HLA Matched Components

John Goodwin
FIMLS, MPhil, DipRCPPath
H&I Laboratory, National Blood Service, Sheffield
HLA Matched Components

- Solid Organ Transplantation
  (Kidney, Heart, Lungs, Pancreas, Liver, Cornea etc)
- Stem Cell Transplantation
  (PBSC, BM, Cord Blood)
- Red Blood Cells
- Platelets
Why is HLA important?

- HLA molecules involved in antigen presentation and are immunogenic
  - Cellular or humoral response
- Extensive tissue distribution and discriminate ‘self and ‘non-self’
  - Great to protect us from invading pathogens but when mismatched in a clinical setting
    - Solid organ transplantation
      - Rejection
    - Stem cell transplantation
      - GVHD
      - Rejection
- RBC
  - HLA antibody formation, transfusion reaction
- Platelets
  - Antibody mediated immune destruction, transfusion reaction
HLA Matched RBC

- Kidney Transplantation
  - Where anaemia (normal feature of CKD) cannot be controlled with drug therapy
  - Living donor setting only
  - Mismatches are known
  - Avoid mismatches with transfused RBC
  - Very time consuming – fully manual process
  - One week notice
Patient Categories for HLA Matched Platelets

- Patients with platelet disorders e.g. Glanzmann’s / Bernard Soulier’s
- Prophylactic to avoid sensitisation e.g. aplastic anaemia, pre renal transplant
- Refractory patient’s
Platelet Refractoriness

Definition
Increase in patient’s platelet count of 
\(<10 \times 10^9/l\) between 10 mins and 24 hours 
after the transfusion of an adult dose of ABO compatible apheresis platelets on two separate occasions
Platelet Refractoriness

**Immune**
- **Platelet alloantibodies**
  - anti HLA (class I - >95%)
  - anti HPA (<5% HPA + HLA, HPA only <1%)
- **Other antibodies**
  - Autoantibodies
  - Drug-dependent antibodies
  - ABO antibodies
- **Immune complexes**

**Non Immune (80%)**
- Splenomegaly
- DIC
- Bleeding
- Consumption (eg ECMO)
- Infection and its treatment e.g. amphotericin B
HLA Matched Platelets

Logistics

- Receive request
  - Fax forms
- Assess request
- Tissue type and HLA antibody screen patient
- Panels searched to select donor
- Issue platelets
- Obtain increment data
- Weekly review meetings
Platelet Selection

- Local and national lists searched manually
  - Tissue type (only 30% fully matched)
  - HLA antibodies
  - CMV status
  - Lysin
  - Availability and location
  - HPA type and antibodies
  - Blood group

- Memos generated and faxed / emailed
Difficult cases

Taking into account the patient’s HLA type and antibody status – no (just a few) matches available nationally

- Cross reactive groups
- Transfuse across known antibodies
  - HLA (1000MFI – 25 000MFI)
  - HPA
- Antigen density on the platelet
<table>
<thead>
<tr>
<th>Antigen</th>
<th>Number of sites per platelet</th>
</tr>
</thead>
<tbody>
<tr>
<td>HPA1 (Ilb/Ilia)</td>
<td>50 - 80 000</td>
</tr>
<tr>
<td>HPA2 (Ib/IX)</td>
<td>25 000</td>
</tr>
<tr>
<td>HPA3 (Ilb/Ilia)</td>
<td>50 - 80 000</td>
</tr>
<tr>
<td>HPA4 (Ilb/Ilia)</td>
<td>50 - 80 000</td>
</tr>
<tr>
<td>HPA5 (Ia/Ila)</td>
<td>800 - 2 800</td>
</tr>
<tr>
<td>HPA15 (CD109)</td>
<td>&lt; 2 000</td>
</tr>
<tr>
<td>HLA Class I</td>
<td>15 - 120 000</td>
</tr>
<tr>
<td>HLA-A*02</td>
<td>4 400 - 10 000</td>
</tr>
<tr>
<td>HLA-Bw4</td>
<td>870 - 8 400</td>
</tr>
<tr>
<td>HLA-Bw6</td>
<td>1 300 - 5 800</td>
</tr>
<tr>
<td>HLA-C</td>
<td>Low</td>
</tr>
<tr>
<td>Blood group A1</td>
<td>2 100 - 16 000</td>
</tr>
<tr>
<td>Blood group A2</td>
<td>very low / not detectable</td>
</tr>
<tr>
<td>Blood group B</td>
<td>1 000 - 8 000</td>
</tr>
</tbody>
</table>

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HLA Matched Platelets

Logistics

• Receive request
• Assess request
• Tissue type and HLA antibody screen patient
• Panels searched to select donor
• Issue platelets
• Obtain increment data
• Weekly review meetings
Increment Return Rates

- National average return rate 2013 only 33.57% (44.39% Sheffield)

- Range 57.68 – 3.43%
Reasons for Incremental Data

- To aid in platelet selection
  - Identify unacceptable antigens
  - Identify acceptable antigen
- To achieve better clinical response
- To identify if HPA testing is required
- To identify if PAS is required
- To identify if further samples are required for HLA antibody testing
- To not waste a precious resource
- To save money
### Platelet increments

**Patient WS  A2 B7  antibodies 96% A3++**

<table>
<thead>
<tr>
<th>Date</th>
<th>Donor type</th>
<th>Pre count</th>
<th>Post count</th>
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<tbody>
<tr>
<td>04/5/05</td>
<td>A2,30B7,40</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>09/5/05</td>
<td>A2 B7,27</td>
<td>7</td>
<td>33</td>
</tr>
<tr>
<td>11/5/05</td>
<td>A2 B40</td>
<td>9</td>
<td>30</td>
</tr>
<tr>
<td>17/5/05</td>
<td>A2,24 B7,39</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>18/5/05</td>
<td>A2 B7,27</td>
<td>3</td>
<td>45</td>
</tr>
<tr>
<td>23/5/05</td>
<td>A2 B7</td>
<td>15</td>
<td>53</td>
</tr>
<tr>
<td>27/5/05</td>
<td>A2 B40</td>
<td>6</td>
<td>34</td>
</tr>
</tbody>
</table>

*Courtesy Andrea Harmer*
Reasons for Incremental Data

- To aid in platelet selection
  - Identify unacceptable antigens
  - Identify acceptable antigen
- To achieve better clinical response
- To identify if HPA testing is required
- To identify if PAS is required
- To identify if further samples are required for HLA antibody testing
- To not waste a precious resource
- To save money
Cost 2013/14

- Platelets (1 adult dose) £208.09

Premium
- HLA matched £180.09
- CMV-ve £8.38
- PAS £31.78
- Irradiated £8.36

- Total £436.70
Additional reasons for incremental data and patient review

Many things we don’t know

- ‘Taboo’ mismatches
- ‘Permissible’ mismatches
- Is HLA-A matching more important than HLA-B?
- What is a significant antibody level (individual and cumulative)?
- Is epitope matching more beneficial?

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Improvements

• OBOS (? May 2015)
  • Increased use of standing orders / avoid late requests
    » Poorer match grade
    » Poorer increment
    » Reduced clinical effect
    » Increase transfusion requirement
    » Not the best product for the patient

• Increase number of A and B1 issued to 80%
• Electronic national searching
• Epitope matching
• More research and studies
• Increase incremental and clinical information return rates leading to better patient review
• Better communication and education
## Number of HLA Matched Platelets Issued

<table>
<thead>
<tr>
<th></th>
<th>2007</th>
<th>2008</th>
<th>2009</th>
<th>2010</th>
<th>2011</th>
<th>2012</th>
<th>2013</th>
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<tr>
<td>Birmingham</td>
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<td>1285</td>
<td>1313</td>
<td>1074</td>
<td>1127</td>
<td>1259</td>
<td>1357</td>
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<tr>
<td>Bristol</td>
<td>1276</td>
<td>1153</td>
<td>1287</td>
<td>1382</td>
<td>1577</td>
<td>1648</td>
<td>1245</td>
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<tr>
<td>Colindale</td>
<td>1780</td>
<td>2123</td>
<td>2647</td>
<td>2912</td>
<td>6685</td>
<td>6004</td>
<td>5555</td>
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<tr>
<td>Newcastle</td>
<td>520</td>
<td>552</td>
<td>512</td>
<td>612</td>
<td>742</td>
<td>453</td>
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<tr>
<td>Sheffield</td>
<td>3231</td>
<td>3442</td>
<td>3313</td>
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<td>4826</td>
<td>4353</td>
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<tr>
<td>Tooting</td>
<td>1858</td>
<td>2730</td>
<td>1167</td>
<td>3199</td>
<td>4127</td>
<td>4721</td>
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<tr>
<td>Unallocated</td>
<td>336</td>
<td>477</td>
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<td>931</td>
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<td>9896</td>
<td>11762</td>
<td>13350</td>
<td>14174</td>
<td>19084</td>
<td>18438</td>
<td>16650</td>
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Summary

- Not an ‘off the shelf’ product
- Can be time consuming
- Regular patient review
- Not cheap
- Still lots of improvements required
- Many people involved
- Communication and education essential
HLA Matched Platelets

- Patient categories
- Definitions and background
- Algorithm
- Logistics
- Statistics
- Troubleshooting / questions
## First Request for HLA Selected Platelets

**PATIENT'S NAME**

<table>
<thead>
<tr>
<th>Dob</th>
<th>Blood Group</th>
<th>CMV status</th>
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<table>
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<tr>
<th>Hospital</th>
<th>Hospital No</th>
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<table>
<thead>
<tr>
<th>Ward</th>
<th>In Patient</th>
<th>Out Patient</th>
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<table>
<thead>
<tr>
<th>Pulse Hosp Code</th>
<th>Hematos Reference</th>
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<table>
<thead>
<tr>
<th>Male</th>
<th>Female</th>
<th>Adult</th>
<th>Paediatric</th>
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<table>
<thead>
<tr>
<th>Male</th>
<th>Female</th>
<th>Adult</th>
<th>Paediatric</th>
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</thead>
</table>

<table>
<thead>
<tr>
<th>Bleep Number</th>
<th>Hospital Phone No</th>
<th>Blood Bank Phone No</th>
<th>Fax No</th>
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**Diagnosis**

**Clinical Details**

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<tr>
<th>Treatment</th>
<th>Chemo</th>
<th>Post Chemo</th>
<th>Post BMT</th>
<th>ATG</th>
<th>IVIG</th>
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<table>
<thead>
<tr>
<th>Reason for Request</th>
<th>Prophylactic</th>
<th>Poor Increments</th>
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<table>
<thead>
<tr>
<th>Previous platelet transfusion</th>
<th>Reaction</th>
<th>Pack type</th>
<th>Fresh</th>
<th>ABO comp</th>
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</table>

<table>
<thead>
<tr>
<th>Last Date</th>
<th>pre.......post.......</th>
<th>Yes/No</th>
<th>Yes/No</th>
<th>Yes/No</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Prev Date</th>
<th>pre.......post.......</th>
<th>Yes/No</th>
<th>Yes/No</th>
<th>Yes/No</th>
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</thead>
</table>

**Other Non Immune Reasons**

<table>
<thead>
<tr>
<th>Bleeding</th>
<th>Fever</th>
<th>Splenomegaly</th>
<th>Infection</th>
<th>DIC</th>
<th>Anticoagulants</th>
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</thead>
</table>

<table>
<thead>
<tr>
<th>Number of Units and Date Required for Initial Request Only</th>
<th>CMV neg required</th>
<th>Yes</th>
<th>No</th>
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</thead>
</table>

<table>
<thead>
<tr>
<th>Signature</th>
<th>Print Name</th>
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</table>

**For NHSBT use only**

<table>
<thead>
<tr>
<th>HLARIPA type</th>
<th>Typing in House</th>
<th>Conf Fax Received</th>
<th>Not typed samples requested</th>
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</thead>
</table>

<table>
<thead>
<tr>
<th>Antibody Results</th>
<th>Pos</th>
<th>Neg</th>
<th>Not tested</th>
</tr>
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</table>

**Antibody Results**

<table>
<thead>
<tr>
<th>Authorised by Name</th>
<th>Date</th>
<th>Time</th>
</tr>
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</table>

<table>
<thead>
<tr>
<th>Comments</th>
</tr>
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</table>

<table>
<thead>
<tr>
<th>Advice given</th>
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</thead>
</table>

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**Key Points**

- Blood group
- Previous transfusion data
- CMV requirement
- FRM559

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Cross-Referenced in Primary Document: SOP3054

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**Key Points**

- **Date and time of transfusion**
- **Latest time for delivery**
- **CMV requirement**
- **Check for updated forms**
HLA Matched Platelets

Logistics

- Receive request
- Assess request
- Tissue type and HLA antibody screen patient
- Panels searched to select donor
- Issue platelets
- Obtain increment data
- Weekly review meetings
Platelet Match Grades

Match Grades (HLA A and B locus)

- **A** = Full match (30%)
- **B1** = 1 MM antigen
- **B2** = 2 MM antigens
- **B3** = 3 MM antigens
- **B4** = 4 MM antigens
- **SEL** = selected
Algorithm for management of patients refractory to random donor platelets

- Refractory to ABO matched <72 hours old
  - Screen for anti-HLA class I

- Exclude non-immune
  - Positive
    - Give HLA class I matched platelets and measure increments after each transfusion
    - Good increment, continue with HLA class I matched platelets and screen for anti-HLA monthly
    - If poor, screen for anti-HPA
      - Positive
        - Give HLA and HPA matched platelets
      - Negative
        - Discuss with NHSBT
    - No increment
      - Consider HPA antibodies

- Negative
  - If refractoriness is confirmed, discuss with blood centre a trial of HLA matched platelets

- Infection and its treatment
  - Splenomegaly
  - Disseminated intravascular coagulation (DIC) bleeding

- Keep in mind non-immune causes and ABO matching
# Increment Data Form

## PATIENT DETAILS

<table>
<thead>
<tr>
<th>Field</th>
<th>Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>Name:</td>
<td>«FirstName» «LastName»</td>
</tr>
<tr>
<td>DOB:</td>
<td>«DateOfBirth»</td>
</tr>
<tr>
<td>ABO/Rh:</td>
<td>«ABO» «Rh»</td>
</tr>
<tr>
<td>Hospital:</td>
<td>«HospitalName»</td>
</tr>
<tr>
<td>Hospital Number:</td>
<td>«HospitalNumber»</td>
</tr>
</tbody>
</table>

## DONATION DETAILS

<table>
<thead>
<tr>
<th>Field</th>
<th>Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>Donation Number:</td>
<td>«Dnt_DonationNo»</td>
</tr>
<tr>
<td>Date Bled:</td>
<td>«Dnt_DateBled»</td>
</tr>
<tr>
<td>Pack Number:</td>
<td>«Dnt_ProductDesc»</td>
</tr>
<tr>
<td>Match Grade:</td>
<td>«MatchGrade»</td>
</tr>
<tr>
<td>Planned transfusion Date:</td>
<td></td>
</tr>
</tbody>
</table>

## TRANSFUSION DETAILS FOR COMPLETION BY THE HOSPITAL

**PLEASE RETURN THIS FORM TO THE ADDRESS OR FAX NUMBER AT THE TOP**

**DATE AND TIME OF TRANSFUSION** .................................................................

Pre transfusion count:............... x10^9/l Date and time:..........................

Post transfusion count:............... x10^9/l Date and time:..........................

**ANY CLINICAL RESPONSE / SYMPTOMS?**

**PLEASE GIVE DETAILS:**

**ADVERSE REACTION TO TRANSFUSION?**  YES/NO

IF YES PLEASE GIVE DETAILS:

**SIGNATURE:.............................................  DATE:........**

---

Who should fill this in?