Age of Molecular Medicine

• Genomics revolution
  – Impacting all areas of laboratory testing
    • Identification of microbes
    • Tumor diagnosis
    • Coagulation Risk and Treatment
      – (Factor V Leiden)

• Transfusion Medicine
  – Genes encoding blood group antigens known
  – “Predict” red cell, platelet, neutrophil antigen expression

• Polymerase Chain Reaction (PCR)
  • Ability to amplify portion of gene of interest
Genetic Approach to Antigen Typing

- Not limited to fresh or intact RBCs – any cellular source
- Do not need a specific and sensitive antibody
- Automated high-throughput typing for minor antigens

Agglutination reactions – difficult to automate
- Molecules carrying antigen part of complex in RBC membrane
- Many RBC antigens need to remain in native conformation
- Epitopes often destroyed on solid surface
PK7300 - Automated Microplate System

“Testing over 90% of the North American blood supply”

- ABO and Rh(D) type, CMV testing, syphilis testing

- Typing for minor antigens - CcEe and K are only antigens licensed
Can do some things serology cannot

• **Type multiply transfused patients**
  – no interference from transfused cells
  – due to assay design

• **Type RBCs coated with immunoglobulin (+DAT)**
  – alternative – chemical treatment
  – labor intensive

• **Type when no commercial reagents**
  – Do(a/b), Hy, Jo(a), Kell system Js(a/b), Co(a), Yt(a), VVS, U, etc.

• **Determine RHD zygosity (one copy or two?)**
  – Test paternal sample when OB patient has anti-D
    • to predict fetal risk for HDN
  – Typing fetus (amniocytes or maternal plasma)
Can do some things serology cannot

- Distinguish weak D from partial D antigen
  - OB patient - determine if candidate for Rh immune globulin
  - Conserved D- blood supply

- RH genotype – patients with sickle cell disease
  - Many have partial D, partial C, or partial e
  - Have complex Rh antibodies
  - Key for antibody identification and selection of donor units

- Determine allo or auto antibody
  - patient RBCs type positive for the antigen
  - has the corresponding antibody in the serum
  - Example: Jk(a)+ with anti-Jka

- Screen for all minor antigens *in a single assay*
  - provide antigen-matched donor units
Samples for molecular testing for DNA extraction

• **Patient sample**
  - Whole blood, buccal swab, urine sediment
  - ~1/2 ml (small quantity WB)
  - EDTA or equivalent (avoid heparin)
  - No sample age requirement
  - Can be post-transfusion

• **Donor sample**
  - Leukoreduced segments do not provide sufficient DNA
  - Need donor testing tube
  - Typing of units cannot be done at the hospital
Laboratory Environment for Testing

- Pre- and Post- PCR areas
  - “Clean” vs “Dirty”

- Power of PCR to amplify contamination from environment
  - Sterile-like techniques
  - Gloves
  - Filter tips for pipets
  - Hood with UV
  - Dedicated equipment and supplies

- 3 separate laboratory areas
  - Sample DNA extraction
  - PCR set-up (“clean”)
  - Post-PCR analysis (“dirty”)
Methods used for molecular testing

**Manual**
- PCR
  - Gel Electrophoresis

**Semi-Automated**
- Real-time PCR
  - automated readout

**Automated**
- DNA probes on colored beads (Luminex)
- DNA probes on miniature beads on silicone chip
- DNA probes on glass slides
- DNA probes in hydrostatic holes
Miniature BeadArray -- DNA on BEADS IN RANDOM ARRAY

8 different samples

20-30 beads each probe

Probe N 128 colors

miniature beads on a silicone chip
AUTOMATED IMAGE ACQUISITION

BARCODE SCANNING
“SNAPSHOT” ACQUISITION
### Human Erythrocyte Antigen (HEA) Phenotyping by DNA Analysis Report

**Steps:**
1. Isolate DNA
2. Multiplex PCR amplification of all targets in one tube
3. Hybridize product to BeadChip – extension reaction
4. Wash/read

#### 35 antigens in single assay
- C/c, E/e, VVS, K/k, J\(s^{a/b}\), K\(p^{a/b}\)
- Jk\(a/b\), Fy\(a/b\), MNSsU, Do\(a/b\), Hy/Jo
- Co\(a/b\), Di\(a/b\), LW\(a/b\), Lu\(a/b\), Sc1/2

*(Not ABO, RhD)*

<table>
<thead>
<tr>
<th>Blood Group</th>
<th>Antigen</th>
<th>Result</th>
<th>Notes</th>
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<tr>
<td>Rh</td>
<td>e</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td></td>
<td>C</td>
<td>+</td>
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<tr>
<td></td>
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<td>+</td>
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<td>k</td>
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<td>Jsb</td>
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<td>Dib</td>
<td>+</td>
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<tr>
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<td>Coa</td>
<td>+</td>
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<td></td>
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<td>+</td>
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<td></td>
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<td>Landsteiner-Wiener</td>
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<td>LW(b)</td>
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<td>Sc(2)</td>
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<td>Hemoglobin S</td>
<td>HbsS</td>
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</table>

**V/VS**
Case 1  Type multiply transfused patients

**HISTORY**: Caucasian female, *myelodysplastic syndrome* receiving multiple transfusions past 9-10 months

**SEROLOGIC WORKUP**: A Pos; previous anti-K
Now: 1+DAT, warm autoantibody, -E or -c?

**ANTIGEN TYPINGS**: on Retic harvest

<table>
<thead>
<tr>
<th>Serologic</th>
<th>Molecular</th>
</tr>
</thead>
<tbody>
<tr>
<td>C</td>
<td>E</td>
</tr>
<tr>
<td>2+/4+ mf</td>
<td>1+ mf</td>
</tr>
<tr>
<td>Pos</td>
<td>Pos</td>
</tr>
</tbody>
</table>

**DNA testing**: C+c+E+e+; DD (R1R2)

Fy (a-b+), Jk (a-b+), Ss

Typing helpful to rule out specificities and determine what pt at risk to make anti-Fya and anti-Jka
Case 2  Type when no commercial reagents

**HISTORY:** 66 yo Female, heart bypass surgery
9/15 – transfused with 6 units ABO & Rh specific; E-
9/28 – suspect DHTR- anemia unresolved (Hgb 6.0)
serum “brown”

**SEROLOGIC WORKUP:** O Positive ; previous **anti-E, new anti-Do**

**PROBLEM:** - Dombock antibodies can cause transfusion reactions
- Screening with patients sera unreliable
- antibodies often weak, present with other specificities
deteriorate on storage, disappear over time

![Gel Electrophoresis](image)

- Do\(^a\) >
- Do\(^b\) >
- Donor units

2/11 units
Do (a-b+)
Confirm pt
Do (a-b+)

Pt.
Case 3  Type when RBCs coated with IgG (+DAT)

**HISTORY:** baby born to RhD-negative woman
   3+ positive DAT due to ABO incompatibility
For RhIG evaluation must do weak D test – invalid when +DAT

**Policy:** Rh immune globulin is given to a mother if the baby’s D type
   is invalid or inconclusive

Complication: mother and baby had been dismissed
   72 hours had passed

**TESTING:** RHD genotyping on baby residual heel stick sample
   To determine maternal risk for sensitization

**RESULTS:** Baby - no RHD gene
   excludes the possibility of maternal sensitization

RHD genotyping used to avoid unnecessary RhIG
RH SYSTEM GENOMICS

EXPANDS DETERMINATION OF Rh ANTIGENS
Rh Antigens - defined by serology

<table>
<thead>
<tr>
<th>Numerical</th>
<th>Symbol</th>
<th>Numerical</th>
<th>Symbol</th>
<th>Numerical</th>
<th>Symbol</th>
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<td>D</td>
<td>Rh20</td>
<td>VS</td>
<td>Rh37</td>
<td>Evans</td>
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<tr>
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<td>C</td>
<td>Rh21</td>
<td>C^G</td>
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<td>c</td>
<td>Rh23</td>
<td>D^w</td>
<td>Rh41</td>
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<td>e</td>
<td>Rh26</td>
<td>c-like</td>
<td>Rh42</td>
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<td>Rh6</td>
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<td>cE</td>
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<td>Rh8</td>
<td>C^w</td>
<td>Rh29</td>
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<td>Riv</td>
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<td>Rh30</td>
<td>Go^a</td>
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<td>Rh34</td>
<td>Hr^B</td>
<td>Rh50</td>
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<td>Rh51</td>
<td>MAR</td>
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<tr>
<td>Rh19</td>
<td>hr^s</td>
<td>Rh36</td>
<td>Be^a</td>
<td>Rh52</td>
<td>BARC</td>
</tr>
</tbody>
</table>

**RH Alleles - defined genetically**

- > 200 different RHD alleles
- > 70 different RHCE alleles

**Challenge:** Reagents detect only 5 principal antigens
others prevalent in ethnic groups with sickle cell disease
"Rh positive"  

**RHD**  
D antigen  

**RHCE**  
Ce, Ce, cE, or CE  

"Rh negative"  

X Deleted X  
Europeans - 15-17%  

RhD  

RhCE  

C/c  
E/e  

32-35 amino acid differences  
Explains why RhD is so immunogenic
**RH LOCUS**

Gene conversion and rearrangement

- hair-pin loop structure
- genetic exchange
  common in duplicated genes/linked

Donor is not changed

New hybrid alleles and proteins
- part of RhD into RhCE
- part of RhCE into RhD
**RHD hybrids encode “Partial D antigen”**

- **RHD exons replaced with RHCE exons**

### RHD

- **DIIIa**: Most common partial D in Blacks
- **DVI type 3**
- **DIIIc**
- **DIVa**
- **DIVb**
- **DIVbIII**
- **DIVbIV**
- **DV**
- **DVI type 1**
- **DVI type 2**
- **DFR1**
- **DFR2**
- **DBT1**
- **DBT2**

### New antigens

- **DAK**
- **BARC**
- **Goα**
- **Evans**
- **Dw**
- **BARC**
- **FPTT**
- **Rh32**
- **Rh32**

### RHCE

- **DIIIa** - Most common partial D in Blacks
- **DVI** - Most common partial D in Caucasians

---

**Serology cannot distinguish these – Type RhD+; Patients make anti-D**

- Females (under age of 50) should receive Rh- blood; are RhIG candidates
Variation in RhD antigen expression

- **Weak D**
  - require antiglobulin phase for detection (or react weaker than conventional)
  - Have single amino acid changes in RhD
    - Majority (>90%) are Type 1 (V270G), Type 2 (G385A), Type 3 (S3C)
    - Most Caucasian
    - NOT at risk for anti-D
    - Rare exceptions (Type 11, 15, 21) have made anti-D
      - NOT associated with hemolytic disease
  
  **NOT CANDIDATES FOR Rh IMMUNE GLOBULIN**

- **Partial D**
  - Many react 3+ : so go undetected by serology
  - AT RISK for anti-D because lack some RhD epitopes
  - Partial DVI – (Caucasians) - fatal hemolytic disease reported
  - Partial DIVa and DIIIa (African American) – 3+ initial spin

**CANDIDATES FOR Rh IMMUNE GLOBIN**
Beth Israel – OB patients RHD genotyping results

- To guide RhIG prophylaxis and selection of blood for transfusion
  - **OB women with D typing discrepancies**
    - positive previously and now negative: or the reverse
    - Rh type from physician office different than hospital
  - **D typing weaker than expected**

<table>
<thead>
<tr>
<th>RHD*</th>
<th>weak D type 1</th>
<th>weak D type 2</th>
<th>weak D type 3</th>
<th>weak D type 4.0</th>
<th>Partial DAR</th>
<th>No RHD</th>
<th>New alleles</th>
<th>Total</th>
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<tbody>
<tr>
<td># OB patients</td>
<td>16</td>
<td>9</td>
<td>2</td>
<td>2</td>
<td>4</td>
<td>1</td>
<td>2</td>
<td>36</td>
</tr>
<tr>
<td>% of total tested</td>
<td>44%</td>
<td>25%</td>
<td>5.5%</td>
<td>5.5%</td>
<td>11%</td>
<td>2.8%</td>
<td>5.5%</td>
<td>100%</td>
</tr>
<tr>
<td>Risk for anti-D</td>
<td>NO</td>
<td>Majority not at risk</td>
<td>YES</td>
<td>YES</td>
<td>UNKNOWN</td>
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<td>Candidate for RhIG</td>
<td>Candidate for RhIG</td>
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</table>

75%  25%

Potential Benefits of *RHD* Genotyping Pregnant Women

Potential Benefit of *RHD* Genotyping Transfusion Recipients

5,000,000 Individuals Transfused Annually in US

730,000 RhD Negative

21,900 Serologic Weak D

17,520 weak D types 1, 2, or 3

Could receive RhD positive RBCs (47,700 units)

*RHD* Genotyping
Case 4

- 20 yo pregnant female with Sickle Cell Disease
- Pain episode
- First pregnancy, gestational age 17 wks
- On chronic exchange transfusion protocol

- ABO/Rh: B negative
- Antibody screen: Positive

<table>
<thead>
<tr>
<th></th>
<th>Galileo</th>
<th>Gel</th>
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<tr>
<td>Sc I</td>
<td>1+</td>
<td>3+</td>
</tr>
<tr>
<td>Sc II</td>
<td>1+</td>
<td>3+</td>
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<tr>
<td>Rh-Hr</td>
<td>Kell</td>
<td>Duffy</td>
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<td>------</td>
<td>-------</td>
</tr>
<tr>
<td>D</td>
<td>C</td>
<td>E</td>
</tr>
<tr>
<td>1 R1R1</td>
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<tr>
<td>Auto</td>
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</table>

Anti-D
Differential for Anti-D in D- pregnant woman

1. **Active anti-D** – possible high risk pregnancy
   - RhD type father (serology)
     if D+: RHD gene zygosity testing
     \[ \text{RHD/RHD} \] – all children D+
     \[ \text{RHD/-} \] – 50% chance D-
   - follow maternal antibody titers
   - type fetus from amniocentesis (or maternal plasma if available)

2. **Passive anti-D** – rule out patient received RhIG
   - anti-D not usually seen in first pregnancy
   - titer of passive antibody is less than 1:8
Paternal *RHD* zygosity: one copy or two?

Rh “positive”  

*RHD*  

Rh “negative”  

Two assays for presence of deletion region  
Father D+/D-  
Possibility that baby could be D negative
Case 4: Additional Testing

**D typing** - positive in AHG phase
- not D-
- possible weak D?
- MF = mixed cell population

**MF= mixed cell population**
- fetal D+ bleed?
- transfused D+?

**anti-D titer: 4** probable passive anti-D

- Presented to another Emergency Department 2 weeks ago
- B neg Antibody screen: negative
- Concern for fetal-maternal hemorrhage
- Received RhIG

**Conclusion: passive anti-D**

KB - fetal hgb = negative (D typing not due to fetal cells)
Case 4: additional history

- Historically B+ at home institution where she receives her exchange transfusions
- History of anti-D detected 8/07
- Anti-D has not demonstrated since 12/07
- Since 2007 on D- transfusion protocol
- Last transfusion 2 months ago
- 3 units B- PRBC

**RHD genotype**

```
\[
\text{RHD} \\
\begin{array}{cccccccccc}
1 & 2 & 3 & 4 & 5 & 6 & 7 & 8 & 9 & 10 \\
\end{array}
\]
```

- 201Arg  223Val
- two amino acid changes in RhD

- When first reported did not appear to lack D epitopes (weak D 4.0)
- Number of patients have made anti-D = partial D (weak partial D 4.0)
- Is at risk for anti-D
- Is she a candidate for additional RhIG?
Common RHCE alleles

RHD

Oldest
African

Asia
Europe

North
America

uncommon

RHCE

1  2  3  4  5  6  7  8  9  10

1  2  3  4  5  6  7  8  9  10

c+  e+
c+  e+
c+  e+
c+  E+
c+  E+
C+/c E/e

ce
Ce
CE
CE
RHCE alleles prevalent in African Blacks

**RHCE*ce alleles**

- **encode** altered/partial e antigen
  - patients type as c+ and e+
  - make anti-e (or anti-c or -ce)
  - often identified as “auto-e” or anti-hrS or –hrB
  - frequently inherited with partial RHD

**RHCE alleles prevalent in African Blacks**

- encode altered/partial e antigen
  - patients type as c+ and e+
  - make anti-e (or anti-c or -ce)
  - often identified as “auto-e” or anti-hrS or –hrB
  - frequently inherited with partial RHD
# Patients with Sickle Cell Disease
## Antibody comparison

**A. 20 patients**  
Receiving antigen-matched for C, E, K and Minority donor units

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<thead>
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<th>Rh common antibodies</th>
<th>0</th>
<th>Complex Rh antibodies</th>
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</tr>
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<tbody>
<tr>
<td></td>
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</tbody>
</table>

|                       |   |                       |    |
|                       |   |                       |    |

<table>
<thead>
<tr>
<th>Other antibodies</th>
<th>9</th>
<th>Other antibodies</th>
<th>56</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 – anti-Jk&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
<td>8 - anti-K</td>
<td></td>
</tr>
<tr>
<td>1 – anti-Fy&lt;sup&gt;a&lt;/sup&gt;</td>
<td></td>
<td>6 - anti-S</td>
<td></td>
</tr>
<tr>
<td>4 – anti-M</td>
<td></td>
<td>6 - anti-Fy&lt;sup&gt;a&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>1 – anti-N</td>
<td></td>
<td>4 - anti-Jk&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>1 – anti-Js&lt;sup&gt;a&lt;/sup&gt;</td>
<td></td>
<td>2 - anti-Jk&lt;sup&gt;a&lt;/sup&gt;</td>
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<tr>
<td></td>
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<td>1 - anti-M</td>
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<tr>
<td></td>
<td></td>
<td>1 - anti-Go&lt;sup&gt;a&lt;/sup&gt;</td>
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<table>
<thead>
<tr>
<th>Total number of antibodies</th>
<th>31</th>
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</table>

**B. 26 patients**  
Not prophylactic antigen-matched  
Receiving random donor units

<table>
<thead>
<tr>
<th>Rh common antibodies</th>
<th>22</th>
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<tbody>
<tr>
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<table>
<thead>
<tr>
<th>Complex Rh antibodies</th>
<th>30</th>
</tr>
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<tbody>
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<table>
<thead>
<tr>
<th>Other antibodies</th>
<th>56</th>
</tr>
</thead>
<tbody>
<tr>
<td>18 - anti-E</td>
<td></td>
</tr>
<tr>
<td>4 - anti-C</td>
<td></td>
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</tbody>
</table>

|                       | 4 |
|                       | 6 |
|                       | 20 |

|                       | 11 |
|                       | 8 |
|                       | 3 |

<table>
<thead>
<tr>
<th>Total number of antibodies</th>
<th>108</th>
</tr>
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</table>

**Average #abs/patient:**  
Group A = 1.5  
Group B = 4.2

**Complex Rh /patient:**  
Group A = 1.1  
Group B = 1.1
Case 5

- 21 yo male with Sickle Cell Disease, type SS, on chronic transfusion protocol
- RBC phenotype: D+ C+c+E-e+
- Transfusion protocol: E-, K-
- From African American Donors

- Antibody screen: Positive after 115 exposures
- Antibody panel: Anti-C ????
Case 5: Differential C+ with anti-C

1. **Autoantibody?**
   - DAT: 2+ IgG

2. **Alloantibody?**
   - RH alleles encoding alter Rh proteins have high prevalence in this ethnic group
Case 5: *RH* genotype

### RHLD

- D/Ce/D hybrid
- D- negative
- encodes altered C

### RHCE

- W16C
- L245V
- G336C
- encodes altered e

- ces
- VS+
- hrB-

- Called r'S or (C)ceS haplotype
- Patients at risk for anti-C and anti-e
- Frequency 8-22% of C+ African Americans
- Patients with this allele are better served with C- donor units
Case 6

- 74 yr old Caucasian woman with intermittent pancreatitis
- Surgical resection of pancreas & spleen to evaluate mass
- No prior transfusion history; 2 pregnancies

- ABO/Rh: O positive
- Antibody screen: negative
- Transfused 3 RBC units, 2 FFP

- + DAT 2 weeks post-transfusion
- Anti-C identified in serum and in the eluate

- Pre-transfusion RBCs type C+c+E+e+
Case 6: Differential C+ with anti-C

1. **Autoantibody?**
   DAT+

2. **Alloantibody?**
   Patient has partial or altered C

3. **Passive antibody due to transfusion of plasma?**
   (2FFP)
Case 6: RH genotype

RHD

RHCE*Ce

DCC^xe

R1^x

High prevalence in Finns
1.8%
C^x+ C+

Change encodes C^x antigen
Antibody directed to conventional RhCe protein

Give C- blood
ABO genotyping

- Not associated with a single polymorphism (SNP)
- Many regions of gene must be sampled

Group O - mutation in A or B transferase that results in non-functional
O - 61 different alleles
  2 O alleles - common in all populations
  13 O alleles - common in Blacks (greatest number)

Group A and B (numerous subgroups)
  A - 47 A alleles
    A1 or A2 common in all populations but many weaker subgroups
  B - 29 B alleles
  cis AB - 5 alleles
  B(A) - 5 alleles

- Problem - still discovering new alleles
- “Prediction” of ABO not enough
- Discrepancies can be resolved by molecular testing
Number of different *ABO* alleles

- **Group A** = 65
- **Group B** = 47
- **Group O** = 58
- **cis AB or B(A)** = 11

Data from Storry and Olsson, Immunohematology 25:48-59, 2009
Case 7  ABO

- Caucasian female
- Healthy kidney donor (thought to be Group O)
- Group B recipient

<table>
<thead>
<tr>
<th>ANTISERA</th>
<th>INTERPRETATION</th>
<th>CELLS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti-A</td>
<td>Anti-B</td>
<td>Anti-A,B</td>
</tr>
<tr>
<td>0</td>
<td>0</td>
<td>0</td>
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</tbody>
</table>

- Forward type: O               Reverse type: A
- ABO discrepancy
Case 7 ABO

- Commercial ABO genotyping kit #1 = A1 / O1
  \textit{normal Group A}
- Commercial ABO genotyping kit #2 = Ae1 / O08
  A subgroup

Our lab uses gene sequencing
- ABO gene sequencing = O52 / O1
  \textit{Predicted Group O}

O52 = “non-deletion” Group O can have low titer anti-A, significance not yet clear
Hosseini-Maaf \textit{et al.}, Transfusion 45:70; Seltsam \textit{et al.}, Transfusion 45:359
ABO sequencing can resolve:

Kidney Donors
• A2 donors can be transplanted to Group O with comparable survival
• A2 antigen reduced in tissues compared to RBC expression levels
• Problem: Group A kidney donors who have been transfused cannot be accurately typed for A1 vs. A2 status

Organ Recipients
• Put on waiting list according to ABO
• Wrong ABO = wrong list; potentially serious complication
• Two types required
• Problem: Discrepancies between serum and cell typing
Case 8: Neonatal Alloimmune Thrombocytopenia

- 38 year old Caucasian female
- Gave birth in 2008 – child with severe thrombocytopenia
- Maternal antibody screen - anti-HPA1a
- Baby required HPA1a- platelet transfusion

What is risk for subsequent pregnancies?

Maternal & Paternal HPA-1 genotyping
- Maternal Genotype: \textit{HPA-1b/1b}
  Phenotype: HPA-1a negative
- Paternal Genotype: \textit{HPA-1a/1a}
  Phenotype: HPA-1a positive (homozygous)

All children of this father are predicted to be HPA-1a positive
Advancing the practice of Transfusion Medicine

Donors

- Expand number of rare units [Hy-, U-, Co(a-), Lu(b-)]
- Screen for multiple antigen-negative unit
- Enable increased provision of antigen-matched products for recipients

Patients

- Complete antigen profile
  - One time testing
  - Begin to address prevention of alloimmunization
Reduce or prevent alloimmunization

- Possibility of extended antigen-matching for patients
  
  - Historically effects ~2-3% of patients
    - Higher in chronic transfused (32%)
    - Higher in minorities undergoing chronic transfusion (35-60%)
  
  - Accepted risk of alloimmunization – delay in transfusion
  
  - Additional Risks
    - Warm autoantibody production
    - Chronic positive DAT
    - Delayed hemolytic or serologic transfusion reaction
Which Patients?

To reduce or prevent alloimmunization

- **Patients with sickle cell disease**
  - C, E, K negative
  - RH genotype for improved Rh matching (D, C)

- **Patients with warm autoantibodies**
  - Decrease number of complex allo and auto adsorptions
  - Eliminate “least incompatible” terminology

- **Patients who have made one alloantibody**
  - 20X increase risk for additional antibodies

- **Females of child-bearing age**
  - Avoid anti-K and anti-c (done in Europe)
    - **Kell** – 10% potentially exposed
      - Anti-Kell - 1/100 pregnancies; 40% K+ babies have anemia
    - **c** – 18% potentially exposed
      - Anti-c associated with 32 fetal deaths in England and Wales (1977-1990)
Frequently Asked Questions

• **CONSENT:** not “genetic” testing
  – Determination of blood group antigens by different method
  – Local regulations apply
  – Prediction of antigen type
    • report as “predicted phenotype”

• **REIMBURSEMENT:** CPT codes for molecular testing apply

• **STANDARDS:**
  – AABB
DNA array technology applied to blood groups

First new technology since monoclonal antibodies

Technology undergoing rapid development

Focus on Personalized Medicine
- treatment based on genetics
- search for gene variations relevant for therapy

Transfusion Medicine will benefit from development of DNA-based testing platforms applied to blood group markers.
Typing for Blood Group Antigens

Agglutination

*phenotype*
Reported as antigen type

DNA

*genotype*
Reported as predicted antigen type