Managing Patients with Antibodies

Melanie Tokessy MLT3
Objectives

• Determine the risks associated with transfusing patients who have developed antibodies
• Assess the complications associated with a patient who has developed antibodies in the chronically transfused patient and consider the best approach to managing
Disclosure

Faculty: Melanie Tokessy, Eastern Ontario Laboratory Association (EORLA)

Relationship with commercial interests: None

Potentials for conflict of interests: None
Risks of Transfusion – Non Infectious

- Minor Allergic: 1 in 100
- TACO: 1 in 100
- Febrile: 1 in 300
- Delayed Hemolytic: 1 in 7,000
- TRALI: 1 in 12,000
- ABO-incompatible: 1 in 40,000
- Serious Allergic: 1 in 40,000
Proper Pretransfusion Testing:

- ABORh
  - ABO most important test
  - Rh second
- Antibody Screen/Identification
  - Incubation time, additives
  - Training/experience/expertise
- Blood selection
- Automation/Barcoding
Patients with Alloantibodies

Varies widely due to:
- Disease of patient
- History of transfusion/pregnancy
- Antigen frequencies of patients vs donors

Estimation:
- 1-2% general population
- 5% multi-transfused
- 20% in transfusion dependent diseases
Patients with Alloantibodies

• Results in delay
  • Antibody workup
  • Finding Ag neg RBC
• HDFNB
  • Anemia
  • Increase bilirubin
• Hemolytic transfusion reactions
  • Decreased cell survival
  • By-products of hemolysis
Patient: DL

- 68y, male
- Liver Failure
- Specimen submitted for 2 PRBC
- History: 2 PRBC transfused 2 weeks ago
  - A positive
  - ABSC: negative
- Hgb today: 80 g/l
Patient: DL

<table>
<thead>
<tr>
<th>Patient</th>
<th>Anti-A</th>
<th>Anti-B</th>
<th>Anti-D</th>
<th>A₁ Cells</th>
<th>B Cells</th>
<th>Inter.</th>
</tr>
</thead>
<tbody>
<tr>
<td>DL</td>
<td>4+</td>
<td>0</td>
<td>4+</td>
<td>0</td>
<td>3+</td>
<td>A pos</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>SI</th>
<th>SII</th>
<th>SIII</th>
<th>Inter.</th>
</tr>
</thead>
<tbody>
<tr>
<td>DL</td>
<td>2+</td>
<td>1+</td>
<td>0</td>
<td>Positive</td>
</tr>
</tbody>
</table>

- Patient booked today in MDU
- Physician is keen to transfuse because the patient has been feeling “sluggish” and tired since last transfusion
Patient: DL

<table>
<thead>
<tr>
<th>Cell</th>
<th>D</th>
<th>C</th>
<th>C</th>
<th>E</th>
<th>e</th>
<th>K</th>
<th>k</th>
<th>Fy&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Fy&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Jk&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Jk&lt;sup&gt;b&lt;/sup&gt;</th>
<th>M</th>
<th>N</th>
<th>S</th>
<th>s</th>
<th>SP</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>+</td>
<td>+</td>
<td>0</td>
<td>0</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>2+</td>
</tr>
<tr>
<td>2</td>
<td>+</td>
<td>+</td>
<td>0</td>
<td>0</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>1+</td>
</tr>
<tr>
<td>3</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>+</td>
<td>0</td>
<td>0</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>0</td>
<td>0</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>2+</td>
</tr>
<tr>
<td>5</td>
<td>0</td>
<td>+</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>0</td>
<td>0</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>0</td>
<td>0</td>
<td>+</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>0</td>
<td>0</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>2+</td>
</tr>
<tr>
<td>9</td>
<td>0</td>
<td>0</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>1+</td>
</tr>
<tr>
<td>10</td>
<td>0</td>
<td>0</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>1+</td>
</tr>
<tr>
<td>11</td>
<td>0</td>
<td>0</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>2+</td>
</tr>
<tr>
<td>12</td>
<td>+</td>
<td>+</td>
<td>0</td>
<td>0</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>AC</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1+</td>
</tr>
<tr>
<td>Cell</td>
<td>D</td>
<td>C</td>
<td>c</td>
<td>E</td>
<td>e</td>
<td>K</td>
<td>k</td>
<td>Fy&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Fy&lt;sup&gt;b&lt;/sup&gt;</td>
<td>Jk&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Jk&lt;sup&gt;b&lt;/sup&gt;</td>
<td>M</td>
<td>N</td>
<td>S</td>
<td>s</td>
<td>SP</td>
</tr>
<tr>
<td>------</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---------</td>
<td>---------</td>
<td>---------</td>
<td>---------</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>----</td>
</tr>
<tr>
<td>1</td>
<td>+</td>
<td>+</td>
<td>0</td>
<td>0</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>0</td>
<td>0</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>2+</td>
</tr>
<tr>
<td>2</td>
<td>+</td>
<td>+</td>
<td>0</td>
<td>0</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>+</td>
<td>1+</td>
</tr>
<tr>
<td>3</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>+</td>
<td>0</td>
<td>0</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>+</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>2+</td>
</tr>
<tr>
<td>5</td>
<td>0</td>
<td>+</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>+</td>
<td>0</td>
<td>0</td>
<td>+</td>
<td>0</td>
</tr>
<tr>
<td>6</td>
<td>0</td>
<td>0</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>7</td>
<td>0</td>
<td>0</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>+</td>
<td>0</td>
<td>0</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>0</td>
</tr>
<tr>
<td>8</td>
<td>0</td>
<td>0</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>+</td>
<td>2+</td>
</tr>
<tr>
<td>9</td>
<td>0</td>
<td>0</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>1+</td>
</tr>
<tr>
<td>10</td>
<td>0</td>
<td>0</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>0</td>
<td>1+</td>
</tr>
<tr>
<td>11</td>
<td>0</td>
<td>0</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>2+</td>
</tr>
<tr>
<td>12</td>
<td>+</td>
<td>+</td>
<td>0</td>
<td>0</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>+</td>
<td>0</td>
</tr>
<tr>
<td>AC</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Next steps to testing:

- Further exclusions
  - selected cells
- Crossmatch Jka- units
  - 23% compatibility
- Full IAT crossmatch
- Direct Antiglobulin Test
- Eluate
# Patient: DL

<table>
<thead>
<tr>
<th>Cell</th>
<th>D</th>
<th>C</th>
<th>c</th>
<th>E</th>
<th>e</th>
<th>K</th>
<th>k</th>
<th>Fy&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Fy&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Jk&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Jk&lt;sup&gt;b&lt;/sup&gt;</th>
<th>M</th>
<th>N</th>
<th>S</th>
<th>s</th>
<th>Peg IAT</th>
</tr>
</thead>
<tbody>
<tr>
<td>2a</td>
<td>+</td>
<td>+</td>
<td>0</td>
<td>0</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>0</td>
<td>0</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>0√</td>
</tr>
<tr>
<td>4a</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>0</td>
<td>0</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>0</td>
<td>0</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>0√</td>
</tr>
<tr>
<td>9a</td>
<td>0</td>
<td>0</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>+</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0√</td>
</tr>
<tr>
<td>10a</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>0</td>
<td>0</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>2+</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Poly</th>
<th>Poly 5’</th>
<th>6% alb</th>
<th>-IgG</th>
<th>-C&lt;sub&gt;3&lt;/sub&gt;</th>
<th>-C&lt;sub&gt;3&lt;/sub&gt; 5’</th>
</tr>
</thead>
<tbody>
<tr>
<td>DL</td>
<td>2+</td>
<td>1+</td>
<td>0</td>
<td>2+</td>
<td>1+</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Cell</th>
<th>D</th>
<th>C</th>
<th>c</th>
<th>E</th>
<th>e</th>
<th>K</th>
<th>k</th>
<th>Fy&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Fy&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Jk&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Jk&lt;sup&gt;b&lt;/sup&gt;</th>
<th>M</th>
<th>N</th>
<th>S</th>
<th>s</th>
<th>Elu</th>
<th>LW</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>+</td>
<td>+</td>
<td>0</td>
<td>0</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>2+</td>
<td>0√</td>
</tr>
<tr>
<td>2</td>
<td>+</td>
<td>+</td>
<td>0</td>
<td>0</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>0</td>
<td>0</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>0√</td>
<td>0√</td>
</tr>
<tr>
<td>3</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>+</td>
<td>0</td>
<td>0</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>+</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0√</td>
<td>0√</td>
</tr>
<tr>
<td>4</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>0</td>
<td>0</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>2+</td>
<td>0√</td>
</tr>
</tbody>
</table>
Patient: DL

- Antigen type pretransfusion specimen
- Repeat pretransfusion antibody screen
- Jka type transfused segments if available
Patient: DL Pretransfusion

<table>
<thead>
<tr>
<th>Cell</th>
<th>Anti-Jk&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Imm25966</th>
</tr>
</thead>
<tbody>
<tr>
<td>DL Pretransfusion</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>C055515485810</td>
<td>3+</td>
<td></td>
</tr>
<tr>
<td>C055515492321</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Jk(a+b+) Positive</td>
<td>3+</td>
<td></td>
</tr>
<tr>
<td>Jk(a-b+) Negative</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>SI</th>
<th>SII</th>
<th>SIII</th>
</tr>
</thead>
<tbody>
<tr>
<td>DL Solid Phase</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>DL PegIAT</td>
<td>0√</td>
<td>0√</td>
<td>0√</td>
</tr>
</tbody>
</table>
Patient: DL

Final Steps

- Keep 2 units on hold when patient in-house
- Antibody card
  - Mailed to patient with letter
- Report TTISS
  - Delayed serological transfusion reaction
Managing Patients with Antibodies

- Most are straightforward and routine
  - But still must be done well and timely
- Sometimes complex and difficult
  - Challenging
  - Rewarding
  - Time consuming: delays
- Know when to refer out: CBS
Chronically Transfusion Patients

- Oncology
- Heme-Onc
  - Leukemia
  - Auto immune
- Thalassemia
- Sickle Cell Anemia
Transfusion Support of Sickle Cell Patients

- Leukoreduced
  - Universal in Canada
- “Fresh” units
  - <10 days old
  - Last longer?
- Sickle trait negative
  - Trait RBCs function normally
  - May cause problems with post measurement of HbS
Transfusion Support of Sickle Cell Patients

- High rate of alloimmunization
  - 19-37% patients
- Racial disparity between donor base and patient population
  - Differences in antigens expressed on RBC
- Higher rate of transfusion
- Most common allo antibodies: Rh (-C, -E) and Kell (-K)
Antigen Matching to Reduce Alloimmunization

• Phenotype all identified sickle cell patients
  • C, c, E, e, K, k, Fya, Fyb, Jka, Jkb, S, s
• Genotype when possible
  • CBS
  • Large centres
• Prophylactically crossmatch to match for Rh and Kell
Antigen Matching to Reduce Alloimmunization

- Full phenotype match for sickle cell patients with one or more allo antibody:
  - Neg for antigen(s) identified
  - C, c, E, e, K, e, Fya, Fyb, Jk, Jkb, S, s
  - Challenging to meet
  - Ok to “drop” some antigens
  - GATA box mutation? Drop Fyb neg requirement
O Negative (mis)Use

- Rh positive sickle cell patients
  - Commonly R_{o}r (ccDee)
  - Crossmatch C-E-
- Rh positive donors
  - 70% C+/30% E+
- Easy to crossmatch Rh neg
  - Most Rh neg C- E-
O Negative Utilization

• High ranking for TOH-General
  • No O negative wastage/discard
• Review of O negative to non-O negative recipients:
  • 2013: 49% O neg to non-O neg
  • Sickle Cell: 44% (444 units)
  • Antibodies: 21% (211 units)
O Negative Utilization

- Stricter O negative crossmatching strategies
- Perform in house phenotyping for common antigen typing
- Discussion with CBS: increase typing of non-O negative donors
- 2014: 24% vs 44%
  - Sickle Cells: 47% (289 units vs 444)
  - Antibodies: 21% (130 units vs 211)
Managing Patient with Special Requirements

- Communication
- Clinical
- CBS
- TM staff
- Assess your patient population
  - Hematological vs trauma
  - Sickle cell
- Don’t always rely on O negative donor units for special typing
Thank you!
My Blood type is

BE NEGATIVE