shrinks donor pool
- Deal with differently
- Agree plan pre offer – Team effort involve whole team

# Peri-Transplant Plans

## Peri Transplant Plan for - D R

Pre Transplant Diagnosis – Cardiomyopathy Prev RV Disarticulation

ABO/Rh group – O Pos

HLA antibodies – 6<sup>th</sup> June 2011 - IgG antibodies to A32, A80, B38, B49, DR53, DQB1\*06:03 and DQA3. Historical specificities detected include A9, B37,B51 and Cw9

Antibody Strategy

ABO compatible Donor

Raw MFI for antibodies (Jun-11) A32 – 750, A80 – 1642, B49 - 1401, B38 – 1052, DR53 – 1525 & 1275, DQB1\*06:03 (also DQA3) – 2164, DQA3 – 852-2164

Avoid known current antibodies as donor DQA type is unknown at time of offer. If all missed then transplant proceeds with low risk due to DQA antibody (2000 MFI), this gives about 60% chance of donor heart being suitable.

Treat historical antibodies as risk factor but transplant against these with increased immunosuppression (which will happen anyway due to potential DQA).

Donor DQA type will be available in lab day after transplant (Sun-Thurs transplant only), treatment can be adjusted accordingly or treat as DQA3 positive on other days.

Post transplant immunosuppression plan is to give ATG day 1 post op if reteroscopic crossmatch is positive or still unknown. Otherwise immunosuppression as per standardised protocol

Plan Drawn up and agreed by VC GMc GP MH

## Peri Transplant Plan for – K B

Pre Transplant Diagnosis – Congenital Heart Disease Pre Valve Surgery

ABO/Rh group – A Pos

HLA antibodies – 9<sup>th</sup> May 2011 - IgG antibodies to A9, A66, B7, B13, B40, B27, B42, B63, B48, B73, B81, DR2, DR7,DR12, DQA\*0501 Historical specificities detected include B17,B47,Cw16,DR1, DR9, DQ4, DQ9, DQA\*01

Antibody Strategy

ABO compatible Donor

Raw MFI for antibodies (May-11) **Class I** 1-2000 SA, Higher on ID tests **Class II** SA DR2 (15,16) – 3500, 1487,1359 DR12 – 2289, DR7 2575, DQA5 – 885

Avoid known current antibodies except DQA as donor DQA type is unknown at time of offer. If all missed then transplant proceeds with low risk due to DQA antibody (<1000 MFI), this gives about 50% chance of donor heart being suitable.

Treat historical antibodies as risk factor but transplant against these with increased immunosuppression (which will happen anyway due to potential DQA). Note - New sample received 04/07/11 not tested as of 06/07/11

Donor DQA type will be available in lab day after transplant (Sun-Thurs transplant only), treatment can be adjusted accordingly or treat as DQA5 positive on other days.

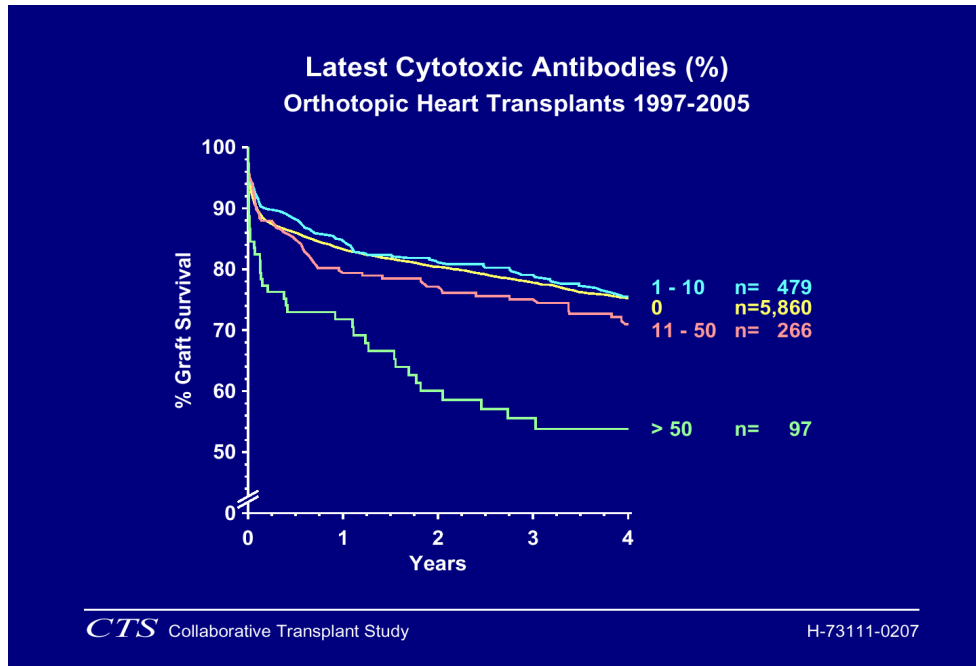
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# Balance

- Need to balance need for transplant against risk of rejection
- Clinicians view “successful transplants before Luminex”
- Laboratory view “reduction in early rejection and no organs wasted”
- Needs the team to buy into the plans

# Conclusions



HLA antibodies are very important and H&I must work with the transplant team to ensure successful transplantation