Providing Rare Blood Products for Complex Immunohematology Cases: A National Perspective

Sandra Nance, MS, MT(ASCP)SBB
Senior Director, IRLs, American Red Cross
Senior Director, American Rare Donor Program
Adjunct Assistant Professor, University of Pennsylvania
Immediate Past Chair, ISBT Working Party on Rare Donors and ISBT Working Party on Immunohematology

The need is constant.
The gratification is instant.
Give blood.™
Providing Rare Blood Products for Complex Immunohematology Cases: A National Perspective

Objectives:

- Enhance decision making for transfusion treatments
- Pro-actively analyze complex antibody cases for blood availability domestically and internationally
Providing Rare Blood Products for Complex Immunohematology Cases: A National Perspective

- Clinical significance of RBC alloantibodies
- Alloimmunization
  - Transfusion
  - Pregnancy
- Pre-transfusion testing and transfusion protocols
- Obtaining blood for complex cases
Providing Rare Blood Products for Complex Immunohematology Cases: A National Perspective

- Clinical significance of RBC alloantibodies
- Alloimmunization
  - Transfusion
  - Pregnancy
- Pre-transfusion testing and transfusion protocols
- Obtaining blood for complex cases
Clinical Significance of RBC Alloantibodies

Pathologic effects of blood group antibodies

- Destruction of:
  - Transfused RBCs - HTR, DHTR, or DSTR
  - Fetal RBCs – HDFN
  - Transplanted tissue – Allograft rejection
  - Autologous RBCs - AIHA

Poole and Daniels, Trans Med Rev 2007;21:58-71

Figure from leavingbio.net
Clinical Significance of RBC alloantibodies

What factors influence clinical significance?

- Temperature of reactivity
  - Reactive at 37°C more likely to be clinically relevant

- Strength (titer)
  - 4+ (vs. 1+) may seem more intimidating, but weakly reactive antibodies have been associated with RBC destruction too

- IgG vs. IgM Antibody
  - 37°C reactivity is what matters, but IgM antibody can be an agglutinin in vivo

- Patient specific factors
  - Inflammation
  - HLA type
  - Number of previous transfusions
  - Previous alloimmunization
Clinical Significance of RBC alloantibodies

How can you tell clinical significance, can we predict?

- Historic information on antibody specificity
  - Literature searches
  - Personal experience - current reports on common antibody significance likely not publishable

- In vivo cell destruction
  - Whole unit transfusion
  - Small aliquot transfusion with or without $^{51}$Cr labeling

- In vitro tests
  - Monocyte Monolayer Assay (MMA)
  - Chemiluminescence
### Poole and Daniels: Scorecard for RBC Alloantibodies

<table>
<thead>
<tr>
<th>ABY</th>
<th>HTR</th>
<th>HDFN</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABO</td>
<td>Yes – severe</td>
<td>Yes – mild</td>
</tr>
<tr>
<td>RH</td>
<td>Yes – severe</td>
<td>Yes – severe</td>
</tr>
<tr>
<td>KEL</td>
<td>Yes – severe</td>
<td>Yes – severe</td>
</tr>
<tr>
<td>FY</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>JK</td>
<td>Yes</td>
<td>Yes – rare</td>
</tr>
<tr>
<td>DI</td>
<td>Yes – Wr&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Yes – severe</td>
</tr>
<tr>
<td>DO</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>
Poole and Daniels: Scorecard for RBC Alloantibodies

<table>
<thead>
<tr>
<th>ABY</th>
<th>HTR</th>
<th>HDFN</th>
</tr>
</thead>
<tbody>
<tr>
<td>MNS</td>
<td>Yes – rare</td>
<td>Yes – rare</td>
</tr>
<tr>
<td>P1</td>
<td>Yes – rare</td>
<td>No</td>
</tr>
<tr>
<td>YT</td>
<td>Yes – rare</td>
<td>No</td>
</tr>
<tr>
<td>LU</td>
<td>Yes - mild</td>
<td>No</td>
</tr>
<tr>
<td>LE</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>SC</td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>
Building the Library on Clinical Significance of Red Cell Antibodies

- [www.notifylibrary.org](http://www.notifylibrary.org) – Collecting publications concerning AHTR and DHTR caused by red cell antibodies
- ISBT Working Party on Rare Donors – Case Reports on Incompatible Transfusion
Goal: Collect data from international sources for outcomes of incompatible transfusion

Use: When there is no antigen negative blood available, clinicians can review reported cases to make more informed decisions about transfusion of Ag+ blood.
<table>
<thead>
<tr>
<th>Anti-</th>
<th>#pos</th>
<th>#neg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Di\textsuperscript{b}</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>GE</td>
<td>15</td>
<td>8</td>
</tr>
<tr>
<td>hr\textsuperscript{B}</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>hr\textsuperscript{S}</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>Hy</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>I</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>Jo\textsuperscript{a}</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td>Kp\textsuperscript{b}</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>Lan</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>LU</td>
<td>19</td>
<td>2</td>
</tr>
<tr>
<td>Lu\textsuperscript{b}</td>
<td>11</td>
<td>1</td>
</tr>
<tr>
<td>U</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Vel</td>
<td>8</td>
<td>2</td>
</tr>
<tr>
<td>Yt\textsuperscript{a}</td>
<td>105</td>
<td>65</td>
</tr>
</tbody>
</table>

Maurer JL, Kavitsky DM, Meny GM, Nance SJ. Monocyte Monolayer Assay (MMA) to Predict Clinical Significance of Alloantibodies: An Update. Transfusion 2011, Supplement
Providing Rare Blood Products for Complex Immunohematology Cases: A National Perspective

- Clinical significance of RBC alloantibodies
- Alloimmunization
  - Transfusion
  - Pregnancy
- Pre-transfusion testing and transfusion protocols
- Obtaining blood for complex cases
Alloimmunization - Transfusion

- Patient risk of Alloimmunization
  - Patient Age
  - Number of Transfusions
  - Phenotype Matched Transfusions
  - Molecular Matched Transfusions
  - Associated with Sickle Cell Disease patient survival?
# Alloimmunization in Transfusion - Thalessemia

## Age range (in years) when RBC antibody first identified

<table>
<thead>
<tr>
<th>ABY</th>
<th>2-5</th>
<th>6-10</th>
<th>11-15</th>
<th>16-20</th>
<th>&gt;20</th>
</tr>
</thead>
<tbody>
<tr>
<td>D C E c C\textsuperscript{w} V</td>
<td>19</td>
<td>18</td>
<td>12</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>K Js\textsuperscript{a} Kp\textsuperscript{a}</td>
<td>11</td>
<td>14</td>
<td>6</td>
<td>5</td>
<td>8</td>
</tr>
<tr>
<td>FY</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>JK</td>
<td>0</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>S</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td><strong>TOTALS</strong></td>
<td><strong>30</strong></td>
<td><strong>36</strong></td>
<td><strong>22</strong></td>
<td><strong>14</strong></td>
<td><strong>16</strong></td>
</tr>
</tbody>
</table>

Ameen et al. Transfusion 2003;43:1604-1610 (Kuwait)
Alloimmunization in Transfusion – Nonhematologic Cohort – The Netherlands

Kaplan-Meier estimate of the rate of additional antibody formation after transfusion in alloimmunized patients

- 80/140 patients (57%) formed additional antibodies after 1 more txn of a median of 2 RBCs (range 1-10 units)
- 31 patients (22%) after 2 additionaltxn episodes of a median of 5 units (range 3-14 units)
- 17 patients (12%) after 3 episodes of a median of 8 units (range 6-18 units)
- 12 patients (9%) after 4-11 transfusion episodes of a median of 19 units (range 7-41 units)

Schonewille H et al. Transfusion 2006;46:630-635
Alloimmunization and Decreased Survival in Sickle Cell Disease (SCD)

Background

- 2006 – Inpatient Sample Data from USA
  - 25% of 100,000 admissions for SCD involved transfusion
  - 27% of patients admitted for vasoocclusive crisis were transfused
  - 37.6% of patients treated for acute chest syndrome were transfused

Telen et al. Transfusion 2015; 55:1378–1387
## Alloimmunization and Decreased Survival

<table>
<thead>
<tr>
<th>ENDPOINT</th>
<th>SUB-ENDPOINT</th>
<th>#</th>
<th>% ALLOIMMUNIZED</th>
<th>% NOT ALLOIMMUNIZED</th>
</tr>
</thead>
<tbody>
<tr>
<td>CNS</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Stroke</td>
<td>289</td>
<td>20%</td>
<td>13%</td>
</tr>
<tr>
<td></td>
<td>Other CV event</td>
<td>286</td>
<td>32%</td>
<td>25%</td>
</tr>
<tr>
<td>PULMONARY</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Acute Chest</td>
<td>298</td>
<td>83%</td>
<td>76%</td>
</tr>
<tr>
<td></td>
<td>Tricuspid regurgitation jet velocity &gt;2.5 m/sec</td>
<td>187</td>
<td>40%</td>
<td>35%</td>
</tr>
<tr>
<td></td>
<td>O₂ Saturation &lt; 92%</td>
<td>272</td>
<td>9%</td>
<td>5%</td>
</tr>
<tr>
<td>OTHER</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Avascular Necrosis H or S</td>
<td>289</td>
<td>48%</td>
<td>33%</td>
</tr>
<tr>
<td></td>
<td>Proteinuria ≥1+</td>
<td>283</td>
<td>23%</td>
<td>25%</td>
</tr>
<tr>
<td></td>
<td>Leg Ulcers</td>
<td>292</td>
<td>26%</td>
<td>23%</td>
</tr>
</tbody>
</table>
Alloimmunization and Decreased Survival

Fig. 4. Survival of alloimmunized and nonalloimmunized patients. Kaplan-Meier estimation of survival in patients with and without alloimmunization showed a median life expectancy of 65 years in nonalloimmunized patients but only 54 years in alloimmunized patients.

Life expectancy 11 years longer in non alloimmunized patients
Providing Rare Blood Products for Complex Immunohematology Cases: A National Perspective

- Clinical significance of RBC alloantibodies
- Alloimmunization
  - Transfusion
  - Pregnancy
- Pre-transfusion testing and transfusion protocols
- Obtaining blood for complex cases
Alloimmunization in Pregnancy

2010 - Italian Society of Immunohematology Survey

- Bennardello F, Curciarello, G. Survey on the prevention and incidence of haemolytic disease of the newborn in Italy. Blood Transfus 2013;11;518-27

1993-2100 Finnish Study

- Dajak S et al. Relationship between previous maternal transfusions and haemolytic disease of the foetus and newborn mediated by non-RhD antibodies. Blood Transfus 2013;11:528-32

The Netherlands Studies

- Schonewille, H et al. High additional maternal red cell alloimmunization after Rhesus and K matched Intrauterine intravascular transfusions for hemolytic disease of the fetus AJOG 2007;196
When to give Antigen Negative Blood

2010 Italian survey by Italian Society of Immunohematology

- 203,384 births
- 13,560 D negative women
  - 245 with anti-D (22 had postnatal RhIg)
  - 111 cases of HDN
    - 40 treated: IUT(8), ExTx(32)
  - 94 cases HDFN due to other alloantibodies
    - 4 IUT, 11 ExTx

Bennardello F, Curciarello, G. Survey on the prevention and incidence of haemolytic disease of the newborn in Italy. Blood Transfus 2013;11;518-27
Bennardello F, Curciarello, G. Survey on the prevention and incidence of haemolytic disease of the newborn in Italy. Blood Transfus 2013;11;518-27
Finnish Study

Study of non-D antibodies and significance of prior transfusion

- 108,000 pregnancies
- 214 clinically significant non-D antibodies
  - Anti-E - 55, anti-K - 54
- 102 prior transfusions (48%)
  - Anti-K 78%, -c 40%, -E 18%
- 44 cases of HDFN, 14 very severe
  - Anti-K 2, -c 7, -E 1, -Rh17 3

Dajak S et al. Relationship between previous maternal transfusions and haemolytic disease of the foetus and newborn mediated by non-RhD antibodies. Blood Transfus 2013;11:528-32
**Finnish Study**

44 cases of HDFN
- 26 no prior transfusion
- 22 anti-c
  - 68% pregnancy immunization
- 14 cases very severe
  - 4 deaths (1 K, 3 Rh17 in D+C-c-E-e-)
  - 8 Ex Tx and transfusion (1K, 6 c, 1E)

Dajak S et al. Relationship between previous maternal transfusions and haemolytic disease of the foetus and newborn Mediated by non-RhD antibodies. Blood Transfus 2013;11:528-32
Finnish Study Summary

- 50% of pregnant women had previous Tx
- Finland women receive K- units for 11 years
- 8/14 very severe were non-transfused, esp K
- Anti-c involved in all cases of severe HDFN with history of Tx

Dajak S et al. Relationship between previous maternal transfusions and haemolytic disease of the foetus and newborn Mediated by non-RhD antibodies. Blood Transfus 2013;11:528-32
The Netherlands Study

- RBC Tx most important risk factor for non-D immunization
- RBC Tx > Parity > Major surgery > Hematologic disease
- Pregnancy related risk and prior male child
- Extending matching antigen will prevent >50% pregnancy immunization
- RhIg did not decrease non-D antibodies which might have been expected if fetal cells were “cleared from circulation” or “receptors blocked”
- History of Tx important risk factor

The Netherlands Study

- 83% of women with anti-c, -K had history of TX
- Of 103 women with anti-K, 9 had K + partner
- Anti-c, RBC Tx and parity important risk factors
- Anti-E, low prevalence partner rate, but authors noted it can be naturally occurring
- Effect of prior male child interesting reading, male fetuses more severely affected, speculated about gender match in transplant
- Recommended extended matching for transfusion for women <45 years old

Fetal Sex and HDFN

86 consecutive pregnancies anti-D titers > 1:16

- Titers did not vary significantly between mothers with male vs. female fetuses,
- Maternal titer at time of IUT were predictive of fetal hematocrits
- 51 fetuses had 1 or more IUT
- Women with male fetuses were twice as likely to have had a previous pregnancy
- Gestational age of male fetuses lower than female at time of first IUT (24.5 vs. 30 weeks)
- Hydrops present in 16 male and 1 female fetuses
- Mortality was 21% in male vs. 7% in female fetuses

Ulm et al NEJM 1998:338:1699-1700
High Additional Maternal RBC ABY after Rh and K matched IUT for HDFN - Netherlands

- Additional antibodies during IUT therapy common
- Not reduced by C c E e K matching
- 17 cases
  - 65% FY JK S and fetus lacked antigen
- Recommended C c E e K Jk\textsuperscript{a} Jk\textsuperscript{b} Fy\textsuperscript{a} Fy\textsuperscript{b} S matching

Schonewille, H et al. High additional maternal red cell alloimmunization after Rhesus and K matched Intrauterine intravascular transfusions for hemolytic disease of the fetus AJOG 2007;196
Antigen Matching Influences Gestational Outcomes

Is there a difference in the incidence of clinically significant hemolytic disease of the newborn (IUT, ExTx) in regions where females of childbearing age are transfused more highly antigen matched red cells compared to regions without such policies?
Red Blood Cell Transfusion Antigen Matching Influence on Gestational Outcomes (AMIGO) Study

- 296 mothers with ≥1 pregnancy or infant that had clinically significant HDFN.
  - 155 (52%) of the mothers were at MATCH centers
  - 141 (48%) of the mothers were at NoMATCH centers.
- Of all 68 anti-K HDFN cases
  - 78% were attributed to paternal antigen
  - 9% to transfusion
  - 13%, it was not possible to identify the origin of the alloimmunization.
- There were 60 transfused mothers
  - 34 at the MATCH centers (cases)
  - 26 at the NoMATCH centers (controls)
  - 13 had HDFN due to anti-K at the MATCH centers
  - 7 at NoMATCH centers

Delaney, et al Transfusion 2015, Supplement
Red Blood Cell Transfusion Antigen Matching Influence on Gestational Outcomes (AMIGO) Study

- 92% of cases at the MATCH centers were known to be paternal antigen positive
- Of those HDFN cases where the corresponding paternal antigen was negative:
  - 1 had anti-K HDFN at a MATCH center
  - 5 at the NoMATCH centers
The etiology of anti-K HDFN is predominantly from paternal inheritance and sensitization during pregnancy. The incidence of anti-K HDFN was not significantly decreased when FCP patients were transfused at MATCH centers, although it suggests a trend for protection. Further, the policy of providing K antigen selected RBC does not seem protective from anti-K HDFN, although small numbers preclude making this determination with adequate power.
Providing Rare Blood Products for Complex Immunohematology Cases: A National Perspective

- Clinical significance of RBC alloantibodies
- Alloimmunization
  - Transfusion
  - Pregnancy
- Pre-transfusion testing and transfusion protocols
- Obtaining blood for complex cases
Pre-Transfusion Testing and Transfusion Protocols

Antibody screening method determines sensitivity level of detection of antibodies

- Manual methods
  - Saline
  - PEG
  - LISS
  - Gel
  - Albumin
  - Enzyme

- Automated
  - Solid Phase
  - Gel
  - Other

Antigen Typing Protocol in Many Centers

- Genotyping
  - Chronic Tx
  - Anti-CD38 therapy
Pre-Transfusion Testing and Transfusion Protocols

Matching protocols

- Testing/matching
  - Phenotype or genotype pretransfusion
  - Matched vs. partially matched units for transfusion

- Patient populations to consider
  - Chronic transfusion patients
  - Pregnant patients
  - Women in childbearing years intending to have children
  - Non-chronic transfusion?
RBC Alloimmunization and the Number of Transfusions

Red-blood-cell alloimmunization incidence:
- in men > 45 years (ABO/D matched)
- In women > 45 years (ABO/D matched)
- women ≤45 years (ABO-/D & K matched) according to number of transfused units.

Zalpuri S. Vox Sang 2012;102:144-148
SCD Patient Antigen Matching Protocol

- Need sufficient supply of antigen negative donor units
  - Chronic transfusion
    - Simple – $21.2 \pm 14.6$ units/3 years
    - Exchange – $61.5 \pm 28.1$ units/3 years
  - Found that 37% of units (607/1637) were D negative, required to meet needs of the patients
    - 69/607 D- unit to pt with anti-D
    - 412/607 D- units to D+ pts who did not form more antibodies
- Early identification of RHD and RHCE variants important

Karafin M et al. Transfusion 2015 early view
Providing Rare Blood Products for Complex Immunohematology Cases: A National Perspective

- Clinical significance of RBC alloantibodies
- Alloimmunization
  - Transfusion
  - Pregnancy
- Pre-transfusion testing and transfusion protocols
- Obtaining blood for complex cases
American Rare Donor Program (ARDP)

- Rare Donor Programs of AABB and ARC started in the 60s by Tibor Greenwalt, MD
- Joint program with AABB Accredited IRLs and Red Cross IRLs, one program for USA, implemented 1998
- Over 900 requests per year
  - For blood with frequency less than 1:1000
  - Antibodies identified
  - No blood found in local centers
American Rare Donor Program (ARDP)

- Rare Categories for ARDP
  - High Prevalence Antigen Negative
    - All ABOs
    - Frequency <1:1000
  - Multiple Antigen Negative
    - Ro, R1, R2, rr AND K- and one of each of the following:
      - Fy(a-) or Fy(b-)
      - Jk(a-) or Jk(b-)
      - S- or s-
      - R1, R2, rr and Fy(a-b-)
  - IgA Deficient
ARDP Member IRLs by State

88 members (2015)

≥ 5 ARDP Members per State
2-4 ARDP Members per State
1 ARDP Member per State

ARDP Member IRLs by State

1 each Brazil, Italy & Kuwait

ARDP Annual Report 2015

Courtesy: Geralyn Meny, MD
Patient Request

Total # of Requests
Total # Filled
Total # Partially Filled
Total # Unfilled

ARDP Annual Report 2015
# Requests and # Unfilled Requests:
Top 20 ARDP Phenotype Requests

January – December, 2014

Total # of Requests

Phenotypes

Top 20 Rare Blood Types
TOTAL UNFILLED

ARDP Annual Report 2015
ISBT Working Party on Rare Donors
Process Flow for Rare Units

Flow Chart to Request Rare Blood from International Rare Donor Panel (IDP)

<table>
<thead>
<tr>
<th>Local Facility</th>
</tr>
</thead>
<tbody>
<tr>
<td>Identify Rare Blood Need</td>
</tr>
<tr>
<td>Available locally? Through facility or siblings? No</td>
</tr>
<tr>
<td>Contact facility managing national requests</td>
</tr>
<tr>
<td>Make blood available to patient</td>
</tr>
<tr>
<td>Inform physician and obtain approval for international search</td>
</tr>
<tr>
<td>Physician approval obtained No</td>
</tr>
<tr>
<td>Manage patient medically</td>
</tr>
<tr>
<td>Yes</td>
</tr>
<tr>
<td>Notify physician</td>
</tr>
<tr>
<td>No units available</td>
</tr>
<tr>
<td>Notify local facility</td>
</tr>
<tr>
<td>Confirm rare blood need</td>
</tr>
<tr>
<td>Yes</td>
</tr>
<tr>
<td>Provide to local facility</td>
</tr>
<tr>
<td>No</td>
</tr>
<tr>
<td>Document Notify local facility</td>
</tr>
<tr>
<td>Contact International Donor Panel or Search International Panel</td>
</tr>
<tr>
<td>Blood donors found and requested No</td>
</tr>
<tr>
<td>Yes</td>
</tr>
<tr>
<td>Notify physician</td>
</tr>
<tr>
<td>Notify local facility</td>
</tr>
<tr>
<td>Notify Local Facility</td>
</tr>
<tr>
<td>Receive Units</td>
</tr>
<tr>
<td>Transfuse Blood</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>National Facility</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rare blood available locally? No</td>
</tr>
<tr>
<td>Notify Local Facility</td>
</tr>
<tr>
<td>Contact country and make shipping arrangements</td>
</tr>
</tbody>
</table>

DOI: 10.1111/vox.12357
<table>
<thead>
<tr>
<th>Country</th>
<th>Definition of Rare Donor</th>
<th>Number of active rare donors</th>
<th>New rare donors 2012 - June 2014</th>
<th>Number of frozen red cell units 2012</th>
<th>Number of rare units shipped 2012 - June 2014</th>
<th>Unfilled requests for rare blood</th>
<th>Cases of incompatible transfusions</th>
<th>Most difficult types to find</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brazil</td>
<td>Not given</td>
<td>892</td>
<td>153</td>
<td>No data</td>
<td>11</td>
<td>4</td>
<td>3</td>
<td>Lan-, K&lt;sub&gt;o&lt;/sub&gt;, U-</td>
</tr>
<tr>
<td>Canada</td>
<td>&lt;1/5000</td>
<td>1,849*</td>
<td>No data</td>
<td>1,250</td>
<td>No data</td>
<td>No data</td>
<td>No data</td>
<td>Di(b-), PP1P&lt;sup&gt;k&lt;/sup&gt;-</td>
</tr>
<tr>
<td>China</td>
<td>1/1000</td>
<td>1,300</td>
<td>230</td>
<td>60</td>
<td>39</td>
<td>3</td>
<td>1</td>
<td>D--, RhD-, Fy(a-)</td>
</tr>
<tr>
<td>Finland</td>
<td>1/500</td>
<td>51</td>
<td>12</td>
<td>171</td>
<td>81</td>
<td>1</td>
<td>1</td>
<td>Vel-, O&lt;sub&gt;n&lt;/sub&gt;, hr&lt;sup&gt;s&lt;/sup&gt;-</td>
</tr>
<tr>
<td>France</td>
<td>1/250</td>
<td>1,600</td>
<td>150</td>
<td>6,315</td>
<td>648</td>
<td>0</td>
<td>7</td>
<td>U-, Vel-, Fy(a-b-), Rh&lt;sub&gt;null&lt;/sub&gt;, Hr-, Hr&lt;sup&gt;B&lt;/sup&gt;-</td>
</tr>
<tr>
<td>Germany</td>
<td>1/1000</td>
<td>500</td>
<td>No data</td>
<td>556</td>
<td>136</td>
<td>0</td>
<td>0</td>
<td>U-, Rh&lt;sub&gt;null&lt;/sub&gt;, D--, K&lt;sub&gt;o&lt;/sub&gt;, Jk(a-b-), Kx-, Ge-, O&lt;sub&gt;n&lt;/sub&gt;, Hy-, Di(b-), PP1P&lt;sup&gt;k&lt;/sup&gt;-</td>
</tr>
<tr>
<td>Iran</td>
<td>1/1000</td>
<td>973</td>
<td>No data</td>
<td>73</td>
<td>93</td>
<td>1</td>
<td>3</td>
<td>RhD-Jk(b-)</td>
</tr>
<tr>
<td>Israel</td>
<td>1/1000</td>
<td>840</td>
<td>264</td>
<td>1,500</td>
<td>301</td>
<td>No data</td>
<td>6</td>
<td>Rh&lt;sub&gt;null&lt;/sub&gt;, Vel-, Jr(a-)</td>
</tr>
<tr>
<td>Italy</td>
<td>&lt;1/1000</td>
<td>10,730</td>
<td>2,492</td>
<td>No data</td>
<td>1,135</td>
<td>1</td>
<td>1</td>
<td>SC:-I, K&lt;sub&gt;o&lt;/sub&gt;, P&lt;sup&gt;k&lt;/sup&gt;-, LW(a-b-), Lan-, Jk(a-b-), I-, P-, Jr(a-), U-, S-s-, hr&lt;sup&gt;B&lt;/sup&gt;- , Hy-, Jo(a-), Kp(b-), Js(b-)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Country</th>
<th>Definition of Rare Donor</th>
<th>Number of active rare donors 2012 - June 2014</th>
<th>New rare donors 2012 - June 2014</th>
<th>Number of frozen red cell units 2012</th>
<th>Number of rare units shipped 2012 - June 2014</th>
<th>Unfilled requests for rare blood</th>
<th>Cases of incompatible transfusions</th>
<th>Most difficult types to find</th>
</tr>
</thead>
<tbody>
<tr>
<td>Japan</td>
<td>1/100 - 1/1000</td>
<td>647</td>
<td>63</td>
<td>No data</td>
<td>137</td>
<td>No data</td>
<td>9</td>
<td>No data</td>
</tr>
<tr>
<td>New Zealand</td>
<td>1/1000</td>
<td>46</td>
<td>15</td>
<td>113</td>
<td>17</td>
<td>0</td>
<td>0</td>
<td>K_0</td>
</tr>
<tr>
<td>Singapore</td>
<td>1/1000</td>
<td>94</td>
<td></td>
<td></td>
<td>11</td>
<td>2</td>
<td>0</td>
<td>Di(b-)</td>
</tr>
<tr>
<td>South Africa</td>
<td>&lt;1/100</td>
<td>88</td>
<td>6</td>
<td>313</td>
<td>54</td>
<td>15</td>
<td>2</td>
<td>Ge-, Lan-, Lu:-5, Jk(a-b-), PPI PK-</td>
</tr>
<tr>
<td>Spain</td>
<td>1/1000</td>
<td>916</td>
<td>135</td>
<td>681</td>
<td>76</td>
<td>0</td>
<td>0</td>
<td>Ge-, Lan-, P-, Co(a-b-), Rhnull, U-, At(a-), SC:-1, Ln(b-), Jk(a-b-)</td>
</tr>
<tr>
<td>Sweden</td>
<td>Not given</td>
<td>74</td>
<td>36</td>
<td>No data</td>
<td>11</td>
<td>0</td>
<td>0</td>
<td>No data</td>
</tr>
<tr>
<td>Switzerland</td>
<td>Not given</td>
<td>800</td>
<td>No data</td>
<td>0</td>
<td>19</td>
<td>No data</td>
<td>0</td>
<td>Lan-, U-, Rhnull, O_r, Jr(a-), K_0</td>
</tr>
<tr>
<td>Taiwan</td>
<td>&lt;1/1000</td>
<td>655*</td>
<td>No data</td>
<td>550</td>
<td>No data</td>
<td>No data</td>
<td>No data</td>
<td>Di(b-)</td>
</tr>
<tr>
<td>The Netherlands</td>
<td>&lt;1/1000</td>
<td>890</td>
<td>337</td>
<td>217</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>K_0, Rhnull, Di(b-)</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>Not given</td>
<td>1,947</td>
<td>540</td>
<td>606</td>
<td>216</td>
<td>2</td>
<td>1</td>
<td>No data</td>
</tr>
<tr>
<td>USA</td>
<td>&lt;1/1000</td>
<td>59,182</td>
<td>10,271</td>
<td>No data</td>
<td>4,250</td>
<td>138</td>
<td>1</td>
<td>E- hr^s-, Lan-, SC:-1,-2, Jr(a-), At(a-), PP1P k-, E- hr^b-, I-</td>
</tr>
</tbody>
</table>

Globally: Toughest Donors to Find

- Rhnull
- Ko
- Lan negative
- U-

USA: Toughest Donors to Find

- E– hrS–
- Lan–
- SC:–1,–2
- Jr(a–)
- At(a–)
- PP1P^k–
- E– hr^B–
- I–

AND ABO/Rh type plays a role
Providing Rare Blood Products for Complex Immunohematology Cases: A National Perspective

- Clinical significance of RBC alloantibodies
- Alloimmunization
  - Transfusion
  - Pregnancy
- Pre-transfusion testing and transfusion protocols
- Obtaining blood for complex cases
Sandra.Nance@redcross.org