(9210-TC) Cases of ABO Discrepancy: Typing and Transplantation

October 13, 2013  ♦  10:30 AM - 12:00 PM
## Event Faculty List

**Event Title:** 9210-TC: Cases of ABO Discrepancy: Typing and Transplantation  
**Event Date:** Sunday, October 13, 2013  
**Event Time:** 10:30 AM to 12:00 PM

<table>
<thead>
<tr>
<th>Director/Moderator/Speaker</th>
<th>Speaker</th>
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</thead>
<tbody>
<tr>
<td>Nicole Draper, MD</td>
<td>Samantha Mack, MD</td>
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<tr>
<td>Assistant Medical Director, Transfusion Services UniPath</td>
<td>UniPath</td>
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<tr>
<td>University of Colorado Hospital</td>
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<tr>
<td><a href="mailto:nicole.draper@ucdenver.edu">nicole.draper@ucdenver.edu</a></td>
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<tr>
<td>Disclosures: No</td>
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**Speaker**  
Glenn Ramsey, MD  
Professor of Pathology  
Northwestern University  
g-ramsey@northwestern.edu  
Disclosures: No
Cases of ABO Typing Discrepancies

Nicole Draper, MD, FCAP, FASCP
Assistant Professor, Department of Pathology, University of Colorado
Assistant Medical Director, Transfusion Services, University of Colorado Hospital

- I have no financial disclosures.

<table>
<thead>
<tr>
<th>Case 1</th>
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**Automated Testing**

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<th>Anti-D</th>
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A     O
Case 1

- 72-year-old woman
- Planned elective right total hip arthroplasty
- Autologous and directed donations 1 week prior to surgery
- Historically A,Rh+ with negative ABSC
- Antibody screen: positive with PEG-AHG

Antibody Panel
Question: Which one of the following would you do next?

A. Phenotype the reagent A1 cells for N-antigen
B. Repeat the antibody screen at 37°C
C. Repeat the serum ABO typing at 4°C
D. Report A,Rh+ with anti-A1 and anti-N antibodies

Repeat Antibody Screen

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- Anti-N reactive at body temperature
- Give N-negative RBC's
- Phenotype the directed donation

Case 1

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Repeat serum type with N-negative red cells

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Case 1

- Transfuse?
  - Compatible with A, Rh+
  - N-antigen negative
  - Autologous unit
  - Directed unit N-positive, put into general inventory

Case 2

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Case 2

- History
  - 38-year-old man with shortness of breath and an apical lung mass. Recent respiratory infection
  - Previous ABO type? A, Rh+ 5 days ago
  - Transfusions? A, Rh+ platelets x2 5 days ago with a platelet count of 15,000/ul

- Interfering antibody?
  - Automated antibody screen: negative
  - DAT: negative
  - Autocontrol by tube testing: 1+
  - IVIG x2 for ITP
Haemolysis after treatment with intravenous immunoglobulin due to anti-A

- 34-year-old A (non-A1) D-positive male with aplastic anaemia. Hgb 11.1 to 5.3 g/dL over 3 days.
- 61-year-old A1 D-negative female with myasthenia gravis. Hgb 12.8 to 7.8 g/dL over 6 days.
- 57-year-old AB D-positive female lung transplant recipient with humoral rejection. Hgb 7.8 to 6.0 g/dL over several hours.
- All three patients
  - negative antibody screen
  - positive direct antiglobulin test for IgG only
  - elute containing anti-A1 reactivity
- The patients were transfused with O RBCs with an appropriate rise in hemoglobin.

Case 2

- Interference due to IVIG
- Unlikely patient has anti-A1
- No evidence of significant hemolysis
  - Per Micromedex 2.0: hemolytic anaemia, delayed, may develop due to enhanced RBC sequestration; increased risk with high doses (2 g/kg or greater), non-O blood group, and underlying inflammation
- Transfusion?
  - IS crossmatch compatible

Case 3

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Antibody Screen

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Technician noted: * “unable to read, cells were permanently adhered to tube.”

Antibody Screen

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AC 2+ 2+ 2+

Question: Which one of the following would you do next?

A. Determine the patient’s red cell phenotype
B. Perform a saline replacement
C. Repeat testing using prewarming technique
D. Wash the reagent red cells
Case 3

- 62-year-old man with symptomatic anemia
- Monoclonal gammopathy identified on SPEP
  - IgA: interfering substance (66-436mg/dL)
  - IgG: <1539 (700-1643mg/dL)
  - IgM: <4995 (43-279mg/dL)
- Waldenstrom macroglobulinemia

Case 3

- Very high IgM interfering with antibody testing
- Washing cells multiple times did not remove the interference on antibody ID
- B,Rh+ on cell type and at OSH
- Clearly c,-E,-K,-Fyb-
- RBC units crossmatch incompatible
- Antibody screen negative after sample at 4°C for 2 days
Apparent Gain of Antibody

- ABO subgroups
- Cold reacting antibodies (auto, anti-M, anti-I)
- Anti-reagent antibodies
- Rouleaux or other nonspecific clumping
- IVIG
- Transfusion (plasma, platelets)
- Transplantation
- Chimera

Case 4

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Case 4

- 65-year-old woman with an abdominal mass
- Blood cultures positive for Gram-negative bacilli
- Acquired B
  - Deacetylating enzyme -- Passenger antigen in vitro

\[ \text{Acetyl} \rightarrow \text{N-Acetylgalactosamine} \rightarrow \text{Galactosamine} \]
Case 4

- Retype
  - Different monoclonal anti-B (not ES4)
  - Acidified (pH 6.0) anti-B (human or monoclonal)
  - Inhibit with GalNH₂-HCl
- Transfuse
  - Type-A compatible red cells and plasma

Apparent Gain of Antigen

- Transplantation
- Rouleaux
- Anti-reagent antibody
- Polyaagglutination
- Acquired B
- B(A) or A(B) phenotype
- Transfusion

Case 5

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Case 5

- 74-year-old man with multiple myeloma
- No recent transfusions
- No recent chemotherapy
- Multiple red cell antibodies (c, E, Fy^a, Jk^a)

Which one would you NOT expect to enhance the strength of reactivity of ABO antibodies?
A. Additional drops of patient plasma
B. Incubation at room temperature for 15 min
C. Incubation at 4°C for 15 min
D. Saline replacement

Case 5

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- ABO antibody enhancement
  - Longer incubation time
  - Incubation at 4°C
  - Additional plasma
Case 5

- Why is the serum type weak?
  - Recent treatment with steroids (dexamethasone)
  - IgA: 191 (66-436 mg/dL)
  - IgG: 617 (700-1643 mg/dL)
  - IgM: <25 (43-279 mg/dL)
  - Kappa free: 3.33 (0.69-2.34 mg/dL)
  - Lambda free: 146.00 (0.51-2.75)

Case 6

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Case 6

- 30-year-old woman, G2P1001
- Initial prenatal visit at 8 weeks gestation
- Routine prenatal type and screen
- Past med/surg history

- Cesarean section
- Gallstones
- MRSA
- Asthma
- Varicella as a child
- 0,Rh+ historically

Medications
- Prenatal vitamin
- Reglan

Case 6

Tube Testing Washed Cells

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Add drops IS
RT 15min
4°C 30min

Probably 0,Rh+ with a very weak serum type

Case 6

Tube Testing >10 Years Ago

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Case 6

- Immunoglobulin levels 2 years previous
  - IgA: <6 (66-436mg/dL)
  - IgG: <200 (700-1643mg/dL)
  - IgM: <25 (43-279mg/dL)
- What prompted immunoglobulin testing?
  - Hospitalized one year ago for pneumonia
  - This admission is for pneumonia with sepsis
  - Diagnosis of asthma
  - Immune deficiency: recurrent infections, chronic lung disease, autoimmune disorders, gastrointestinal disease

Case 6

- DISCHARGE DIAGNOSES:
  - Severe sepsis.
  - Community-acquired pneumonia.
  - Acute kidney injury
  - Anemia
  - Asthma
  - Common variable immunodeficiency (impaired B cell differentiation with defective immunoglobulin production), but could be due to systemic illness causing bone marrow suppression

Case 6

- Ask OB to get current immunoglobulin levels—unchanged
  - IgA: <6 (66-436mg/dL)
  - IgG: <200 (700-1643mg/dL)
  - IgM: <25 (43-279mg/dL)
- What does this mean for future transfusions?
  - May not see a serum ABO type—should be clearly noted in her record in the blood bank
  - IgA deficient, may want anti-IgA antibody testing for risk of emergent transfusion and IVIG
Loss of Antibody

- Neonate
- Immunosuppressed
- Immunodeficient
- Leukemia/lymphoma/myeloma
- ABO subgroup
- Transfusion (plasma, platelets)
- Transplantation

Case 7

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Case 7

- A 62-year-old man with metastatic pancreatic cancer and liver failure has abnormal coagulation function testing
- 2 units of plasma are requested for transfusion
- B, Rh- two years ago
What is NOT a likely explanation for this typing discrepancy of apparent loss of B-antigen?

A. Weak B subgroup  
B. Massive transfusion with type O red cells  
C. Excess soluble B-antigen in the plasma  
D. Transfusion with type A platelets

Case 7

- Adenocarcinomas of the pancreas, biliary system, stomach and ovary are known to sometimes produce soluble A and B substance.

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Apparent Loss of Antigen

- Transplantation
- Massive transfusion
- A or B subgroups
- Leukemia/lymphoma
- Red cell aplasia
- Excessive soluble blood group substance
- Chimera

Case 8: Patient

- 61-year-old man
- Nephrectomy for multilocular renal cell carcinoma of the right kidney
- Patient's blood type O, Rh+ with negative antibody screen
- Transfused 2 units (O+, O-) RBC's post-op
- 30 minutes post-transfusion: chills, tachypnea, tachycardia, hemoglobinuria

Case 8: RBC Unit

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<td>4+mf</td>
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B? B

Why was the unit labeled O-?
Case 8: Donor

- 24-year-old man
- Transfusion/Transplantation? No
- Donor has a twin sister

Type O- (95%) and Type B+ (15%)

Mixed Field Agglutination

- Chimera
  - Transplant
  - Transplacental exchange of hematopoietic stem cells
  - Full chimera
Case 8

- Donation?
  - RBC type cannot be type confirmed by another institution → discarded
- Platelets?
- Plasma?
- Transfusion?
  - Has anti-A

Case 9

<table>
<thead>
<tr>
<th>Automated Testing</th>
<th>Anti-A</th>
<th>Anti-B</th>
<th>Anti-D</th>
<th>A₁ Cells</th>
<th>B Cells</th>
</tr>
</thead>
<tbody>
<tr>
<td>3+ mf</td>
<td>0</td>
<td>3+</td>
<td>1+</td>
<td>4+</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Tube Testing</th>
<th>Anti-A</th>
<th>Anti-B</th>
<th>Anti-A₁ Lectin</th>
<th>A₁ Cells</th>
<th>A₂ Cells</th>
<th>B Cells</th>
</tr>
</thead>
<tbody>
<tr>
<td>4+ mf</td>
<td>0</td>
<td>3+ mf</td>
<td>1+</td>
<td>1+</td>
<td>4+</td>
<td></td>
</tr>
</tbody>
</table>

Case 9

- A 32-year-old woman is seen in the emergency room and determined to have symptomatic anemia
- Type and crossmatch of 2 units of RBC's
- She had a hematopoietic stem cell transplant 6 weeks ago at another facility
Case 9

Automated Testing

<table>
<thead>
<tr>
<th>Anti-A</th>
<th>Anti-B</th>
<th>Anti-D</th>
<th>A1 Cells</th>
<th>B Cells</th>
</tr>
</thead>
<tbody>
<tr>
<td>3+ mf</td>
<td>0</td>
<td>3+</td>
<td>1+</td>
<td>4+</td>
</tr>
</tbody>
</table>

Tube Testing

<table>
<thead>
<tr>
<th>Anti-A</th>
<th>Anti-B</th>
<th>Anti-A Lectin</th>
<th>A1 Cells</th>
<th>A2 Cells</th>
<th>B Cells</th>
</tr>
</thead>
<tbody>
<tr>
<td>4+ mf</td>
<td>0</td>
<td>4+ mf</td>
<td>1+</td>
<td>1+</td>
<td>4+</td>
</tr>
</tbody>
</table>

Case 9

- Transfuse?
  - Has anti-A and anti-B
- When can we officially change the patient’s blood type to A?
  - No longer making anti-A on two consecutive ABO typings

Mixed Field

- ABO subgroups
- Fetuses and neonates
- Chimeras
- Transplantation
- Transfusion of red cells
Summary

• ABO antibodies are expected
• The weaker reactions are typically the aberrant reactions
• History is very important in resolving these discrepancies
• Until an ABO discrepancy is resolved O RBC’s and AB plasma should be issued

General References

• AABB Technical Manual, Seventeenth Edition
• Immucor Gamma package inserts: reagent red blood cells, blood grouping reagent, anti-A, lectin
• Issitt. Applied Blood Group Serology, Third Edition
• Judd. Judd’s Methods in Immunohematology, Third Edition
ABO Typing Discrepancies

Samantha E Mack, MD, FCAP
Pediatric and Blood Bank Pathologist
UniPath, Denver Colorado

Overview

- Review basics of ABO
- Go through several cases

Who has ABO?
ABO Blood Group System

- Defined by antigens: A and B
- Four major blood group phenotypes: A, B, AB, and O
- Antigens on glycoproteins and glycolipids in red cell membranes, on most cells and tissues, and secretory fluids of most individuals

![ABO Blood Group System Diagram](http://www.dbriers.com/tutorials/2013/02/blood-types-simplified/)

ABO Blood Group Antigens

- Enzyme adds sugar to the H antigen to create A or B antigen


ABO Blood Group Systems

- Inheritance
  - Mendelian, co-dominant
  - One haplotype from each parent is inherited
  - Chromosome 9q34

ABO Antibodies

- Naturally occurring
- Formed by 4-6 months of age
- Make antibodies to the antigens you lack
- Cause intravascular hemolysis
- IgM type

ABO Antigens & Antibodies

<table>
<thead>
<tr>
<th>RBC Antigens</th>
<th>A (AA, AO)</th>
<th>B (BB, BO)</th>
<th>AB (AB)</th>
<th>None (OO)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plasma Antibodies</td>
<td>Anti-B</td>
<td>Anti-A</td>
<td>None</td>
<td>Anti-A</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Anti-B</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Anti-A,B</td>
</tr>
</tbody>
</table>

ABO Typing

<table>
<thead>
<tr>
<th>Front Type</th>
<th>Back Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reagent</td>
<td>Anti-A</td>
</tr>
<tr>
<td>Results</td>
<td>+</td>
</tr>
<tr>
<td></td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>+</td>
</tr>
<tr>
<td></td>
<td>0</td>
</tr>
</tbody>
</table>
**Plasma Compatibility**

<table>
<thead>
<tr>
<th>Donor</th>
<th>A</th>
<th>B</th>
<th>AB</th>
<th>O</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Y</td>
<td>N</td>
<td>N</td>
<td>Y</td>
</tr>
<tr>
<td>B</td>
<td>N</td>
<td>Y</td>
<td>N</td>
<td>Y</td>
</tr>
<tr>
<td>AB</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>O</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>Y</td>
</tr>
</tbody>
</table>

Type O is the universal plasma recipient
Type AB is the universal plasma donor

---

**RBC Compatibility**

<table>
<thead>
<tr>
<th>Donor</th>
<th>A</th>
<th>B</th>
<th>AB</th>
<th>O</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Y</td>
<td>N</td>
<td>Y</td>
<td>N</td>
</tr>
<tr>
<td>B</td>
<td>N</td>
<td>Y</td>
<td>Y</td>
<td>N</td>
</tr>
<tr>
<td>AB</td>
<td>N</td>
<td>N</td>
<td>Y</td>
<td>N</td>
</tr>
<tr>
<td>O</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
</tr>
</tbody>
</table>

Type O is the universal red cell donor
Type AB is the universal red cell recipient

---

**Case 1**

<table>
<thead>
<tr>
<th>Automated Testing</th>
<th>Anti-A</th>
<th>Anti-B</th>
<th>Anti-D</th>
<th>A₁ Cells</th>
<th>B Cells</th>
</tr>
</thead>
<tbody>
<tr>
<td>3+</td>
<td>0</td>
<td>0</td>
<td>1+</td>
<td>3+</td>
<td></td>
</tr>
</tbody>
</table>
Q1: Which reaction is likely discrepant?

A. Front type
B. Back type
C. Neither, they are concordant

Case 1

**Automated Testing**

<table>
<thead>
<tr>
<th>Anti-A</th>
<th>Anti-B</th>
<th>Anti-D</th>
<th>A₁ Cells</th>
<th>B Cells</th>
</tr>
</thead>
<tbody>
<tr>
<td>3+</td>
<td>0</td>
<td>0</td>
<td>1+</td>
<td>3+</td>
</tr>
</tbody>
</table>

**Tube Testing**

<table>
<thead>
<tr>
<th>Anti-A</th>
<th>Anti-B</th>
<th>Anti-A₁ Lectin</th>
<th>A₁ Cells</th>
<th>A₂ Cells</th>
<th>B Cells</th>
</tr>
</thead>
<tbody>
<tr>
<td>4+</td>
<td>0</td>
<td>0</td>
<td>1+</td>
<td>0</td>
<td>3+</td>
</tr>
</tbody>
</table>

**Automated Testing**

<table>
<thead>
<tr>
<th>Anti-A</th>
<th>Anti-B</th>
<th>Anti-D</th>
<th>A₁ Cells</th>
<th>B Cells</th>
</tr>
</thead>
<tbody>
<tr>
<td>3+</td>
<td>0</td>
<td>0</td>
<td>1+</td>
<td>3+</td>
</tr>
</tbody>
</table>

**Tube Testing**

<table>
<thead>
<tr>
<th>Anti-A</th>
<th>Anti-B</th>
<th>Anti-A₁ Lectin</th>
<th>A₁ Cells</th>
<th>A₂ Cells</th>
<th>B Cells</th>
</tr>
</thead>
<tbody>
<tr>
<td>4+</td>
<td>0</td>
<td>0</td>
<td>1+</td>
<td>0</td>
<td>3+</td>
</tr>
</tbody>
</table>

A Anti-A₁
**Dolichos biflorus**
- Fast growing annual herb sometimes with pea-like yellow flowers and curved seed pods.
- Lectin specific for N-acetylgalactosamine residues.
- Agglutinates only A₁ at proper dilution.

**Case 1**
- 25-year-old woman with prenatal type and screen
- Transfusion 10 years ago following MVA
- 80% A₁ 20% A₂
- The A₂ allele has a substitution at nucleotide 467 (C>T) and a deletion involving nucleotides 1059 to 1061, causing a less effective enzyme (75% less A).

**Precursor Structures**
- Type 1: Galβ3GlcNAcβ - R
- Type 2: Galβ4GlcNAcβ - R
- Type 3: Galβ3GalNAco3 - R
- Type 4: Galβ3GalNAcβ3 - R

[Link: https://gupea.ub.gu.se/bitstream/2077/26276/1/gupea_2077_26276_1.pdf]
Case 1

- Diagnosis
  - Type A₂ with an anti-A₁ antibody
    - Anti-A₁
    - 1-8% of A₂ (our case)
    - 22-35% of A₂B
    - Typically cold reacting

- Transfusion
  - Type A
  - Type O cells if anti-A₁ agglutination at 37°C

Case 2

Automated Testing

<table>
<thead>
<tr>
<th>Anti-A</th>
<th>Anti-B</th>
<th>Anti-D</th>
<th>A₁ Cells</th>
<th>B Cells</th>
</tr>
</thead>
<tbody>
<tr>
<td>3+</td>
<td>4+</td>
<td>3+</td>
<td>1+</td>
<td>0</td>
</tr>
</tbody>
</table>

Tube Testing

<table>
<thead>
<tr>
<th>Anti-A</th>
<th>Anti-B</th>
<th>Anti-A₁ Lectin</th>
<th>A₁ Cells</th>
<th>A₂ Cells</th>
<th>B Cells</th>
</tr>
</thead>
<tbody>
<tr>
<td>4+ mf</td>
<td>4+</td>
<td>0</td>
<td>2+</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>
Case 2

<table>
<thead>
<tr>
<th>Automated Testing</th>
<th>Anti-A</th>
<th>Anti-B</th>
<th>Anti-D</th>
<th>A₁ Cells</th>
<th>B Cells</th>
</tr>
</thead>
<tbody>
<tr>
<td>AB</td>
<td>3+</td>
<td>4+</td>
<td>3+</td>
<td>1+</td>
<td>0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Tube Testing</th>
<th>Anti-A</th>
<th>Anti-B</th>
<th>Anti-A₁ Lectin</th>
<th>A₁ Cells</th>
<th>A₂ Cells</th>
<th>B Cells</th>
</tr>
</thead>
<tbody>
<tr>
<td>4+ mf</td>
<td>4+</td>
<td>0</td>
<td>2+</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

A₂B? Anti-A₁

---

Case 2

- History
  - 35-year-old G1 at 8 weeks gestation with vaginal spotting
  - Transfusion? No
  - Previous ABO type? AB+ 3 weeks previous
- Interfering antibody?
  - Antibody screen negative
- A-subgroup?
  - Most commonly A₂ with anti-A₁

---

A-Subgroups

<table>
<thead>
<tr>
<th></th>
<th>Anti-A</th>
<th>Anti-B</th>
<th>Anti-A₁</th>
<th>Anti-H</th>
<th>A₁ Cells</th>
<th>B Cells</th>
</tr>
</thead>
<tbody>
<tr>
<td>A₁</td>
<td>4+</td>
<td>0</td>
<td>4+</td>
<td>0</td>
<td>0</td>
<td>4+</td>
</tr>
<tr>
<td>A₂</td>
<td>4+</td>
<td>0</td>
<td>4+</td>
<td>2+</td>
<td>0/2+</td>
<td>4+</td>
</tr>
<tr>
<td>A₃</td>
<td>2+ mf</td>
<td>0</td>
<td>2+ mf</td>
<td>3+</td>
<td>0/2+</td>
<td>4+</td>
</tr>
<tr>
<td>A₄</td>
<td>0/+</td>
<td>0</td>
<td>1-2+</td>
<td>4+</td>
<td>0/2+</td>
<td>4+</td>
</tr>
<tr>
<td>A₅</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>4+</td>
<td>0/2+</td>
<td>4+</td>
</tr>
</tbody>
</table>

Case 2

- Diagnosis
  - Type A, B with anti-A₁ antibody
- Transfuse...

Q2: What red cells should be selected for transfusion?

A. AB
B. A
C. O or B

Amount of antigen present

- Ranges due to
  - ABO genotype
  - Non-ABO genetics
  - Environmental factors
ABO Genotype

- Hundreds of different alleles have been described at the ABO locus
- They have varying strengths

Non-ABO genetic mutations

- Mutations in
  - Regulatory genes
  - Promoter sequence
  - Splicing sites
  - Insufficient precursor
- Precursor structure mutations
- Acquired antigens
- Non-ABO glycosyltransferases making ABO antigens
- ABO glycosyltransferases making the wrong ABO antigens

Environmental factors

- Non-ABO antigens reacting with ABO reagents
- Insensitive detection systems
- Chimera/Transfusion/Transplantation
- Infection
- Physiologic – Pregnancy, Age, Cancer
Case 3

Tube Testing

<table>
<thead>
<tr>
<th>Anti-A</th>
<th>Anti-B</th>
<th>Anti-A,B</th>
<th>Anti-D</th>
</tr>
</thead>
<tbody>
<tr>
<td>2+ mf</td>
<td>0</td>
<td>4+</td>
<td>4+</td>
</tr>
</tbody>
</table>

- Looks like the A₂ we just saw in the last case...
- Why isn’t there a back type?

Case 3

- History
  - 26 week gestational age infant
  - Delivered by C-section 5 days ago due to HELLP syndrome
  - Infant has bowel perforation
  - No transfusions
  - Mother is A+

Case 3

- Wharton’s Jelly
  - Coats newborn cord cells
  - Package insert for reagent states “Cord red blood cells contaminated with Wharton’s jelly may give falsely positive reactions”
  - Wash at least 4-5 times

<table>
<thead>
<tr>
<th></th>
<th>Anti-A</th>
<th>Anti-B</th>
<th>Anti-D</th>
</tr>
</thead>
<tbody>
<tr>
<td>15</td>
<td>2+ mf</td>
<td>0</td>
<td>4+</td>
</tr>
<tr>
<td>8 washes</td>
<td>2+ mf</td>
<td>0</td>
<td>4+</td>
</tr>
<tr>
<td>12 washes</td>
<td>2+ mf</td>
<td>0</td>
<td>4+</td>
</tr>
</tbody>
</table>
Case 3

Heel Stick

<table>
<thead>
<tr>
<th></th>
<th>Anti-A</th>
<th>Anti-B</th>
<th>Anti-D</th>
</tr>
</thead>
<tbody>
<tr>
<td>IS</td>
<td>2+ mf</td>
<td>0</td>
<td>4+</td>
</tr>
<tr>
<td>8 washes</td>
<td>2+ mf</td>
<td>0</td>
<td>4+</td>
</tr>
<tr>
<td>12 washes</td>
<td>2+ mf</td>
<td>0</td>
<td>4+</td>
</tr>
</tbody>
</table>

Case 3

Development of ABO antigens

Not fully developed in newborn infants

Number of A and B antigen sites per red cell of adults and newborn infants of different ABO phenotypes

<table>
<thead>
<tr>
<th>Phenotype</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>A1 Adult</td>
<td>810,000 to 1,170,000</td>
</tr>
<tr>
<td>A1 Cord</td>
<td>250,000 to 370,000</td>
</tr>
<tr>
<td>A2 Adult</td>
<td>240,000 to 260,000</td>
</tr>
<tr>
<td>A2 Cord</td>
<td>140,000</td>
</tr>
<tr>
<td>A1B Adult</td>
<td>460,000 to 850,000 A sites</td>
</tr>
<tr>
<td></td>
<td>310,000 to 560,000 B sites</td>
</tr>
<tr>
<td>A1B Cord</td>
<td>220,000 A sites</td>
</tr>
<tr>
<td>A2B Adult</td>
<td>120,000 A sites</td>
</tr>
<tr>
<td>B Adult</td>
<td>610,000 to 830,000</td>
</tr>
</tbody>
</table>


Case 3

Diagnosis

Most likely weak type A

Transfusion

Type O
Case 4

- History:
  - NHL
  - No recent transfusions
  - Previously typed as "O" at an outside hospital

Case 4

Is this an antibody problem (back type problem)?

<table>
<thead>
<tr>
<th></th>
<th>A1 Cell</th>
<th>B Cell</th>
<th>Screening Cells (I, II, and III)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IS</td>
<td>0</td>
<td>1+</td>
<td></td>
</tr>
<tr>
<td>RT (10 min)</td>
<td>0</td>
<td>2+</td>
<td></td>
</tr>
<tr>
<td>RT (30 min)</td>
<td>0</td>
<td>1+</td>
<td>0</td>
</tr>
<tr>
<td>4°C</td>
<td>0</td>
<td>2+</td>
<td>0</td>
</tr>
</tbody>
</table>
Case 4

- Is there a missing antigen (front type problem)?

<table>
<thead>
<tr>
<th>4 drops</th>
<th>Anti-A</th>
<th>Anti-B</th>
<th>Anti-A,B</th>
</tr>
</thead>
<tbody>
<tr>
<td>RT</td>
<td>0</td>
<td>0</td>
<td>3+</td>
</tr>
<tr>
<td>RT 10 min</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>RT 30 min</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>4 C</td>
<td>1+ (then shook off)</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

A-Subgroups

<table>
<thead>
<tr>
<th></th>
<th>Anti-A</th>
<th>Anti-B</th>
<th>Anti-A,B</th>
<th>Anti-H</th>
<th>A_1 Cells</th>
<th>B Cells</th>
</tr>
</thead>
<tbody>
<tr>
<td>A_1</td>
<td>4+</td>
<td>0</td>
<td>4+</td>
<td>0</td>
<td>0</td>
<td>4+</td>
</tr>
<tr>
<td>A_2</td>
<td>4+</td>
<td>0</td>
<td>4+</td>
<td>2+</td>
<td>0/2+</td>
<td>4+</td>
</tr>
<tr>
<td>A_3</td>
<td>2+ mf</td>
<td>0</td>
<td>2+ mf</td>
<td>3+</td>
<td>0/2+</td>
<td>4+</td>
</tr>
<tr>
<td>A_x</td>
<td>0/+</td>
<td>0</td>
<td>1-2+</td>
<td>4+</td>
<td>0/2+</td>
<td>4+</td>
</tr>
<tr>
<td>A_1l</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>4+</td>
<td>0/2+</td>
<td>4+</td>
</tr>
</tbody>
</table>

AABB Technical Manual, Seventeenth Edition

Case 4: Adsorption Elution

Verification of A cells on A1 cells - testing with A1 reagents:

<table>
<thead>
<tr>
<th>Specimen</th>
<th>O cells</th>
<th>A cells</th>
<th>A_1 Cells</th>
<th>A_2 Cells</th>
<th>A_3 Cells</th>
<th>A_x Cells</th>
<th>A_1l Cells</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group A, B</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>5% RBC</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Anti-A</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Anti-B</td>
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<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Anti-A,B</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Anti-H</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
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<td>0</td>
</tr>
</tbody>
</table>

Verification of A cells on A1 cells - testing with A1 reagents:

<table>
<thead>
<tr>
<th>Specimen</th>
<th>O cells</th>
<th>A cells</th>
<th>A_1 Cells</th>
<th>A_2 Cells</th>
<th>A_3 Cells</th>
<th>A_x Cells</th>
<th>A_1l Cells</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group A, B</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>5% RBC</td>
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<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Anti-A</td>
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<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Anti-B</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Anti-A,B</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Anti-H</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>
Case 4: Diagnosis

- Diagnosis
  - Type A variant, likely A_{x}
- Transfuse
  - Type A

Summary

Importance of discussing ABO discrepancies
- Interpretation in a timely manner
- ABO type resulting is delayed
- Possibility of using up stock

Questions?
References

- Immucor Gamma package insert for Anti-A, Anti-B, and Anti-A,B blood grouping reagents.

Contributors: Nicole Dirner, MD & Micah Will, MD
ABO Typing and Transfusions in Allogeneic Stem Cell Transplants

Glenn Ramsey, MD
Northwestern Memorial Hospital
Feinberg School of Medicine
Northwestern University
Chicago, Illinois

Introductory Overview

Rocky Mountain National Park
Near Alpine Visitor Center, altitude 11,796'

Outline

ABO Factors in Stem Cell Transplants
Timing of Blood Group Conversion
Transfusion Protocols and Practices
Cases with Conundrums
### ABO and Allogeneic Stem Cell Transplants (SCT)

- Donor selection: first priority—HLA match
- A, B antigens not on earliest hematopoietic progenitor cells
- Engraftment often not affected by ABO mismatch
  - To be discussed further
- Minor and major ABO mismatches are common
- Transfusion services have policies and procedures for selecting ABO type of blood components
  - Depending on phase of ABO conversion

### How do you perform routine crossmatches (no alloantibodies) in patients switching blood types after an allogeneic stem cell transplant?

1. Give group O RBCs, no crossmatch needed
2. Electronic crossmatch
3. Immediate-spin crossmatch
4. Antiglobulin crossmatch

### Computer Crossmatch

FDA Guidance, April 2011

- “If ABO typing discrepancies exist, you should not rely on a computer crossmatch. This is particularly important if there is mixed field red cell reactivity, missing serum reactivity, or apparent change in blood type following hematopoietic stem cell transplantation. Under those circumstances, your procedures should provide for compatibility testing using serologic crossmatch techniques.”
ABO Blood Group Physiology

- ABO antigens on
  - RBCs
  - Platelets and WBCs
    - [Group A, platelets have ~no group A]
  - Endothelial cells—all organs
  - Plasma glycosphingolipids, secretion glycolipids
- Allogeneic SCT
  - Changes hematopoietic cell ABO type
  - But endothelial cells and secretions retain recipient type

Allogeneic SCT Variables

- Immunosuppression
  - Myeloablative—old marrow stops production
  - Non-myeloablative—older or co-morbidity patients
    - More chance for native marrow persistence
- Progenitor cells
  - Bone marrow
  - Peripheral stem cells
  - Umbilical cord cells
    - Double-donor transplants in adults

Two Cords, One Winner

- WBC chimerism:
  - Within 21 days, one cord usually predominates
- Winning factors:
  - CD3+ cell dose
  - HLA match (in non-myeloablative cases)
- Ramirez P: Bone Marrow Transplant 47:799, 2012
Patient-Donor Chimerism Testing

- Marrow or peripheral blood
- WBC DNA
  - Not RBCs
- Methods
  - XX or XY in SCTs from different gender
  - Short tandem repeats
After a group A1 patient receives a group O SCT, what most often happens with anti-A production?

1. Anti-A appears as expected when donor O RBCs emerge
2. Anti-A is weak or not detected
3. Anti-A rapidly appears before donor O RBCs
4. Anti-A2 appears
Variations from the Expected

- Major-incompatible (e.g., A graft to O recipient)
  - Delayed RBC engraftment, pure red cell aplasia
  - Incidence 3-29%
  - ↑ odds: nonmyeloablative SCT; no anti-B-cell therapy

- Minor-incompatible (e.g., O graft to non-O recipient)
  - Passenger-lymphocyte antibody, hemolysis
  - Cited incidence 10-15%; ↑ odds: related donor
  - nonmyeloablative SCT; no anti-B-cell therapy
  - Less likely: umbilical cord grafts
  - Snell M, Bone Marrow Transplant 38:135,2006

Minimum Requirements During ABO Blood Group Switch

Desired Compatibility: Green Arrows

Recipient Transfusions Donor

- Plasma
  - Anti-A, -B
  - A, B, AB, O
  - Anti-A, -B
  - A, B, AB, O

- RBCs
  - Anti-A, -B
  - A, B, O
  - Anti-A, -B
  - A, B, O
The Platelet ABO Dilemma

- ABO antigens on platelets
  - Major-incompatible plt's average 2/3 of normal response
  - A few persons are refractory to major-incompatible plt's

- Anti-A, -B in plasma of platelets
  - Minor-incompatible platelets give reduced responses
    - Immune complexes from anti-A,B/soluble A,B antigens
    - [Platelet additive solution removes ⅔ of plasma]

Traditional Compatibility During ABO Switch
E.g., Tormey CA, AABB Technical Manual, 2011, Table 25-2
Traditional Compatibility

- Avoid plasma, platelet anti-A/B vs graft A or B
- O patient, A graft
  - Give A platelets
- A patient, O graft
  - Give A platelets until O RBCs engraft
  - Then switch all products to group O
- A patient, B graft
  - Prefer AB platelets until B RBCs
  - Then switch all products to group B

Group A patient received group B SCT 10 days ago, now needs 2 platelet doses stat for pulmonary bleeding with platelet count 9,000/μL. No group AB platelets are available. What is your next best choice?

1. Group A platelets
2. Group B platelets
3. Group O platelets

Blood & Tissue Compatibility During & After ABO Switch

NIH: O'Donghaille D, Transfusion 52:456, 2012

Recipient  Transfusions  Donor

Plasma
Anti-A, B

Tissue/Soluble A, B

Anti-A, B

Platelets
A, B, O

RBCs
A, B, O
Avoid Anti-Tissue Antibody

- NIH approach
- Avoid platelet and plasma anti-A/B vs recipient and graft
- Lifelong

- O patient, A graft
  - Give group A platelets
- A patient, O graft
  - Give group A platelets lifelong
- A patient, B graft
  - Prefer AB platelets lifelong
  - [Give patient instructions/card?]

Pan-Compatible Transfusions in ABO Switch

Univ Rochester: Heal JM, Bone Marrow Transpl 36:747, 2005

Avoid any ABO incompatibility

- Univ Rochester findings after protocol instituted:
  - Less platelet refractoriness, including HLA
  - Less major bleeding
  - Improved overall survival

- Also see: Surgical patients: Henrichs KF, Transfusion 52:635, 2012  
  - Less febrile, allergic reactions; less RBC antibodies
Challenging Cases

Cases From Northwestern Memorial Hospital

Adult allogeneic stem-cell transplants:

A1, A2, and anti-A1

Disappearing RBCs

Double-cords, triple blood groups

Case 1: A1 and A Subgrouping

- O recipient ← A graft—matched unrelated
  - Week 8: group A RBCs appeared
    - But anti-A continued, with negative DAT
    - ???
  - RBCs type A1-negative; "anti-A" is anti-A1-specific
Case 1: \( A_1 \) and \( A \) Subgrouping

- \( O \) recipient \( \rightarrow \) \( A \) graft—matched unrelated
  - Week 8: group \( A \) RBCs appeared
    - But anti-\( A \) continued, with negative DAT
    - ???
  - RBCs type \( A_1 \)-negative; “anti-\( A \)” is anti-\( A_1 \)-specific
  - \( A_2 \) phenotype with anti-\( A_1 \)
  - SCT donor presumably \( A_2 \)

Case 2: \( A_1 \) and \( A \) Subgrouping

- \( B \) recipient \( \rightarrow \) \( A \) graft—matched unrelated
  - Week 8 (1\textsuperscript{st} specimen): group A RBCs present
    - But anti-\( A \) continued, with negative DAT
    - ???
  - RBCs typed \( A_1 \)-positive with \( A_1 \) lectin
    - Anti-\( A \) appeared to be anti-\( A_1 \)-specific
      - DAT was negative

B patient, A SCT graft. 
\( A_1 \) RBCs, anti-\( A_1 \) in plasma, negative DAT.
Which is the most likely explanation?

1) Anti-I\( H \)
2) False-negative DAT
3) Sd(a++) polyagglutination
4) Acquired \( A \) variant
5) I have no idea
Case 2: A₁ and A Subgrouping

- B recipient ← A graft—matched unrelated
  - Week 8 (1st specimen): group A RBCs present
    - But anti-A continued, with negative DAT
    - ???
  - RBCs typed A₁-positive with A₂ lectin
    - Anti-A appeared to be anti-A₁-specific
      - DAT was negative
  - Findings persisted through last followup, 5 mo post-SCT
  - ?!??!?----RBCs not truly A₁⁺? Plasma not truly anti-A₁?

Case 3: Disappearing RBCs

- O recipient ← O and B double-cord grafts
  - WBC chimerism: group B donor, 6 weeks
- B RBCs, 3 months to 6.5 months
- Blood type switched to group B
- 8.5 months:
  - No group B RBCs

Case 3: Disappearing RBCs

- O recipient ← O and B double-cord grafts
  - WBC chimerism: group B donor, 6 weeks
- B RBCs, 3 months to 6.5 months
- Blood type switched to group B
- AML relapse: 6 months;
  - WBCs 83% group B donor, 17% recipient
- 8.5 months:
  - No group B RBCs
Case 4: Double Cords, Triple Blood Groups

- B+ recipient ← O-neg and A+ double-cord grafts
  - Transfuse O-neg RBCs
- WBCs: 100% A+ donor from 3 weeks on
- B+ RBCs present through 8 weeks
- Only group O-neg RBCs (transfusions) in weeks 8-12
- Group A RBCs appear at 12 weeks, but anti-A persists
  - DAT negative--???
  - Rh typings negative to weak--???

Case 4: Double Cords, Triple Blood Groups

- B+ recipient ← O-neg and A+ double-cord grafts
  - Transfuse O-neg RBCs
- WBCs: 100% A+ donor from 3 weeks on
- B+ RBCs present through 8 weeks
- Only group O-neg RBCs (transfusions) in weeks 8-12
- Group A RBCs appear at 12 weeks, but anti-A persists
  - DAT negative--???
  - Rh typings negative to weak--???
- 12-16 weeks: RBCs A1-negative, weak-D+; Plasma anti-A1
- Cord donor presumably A2 and weak-D variant

Outline

- ABO Factors in Stem Cell Transplants
- Timing of Blood Group Conversion
- Transfusion Protocols and Practices
- Cases with Conundrums
Upon Reflection...
Questions?

Near Fall River Pass