Understanding the Complexities of Rh

South Central Association of Blood Banks
Pre-Meeting Symposium
June 6, 2012
Susan T. Johnson, MSTM, MT(ASCP)SBB
Director, Clinical Education
BloodCenter of Wisconsin

Objectives
• Discuss the biochemical characteristics of RhD and RhCE proteins and RHAG glycoprotein.
• Describe the molecular characteristics of the RHD, RHCE & RHAG genes
• List the reasons for Rh typing discrepancies
• Understand the differences among partial, weak, D_e variants and D epitopes on RhCe protein

IMMUNOGENICITY OF D
• D is second most important antigen
• Immunogenicity - D- people given ≥1 unit of D+ blood make anti-D
  • Volunteers
    • 50-80%
  • Patients
    • 21-22%
• Antibodies cause HDFN and HTR
IMMUNOGENECITY OF “OTHER” COMMON Rh ANTIGENS

<table>
<thead>
<tr>
<th>ANTIGEN</th>
<th>FREQUENCY (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>C</td>
<td>70%</td>
</tr>
<tr>
<td>E</td>
<td>30%</td>
</tr>
<tr>
<td>c</td>
<td>80%</td>
</tr>
<tr>
<td>e</td>
<td>98%</td>
</tr>
</tbody>
</table>

- Incidence of antibody formation to C, E, c, e < 1%

Weiner Haplotype Terminology

<table>
<thead>
<tr>
<th>Symbol</th>
<th>D</th>
<th>C</th>
<th>E</th>
<th>c</th>
<th>e</th>
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<td>+</td>
<td>R₁</td>
</tr>
<tr>
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<td>0</td>
<td>+</td>
<td>0</td>
<td>0</td>
<td>+</td>
<td>r'</td>
</tr>
<tr>
<td>R₂</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>+</td>
<td>0</td>
<td>R₂</td>
</tr>
<tr>
<td>r''</td>
<td>0</td>
<td>0</td>
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<td>+</td>
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<td>r''</td>
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<tr>
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<tr>
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<td>0</td>
<td>0</td>
<td>+</td>
<td>+</td>
<td>R₂₂</td>
</tr>
</tbody>
</table>

RH GENES

<table>
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<tr>
<th>GENE</th>
<th>CHROMOSOME</th>
<th>Status</th>
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<tbody>
<tr>
<td>RHD</td>
<td>1</td>
<td>Polymorphic</td>
</tr>
<tr>
<td>RHCE</td>
<td>1</td>
<td>Polymorphic</td>
</tr>
<tr>
<td>RHAG</td>
<td>6</td>
<td>Monomorphic</td>
</tr>
</tbody>
</table>

RHAG is ancestral gene
**RH Genes – Rh Positive**

Chromosome 1

- **Locus 1**
  - **RHD**
  - Exons
  - Locus 1 - presence of RHD codes for the presence of D or no D. Differs from RHCE by 34 to 37 amino acids (C or c)

- **Locus 2**
  - **RHCE**
  - Exons

**RH Genes – Rh Positive**

Chromosome 1

- **Locus 1**
  - **RHD**
  - Exons

- **Locus 2**
  - **RHCE**
  - Exons

**Rh Protein**

Multi-pass membrane protein

- Crosses RBC membrane 12 times
- No sugars attached

http://www.jic.ac.uk/corporate/about/publications/advances/images_10/protein.jpg
Rh DESIGNATION

Rh Positive 85%
Rh Negative 15%

RhD Negative
- Deletion of RHD – in European ancestry
- Inactivating mutations of RHD
  - RHD\(\psi\) in African Americans
- Hybrid RHD-CE-D in African backgrounds

RH Genes in Rh Negative Caucasians
Chromosome 1

Locus 1 deletion of RHD therefore, no D antigen.
RhD Negative – African Background

19%  \( RHD \) deletion
66%  \( RHD\psi \)
19%  Hybrid \( RHD-CE-D \)

Rh Genes in Rh Negative - African Background

*Chromosome 1*

- **Locus 1**: \( RHD\psi \) (No D antigen, several mutations in RHCE results in no product)
- **Locus 2**: RHCE (C/c and E/e antigens)

66% of AAs have \( RHD\psi \)

Rh (D) Negative – African Background

*Chromosome 1*

- **Locus 1**: \( RHCE \) inserted in \( RHD \) results in no D antigen and weak C.
- **Locus 2**: RHCE (C/c and E/e antigens)

15% of AAs have hybrid \( RHD-CE-D \)
### RH Genes – RhCE

Chromosome 1

**RH Genes**

- **RHD**
- **RHCE**

**Locus 1**

- 1
- 2
- 3
- 4
- 5
- 6
- 7
- 8
- 9
- 10

**Locus 2**

- 1
- 2
- 3
- 4
- 5
- 6
- 7
- 8
- 9
- 10

### ALLELES OF RHCE

<table>
<thead>
<tr>
<th>GENE</th>
<th>PROTEIN</th>
<th>PHENOTYPE</th>
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<tbody>
<tr>
<td>RHce</td>
<td>Rhce</td>
<td>c+e+</td>
</tr>
<tr>
<td>RHCe</td>
<td>RhCe</td>
<td>C+e+</td>
</tr>
<tr>
<td>RHcE</td>
<td>RhcE</td>
<td>c+E+</td>
</tr>
<tr>
<td>RHCE</td>
<td>RhCE</td>
<td>C+E+</td>
</tr>
</tbody>
</table>
Rh GLYCOPROTEIN (RhAG)

- Chromosome 6 - RhAG gene
- 409 a.a.
- Crossed RBC membrane 12 times
- Recognized blood group system – RHAG
  - Carries blood group antigens
- Absent on Rhnull, U- red cells

Tilley et. al, Vox Sanguinis (2010) 98, 151–159

RhAG

Rh Complex

The gene product of RHAG is required for the expression of the Rh proteins
Rh Typing Discrepancies

- Rh antigen expression
- \textit{RHD} & \textit{RHCE} gene mutations
- Reagent differences
  - Monoclonal vs. Polyclonal
  - Method variability – Anti-D

Polyclonal vs. Monoclonal Antibody
What’s the Difference?

- \textbf{Polyclonal Antibody}
  - Consists of Ig molecules from many different clones of B lymphocytes
  - A “cocktail” of antibodies which may be aimed at different epitopes on the same antigen
Polyclonal Antibodies

Normal immune response stimulates the production of many different immunoglobulins recognizing different epitopes on antigen

\[ \gamma = \text{immunoglobulin} \]

Monoclonal Antibody

Monoclonal antibody is specific for 1 epitope

\[ \gamma = \text{immunoglobulin} \]

Monoclonal versus Polyclonal

- Expansion
- Antigen
- B cells
- Antibodies

Monoclonal

Polyclonal
Monoclonal Reagent Types

- Blend of monoclonal & polyclonal antibodies
- Blend of two or more monoclonal antibodies, each secreted by a different cell line
- IgG or IgM, or combination of IgG + IgM
- Why?
  - D antigen has >30 different epitopes
  - Variant D antigens

Variables Impacting RhD Typing

<table>
<thead>
<tr>
<th>CONTRIBUTORS OF VARIABILITY</th>
<th>VARIABLES</th>
</tr>
</thead>
<tbody>
<tr>
<td>RhD Gene</td>
<td>Week D</td>
</tr>
<tr>
<td></td>
<td>2-4 microtransfused RhD</td>
</tr>
<tr>
<td></td>
<td>Partial D</td>
</tr>
<tr>
<td></td>
<td>Dp</td>
</tr>
<tr>
<td></td>
<td>Dp or ABO</td>
</tr>
<tr>
<td></td>
<td>RhCE Protein</td>
</tr>
<tr>
<td></td>
<td>Polyspecific</td>
</tr>
<tr>
<td></td>
<td>Monoclonal IgG</td>
</tr>
<tr>
<td></td>
<td>Monoclonal IgM</td>
</tr>
<tr>
<td></td>
<td>Monoclonal Human IgG</td>
</tr>
<tr>
<td></td>
<td>Monoclonal Blends</td>
</tr>
<tr>
<td>Anti-D Reagents</td>
<td>RhCE Protein</td>
</tr>
<tr>
<td></td>
<td>Polyspecific</td>
</tr>
<tr>
<td></td>
<td>Monoclonal IgG</td>
</tr>
<tr>
<td></td>
<td>Monoclonal IgM</td>
</tr>
<tr>
<td></td>
<td>Monoclonal Human IgG</td>
</tr>
<tr>
<td></td>
<td>Monoclonal Blends</td>
</tr>
<tr>
<td>Testing Platform</td>
<td>RhCE Protein</td>
</tr>
<tr>
<td></td>
<td>Polyspecific</td>
</tr>
<tr>
<td></td>
<td>Monoclonal IgG</td>
</tr>
<tr>
<td></td>
<td>Monoclonal IgM</td>
</tr>
<tr>
<td></td>
<td>Monoclonal Human IgG</td>
</tr>
<tr>
<td></td>
<td>Monoclonal Blends</td>
</tr>
<tr>
<td>Individual being Rh Typed</td>
<td>RhCE Protein</td>
</tr>
<tr>
<td></td>
<td>Polyspecific</td>
</tr>
<tr>
<td></td>
<td>Monoclonal IgG</td>
</tr>
<tr>
<td></td>
<td>Monoclonal IgM</td>
</tr>
<tr>
<td></td>
<td>Monoclonal Human IgG</td>
</tr>
<tr>
<td></td>
<td>Monoclonal Blends</td>
</tr>
</tbody>
</table>
| Why is Detecting RhD so challenging?
WEAK EXPRESSION OF RhD

HISTORY

• D\text{\textsuperscript{u}}
• D mosaics
• Weak D – general term used
• Partial D
• Weak D
  • Specific group of RhD variants
  • D-elution alleles

WEAK D

HISTORY

• Described by Stratton (1946)
• D antigen not detected by all anti-D
• Mistakenly called the D\text{\textsuperscript{u}} antigen
• D\text{\textsuperscript{u}+} blood to a D- person causes production of \textit{anti-D not anti-D\text{\textsuperscript{u}}}

WEAK D

Reactivity with Anti-D

• Agglutinated with some anti-D on direct agglutination (IS)
• Negative on direct agglutination (IS)
• D antigen detected by IAT only
Frequency of Weak Expression

<table>
<thead>
<tr>
<th>Location</th>
<th>Year</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hopkins Scotland</td>
<td>1967</td>
<td>0.56%</td>
</tr>
<tr>
<td>Garretta France</td>
<td>1974</td>
<td>0.66%</td>
</tr>
<tr>
<td>Beck USA</td>
<td>1990</td>
<td>0.2%</td>
</tr>
<tr>
<td>Jenkins USA</td>
<td>2004</td>
<td>0.4%</td>
</tr>
<tr>
<td>Flegel Germany</td>
<td>2006</td>
<td>0.4%</td>
</tr>
</tbody>
</table>

WEAK D
Variation in RhD Expression

- Do not make anti-D
- Able to make anti-D

Weak Expression of D
*Do Not Make Anti-D*

- C in *trans* with *RHD* (Ceppellini effect)
  - r' haplotype
- Weak D “Types”: single amino acid changes
Ceppelini Effect

- D\textsuperscript{+} Ce\textsuperscript{+} Ce/ce
- Ce/ce Ce/ce D\textsuperscript{+} Ce/ce
- Ce/ce ce/ce Ce/ce D\textsuperscript{+} Ce/ce

**Weak D Types**

*Most Do Not Make Anti-D*

- Missense mutations in regions of *RHD* encoding transmembrane/cytoplasmic portion of D
- Less protein inserted into RBC membrane
- Can type as Rh-positive or Rh-negative by direct agglutination with monoclonal (IgM) anti-D reagents

<table>
<thead>
<tr>
<th>IS</th>
<th>D IAT</th>
<th>C IAT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti-D</td>
<td>3+</td>
<td>Anti-D</td>
</tr>
</tbody>
</table>

**Some Weak D Types**

- Type 1
- Type 2
- Type 3
- Type 4.0
- Type 4.2
- Type 5
- Type 11
- Type 15
- Type 19
- Type 20

- Account for 90% of Weak D; Do not produce Anti-D
- Known to form Anti-D when exposed to D\textsuperscript{+} RBCs
**Molecular Basis of Weak D**

Types 1 and 2
- Most common weak D types
- Weak D Type 1
  - $R_1r (D+C+E-c+e^+)$
- Weak D Type 2
  - $R_2r (D-C-E+c+e^+)$

**Weak D Types 1 and 2**

<table>
<thead>
<tr>
<th>IS</th>
<th>D IAT</th>
<th>CI IAT</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>3</td>
<td>0</td>
</tr>
</tbody>
</table>
D Antigen Copy Number

Weak Expression of D
Able to Make Anti-D

- Partial Ds: hybrid RHD alleles
  - DVI
  - DIIIa
  - DIVa, DIVb, others
- Weak D Type 4, 2, 5, 11, 15, 19, 20
- Del: detection by adsorption/elution
- D epitopes on RHCE gene

Rhesus Pieces
PARTIAL D

- Partial D
- Lack exofacial epitopes
  - Hybrid proteins
  - Missense mutations affecting exofacial protein

---

PARTIAL D

CM Westhoff

<table>
<thead>
<tr>
<th>IS</th>
<th>D IAT</th>
<th>Cl. IAT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti-D</td>
<td>0</td>
<td>3</td>
</tr>
</tbody>
</table>

or

<table>
<thead>
<tr>
<th>IS</th>
<th>D IAT</th>
<th>Cl. IAT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti-D</td>
<td>3+</td>
<td></td>
</tr>
</tbody>
</table>

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PARTIAL DVI

Normal RHD Normal RHCE

Partial DVI

One example of Partial DVI gene where 3 exons of RHCE gene are inserted into RHD gene.

<table>
<thead>
<tr>
<th>IS</th>
<th>D IAT</th>
<th>Cl. IAT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti-D</td>
<td>0</td>
<td>3</td>
</tr>
</tbody>
</table>
Del

- Type as D-negative (IS & IAT), only adsorb & elute anti-D
- Severely reduced protein
- 2 individuals have made anti-D after receiving D+ blood

Deletion of exon 9 in Asians occurs in 10-30%

D Epitope on RHCE Genes

- Crawford (ceCF) phenotype
- $R_0^{Har}$, also known as $D^{HAR}$

D Epitope on RHce Gene - $D^{CF}$

$D^{CF}$ results from 3 nucleotide changes: 486G>C, 697C>G, 733C>G in RHce gene.
Anti-D Reagents: Reactions with Crawford Phenotype RBCs

<table>
<thead>
<tr>
<th>Reagent</th>
<th>Anti-D</th>
<th>IgM</th>
<th>IgG</th>
<th>Crawford</th>
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<tr>
<td>GammaClone</td>
<td>Pos</td>
<td>F8D8</td>
<td></td>
<td>Pos</td>
</tr>
<tr>
<td>Immucor-4</td>
<td>Pos</td>
<td>MS26</td>
<td></td>
<td>Neg</td>
</tr>
<tr>
<td>Immucor-5</td>
<td>Neg</td>
<td>MS26</td>
<td></td>
<td>Neg</td>
</tr>
<tr>
<td>Ortho Bioclone</td>
<td>Neg</td>
<td>MAD2</td>
<td>Human</td>
<td>Neg</td>
</tr>
<tr>
<td>Ortho (ID-MTS)</td>
<td>Neg</td>
<td>MS201</td>
<td></td>
<td>Neg</td>
</tr>
</tbody>
</table>

Reactive clones in some European reagents: RUM-1, D175-2, F5S, H2D5D2F5, MCAD-6

D Epitope on RHCE Gene - $D^{HAR}$

- $D^{HAR}$ results from one RHD exon inserted into the RHCE gene.

<table>
<thead>
<tr>
<th>Exons</th>
<th>No D antigens or antigens</th>
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<tr>
<td>1</td>
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</tr>
<tr>
<td>2</td>
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<td>3</td>
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<td>4</td>
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<tr>
<td>9</td>
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</tr>
<tr>
<td>10</td>
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</tbody>
</table>

IS

Anti-D

3+

R$_o$ Har Phenotype: Reactivity with Reagent Anti-D

<table>
<thead>
<tr>
<th>Reagent</th>
<th>Anti-D</th>
<th>IgM</th>
<th>IgG</th>
<th>R$_o$ Har</th>
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<tr>
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<td>Pos</td>
<td>F8D8</td>
<td></td>
<td>Pos*</td>
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<tr>
<td>Immucor-4</td>
<td>Pos</td>
<td>MS26</td>
<td></td>
<td>Pos*</td>
</tr>
<tr>
<td>Immucor-5</td>
<td>Pos</td>
<td>MS26</td>
<td></td>
<td>Pos*</td>
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<tr>
<td>Ortho Bioclone</td>
<td>Neg</td>
<td>MAD2</td>
<td>Human</td>
<td>Neg</td>
</tr>
<tr>
<td>Ortho (ID-MTS)</td>
<td>Pos</td>
<td>MS201</td>
<td></td>
<td>Pos</td>
</tr>
<tr>
<td>Biotest (Bio-Rad)</td>
<td>Pos</td>
<td>BS221</td>
<td>H41</td>
<td>Pos</td>
</tr>
<tr>
<td>Quotient - Alpha</td>
<td>Pos</td>
<td>LDM1</td>
<td></td>
<td>Pos</td>
</tr>
<tr>
<td>Quotient - Delta</td>
<td>Pos</td>
<td>LDM1</td>
<td>ESD1M</td>
<td>Pos</td>
</tr>
</tbody>
</table>

*Positive reactions often weaker at IAT
Confusion Over Weak Expression of D

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>Donor</td>
<td>Rh+</td>
</tr>
<tr>
<td>Recipient</td>
<td>Rh-</td>
</tr>
<tr>
<td>Prenatal</td>
<td>RhIG?</td>
</tr>
<tr>
<td>Newborn</td>
<td>Postpartum RhIG?</td>
</tr>
<tr>
<td>Autologous Donor</td>
<td>@#f&amp;~?</td>
</tr>
</tbody>
</table>

Reasons to Resolve Weak Expression

- Conserve Rh-negative blood for D-negative recipients (high risk of making anti-D).
- Avoid giving RhIG to women who do not need it (Rh status is confirmed for historical discrepancies)
- Resolve early in pregnancy to eliminate false-positive rosette tests.

Rh Discrepancies - MSH, Toronto


Discrepancy between two anti-D direct tests
- 33,864 RhD phenotypings performed over an 18 month interval
- 55 of 5672 potential Rh-negative patients were tube test positive for one anti-D (0.98%)
  - 54 were tube test negative using one FDA-approved reagent but positive (2+ or less) using another government approved antisera
### Summary of the Toronto Study


20 functional RHD alleles detected; 1 wildtype (HDN)

- 34 Weak D Types (PCR-RFLP):
  - 16 weak D Type 1
  - 8 weak D Type 2
  - 1 weak D Type 3
  - 6 weak D Type 4
  - 2 weak D Type 42
- 7 DAR (exon mapping plus sequencing)
- 6 D^V^a or D^V^a-like alleles:
  - 3 D^V^a(Kou.)
  - 1 D^V^a(HK(E233K))
  - 1 D^V^a-like
  - 1 DTO (Novel)
- DFR, DAU-4, DAU-5 (Novel), DAU-6 (Novel)
- DAR/DAU-2, DAU-0/Cdes (compound heterozygotes)
- 1 not identified (possible Dilla, Dva, DAR, DOL)

57% were Weak D types 1, 2, 3 and 4

---

### Impact if deemed Rh-negative


Inappropriate use of blood products

<table>
<thead>
<tr>
<th>RHD Allele</th>
<th>OB</th>
<th>TR</th>
<th>NB</th>
<th>Impact</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weak D Types 1-4</td>
<td>12</td>
<td>8</td>
<td>5</td>
<td>12 OB patients received Rhig 4 transfusion recipients received 12 Rh-neg RBCs</td>
</tr>
<tr>
<td>Weak D Type 42</td>
<td>1</td>
<td>1</td>
<td>-</td>
<td>OB patient received Rhig 1 transfusion recipient received 11 Rh-neg RBCs</td>
</tr>
<tr>
<td>DAR</td>
<td>3</td>
<td>1</td>
<td>3</td>
<td>3 OB patients received Rhig Potential transfusion recipient was not transfused</td>
</tr>
<tr>
<td>D^v^ and D^v^like</td>
<td>1</td>
<td>1</td>
<td>5</td>
<td>1 OB patient who delivered an Rh-neg infant Potential transfusion recipient was not transfused</td>
</tr>
<tr>
<td>DAU, DFR, DTO</td>
<td>3</td>
<td>2</td>
<td>2</td>
<td>2 OB patients delivered an Rh-infant Neither potential transfusion recipient transfused</td>
</tr>
<tr>
<td>Total</td>
<td>21</td>
<td>23</td>
<td>7</td>
<td>7 Rhig 0 Rh-negative RBCs</td>
</tr>
</tbody>
</table>

---

### Monoclonal Anti-D Panel

Interpretation: DVI
Investigation strategy for RhD typing discrepancies using a combination of PCR-SSP and serological techniques

- Lay See Er, MSTM, (ASCP)SBB

- [http://www.aabb.org/development/awardsscholarships/scholarships/Pages/pastwinners.aspx](http://www.aabb.org/development/awardsscholarships/scholarships/Pages/pastwinners.aspx)
Bagene Weak D Kit Results

Lane 2: DNA ladder
Start reading from lane 3
Lane 1, 11,12: buffer load (no bands)

Weak D type 1

Bagene Weak D Kit Results

Lane 2: DNA ladder
Start reading from lane 3
Lane 1, 11,12: buffer load (no bands)

Weak D type 2

Guideline for Interpreting Discordant Rh Typing Results

Rh typing results are evaluated at immediate spin (direct agglutination) and Rh typing is repeated with identical results.

<table>
<thead>
<tr>
<th>If individual types...</th>
<th>And individual is a...</th>
<th>And...</th>
<th>Then, consider molecular typing...</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rh-negative</td>
<td>Transfusion recipient</td>
<td>Donor record is Rh-positive</td>
<td>Interpret Rh-negative</td>
</tr>
<tr>
<td>Rh-negative</td>
<td>Obstetrical patient</td>
<td>Donor record is Rh-positive</td>
<td>Interpret Rh-neg or Rh-pos?</td>
</tr>
<tr>
<td>Rh-negative</td>
<td>Post delivery</td>
<td>Donor record is Rh-positive</td>
<td>Perform anti-D IAT*</td>
</tr>
<tr>
<td>Rh-negative</td>
<td>Transfusion recipient</td>
<td>Facility history is Rh-positive</td>
<td>Interpret Rh-negative</td>
</tr>
<tr>
<td>Rh-negative</td>
<td>Obstetrical patient</td>
<td>Facility history is Rh-positive</td>
<td>Interpret Rh-neg or Rh-pos?</td>
</tr>
<tr>
<td>Rh-negative</td>
<td>Post delivery</td>
<td>Facility history is Rh-positive</td>
<td>Perform anti-D IAT*</td>
</tr>
</tbody>
</table>

Modified from Transfusion Technology Report Vol. #013 Immucor, Inc.
**Guideline for Interpreting Discordant Rh Typing Results**

Rh typing results are evaluated at immediate spin (direct agglutination) and Rh typing is repeated with identical results.

<table>
<thead>
<tr>
<th>Rh-positive</th>
<th>And individual is a...</th>
<th>And...</th>
<th>Then, consider molecular typing...</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rh-positive</td>
<td>Transfusion recipient</td>
<td>Rh Negative at another facility</td>
<td>Type with different anti-D reagent</td>
</tr>
<tr>
<td>Rh-positive</td>
<td>Obstetrical patient</td>
<td>Rh Negative at another facility</td>
<td>Type with different anti-D reagent</td>
</tr>
<tr>
<td>Rh-positive</td>
<td>Post delivery</td>
<td>Rh Negative at another facility (regardless of history)</td>
<td>Type with different anti-D reagent</td>
</tr>
</tbody>
</table>

Modified from Transfusion Technology Report Vol. #013 Immucor, Inc.

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**RHCE *ceCF**

Transfusion 2011 Jan;51(1):25-31

- Trp16Cys Gln233Glu
- L245V
- Rh43 (Crawford) positive
- Encodes for partial c, partial e, hR6
- hR6 negative
- Negative for new high prevalence antigen, CELO (Rh58)
- CELO is antithetical to Crawford

---

**RHCE *ceCF**

Transfusion 2011 Jan;51(1):25-31

- 12 anti-c were all positive
- Molecular analysis indicated partial c
Objectives

- Discuss the biochemical characteristics of RhD and RhCE proteins and RHAG glycoprotein.
- Describe the molecular characteristics of the RHD, RHCE & RHAG genes.
- List the reasons for Rh typing discrepancies.
- Understand the differences among partial, weak, D_0 variants and D epitopes on RhCe protein.

References

- Flegel WA. Molecular genetics and clinical applications for RH. Transfusion and Apheresis Science 2011;44:81-91. 2.

Thank You

sue.johnson@bcw.edu