Transfusion Associated Acute Lung Injury (TRALI)

Chris Beritela, MS, MT(ASCP)SBB
Area Technical Consultant
Immucor, Inc.

Objectives

- Define Transfusion-Related Acute Lung Injury (TRALI) and the role of HLA antibodies in TRALI
- Describe the properties of HLA antibodies and how these properties are incorporated into TRALI mitigation strategies
- Review the incidence, potential causes, and differential diagnosis of TRALI.
- Discuss the current AABB Standards and Recommendations related to the prevention, reduction, and investigation of TRALI.
- Discuss HLA antibody testing methods and the TRALI reduction program at Rhode Island Blood Center

TRALI – Basic Definition

Transfusion Related Acute Lung Injury
TRALI is an acute, often life-threatening, reaction characterized by respiratory distress, hypo- or hypertension and non-cardiogenic pulmonary edema that occurs within 6 hours of a blood component transfusion.
History of TRALI

1951, Dr. Barnard described a transfusion (tr xn) related non-cardiogenic pulmonary edema.

1967, Dr. Asbaugh et al, described acute respiratory distress syndrome.

1980, Popovsky et al, described TRALI as a distinct clinical entity.

2004, Canadian Consensus Conference define TRALI.

2005, NHLBI define TRALI.

AABB Association Bulletin #05-09

- Acute onset < 6hrs
- No evidence of left atrial hypertension
- No pre-existing Acute Lung Injury
- Pulmonary artery occlusion pressure <18 mm Hg, or lack of clinical evidence of left atrial hypertension
- Bilateral infiltrates

Pathogenesis of TRALI

- Two immune-mediated hypotheses
  - HLA and HNA antibodies
  - Biologic Response Modifiers (BRM)

- Non-immune mediated TRALI
**Immune Mediated: HLA/HNA antibodies**

- Antibodies originate in the donor product (90%)
  - Antibodies directed against HLA (Class I / II) or HNA

**Immune Mediated: HLA/HNA antibodies**

- Antibody originates in the recipient (10%)

**Immune Mediated: Two-hit model**

**Risk hit (patient factors)**
- Sepsis
- Haematological malignancy
- Heart surgery
- Mechanical ventilation
- Massive blood transfusion
- Chronic alcohol abuse
- Age of patient
- Shock
- Acute renal failure
- Severe burn disease
- Graft surgery
- Liver surgery

**Second hit (transfusion factors)**
- RBC
  - HLA or HNA
  - Biactive Spots
  - vWdAB
  - Aged erythrocyte
- FFP
  - HLA or HNA
- PLT
  - HLA or HNA
  - Biactive Spots
  - vWdAB
Pathogenesis of TRALI

- Vascular endothelial growth factor (VEGF)
- Neutropenic patients.

Clinical Presentation- Transfusionist

- TRALI
  - Onset within 2 hours
  - Fever
  - Hypotension
  - Dyspnea
  - Cyanosis
  - Bilateral infiltrates
- Transfusion Associated Circulatory Overload (TACO)
- Anaphylactic Transfusion Reactions
- Transfusion Related Sepsis
### Most Common Symptoms

<table>
<thead>
<tr>
<th>Symptom</th>
<th>TRALI</th>
<th>TACO</th>
<th>Anaphylaxis</th>
<th>Sepsis</th>
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<tbody>
<tr>
<td>Cyanosis</td>
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<tr>
<td>Hypotension</td>
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<tr>
<td>Respiratory distress/failure</td>
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<tr>
<td>Hypoxemia</td>
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<tr>
<td>Hypertension</td>
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<tr>
<td>Fever</td>
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<tr>
<td>Pulmonary edema</td>
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<tr>
<td>Chills</td>
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<tr>
<td>Dyspnea</td>
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<tr>
<td>Cyanosis</td>
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<tr>
<td>Headache</td>
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<tr>
<td>Urticaria</td>
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<tr>
<td>Bronchospasm</td>
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### Treatment for TRALI

- Intensive respiratory support.
  - Supplemental oxygen
  - Mechanical respirator
- Intensive circulatory support.
  - Pressors
  - Corticosteroids
  - Diuretic

### Incidence of TRALI

- Not well established
  - Under reported
  - Passive reporting
  - Difficult to diagnose
- Rates vary widely
  - 1 in 432 to 1 in 88,000 per platelet transfusion
  - 1 in 4,000 to 1 in 557,000 per unit of RBC
  - TRALI > 0.1% of transfusions
Why Is This Such A Big Deal?

- Longer ICU stays
- Higher mortality
- Leading cause of transfusion-related death reported to the FDA since 2008

Reported Data from FDA Website

Finding Our Way to Less HLA

- How to reduce the incidence of TRALI?
  - Understand how prevalence
  - Male vs female donors
  - Preserve donor pool
Prevalence of HLA Antibody

- Highly polymorphic
- Approximately 33% of people exposed to HLA antigens make antibodies to HLA
  - Transfusions
  - Tissue/organ transplant
  - Pregnancy

Prevalence of HLA Antibody

- About 10% of blood donations contain HLA/HNA abys
  - Primarily platelets and plasma
  - Approximately 35% of TRALI due RBC
  - Multiparous women

Mitigation of TRALI

- 2003 NBS in the UK: male only plasma
- 29th Ed. AABB Standards: 5.4.1.2
  - 5.4.1.2.1 Effective date Oct 2016
  - Males
  - Females who have not been pregnant
  - Females negative for HLA antibodies.
### Additional AABB and CAP Standards

<table>
<thead>
<tr>
<th>Processes to evaluate</th>
<th>AABB</th>
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<tr>
<td>Lab policies to evaluate and report</td>
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<tr>
<td>Notification of blood supplier</td>
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<tr>
<td>Plan to reduce risk of TRALI</td>
<td>7.4.2.3</td>
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<tr>
<td>Track the frequency of TRALI</td>
<td>7.4.2.4</td>
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<th>Processes to evaluate</th>
<th>CAP</th>
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<tr>
<td>TRM41700 to TRM42185</td>
<td>TRM 42050</td>
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<td>TRM 42100</td>
<td>TRM.42110</td>
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### FDA

- Section 606.170(b) of Title 21, Code of Federal Regulations (21 CFR 606.170(b))
- Report of the investigation within 7 days
- Division of Inspections and Surveillance.
  - Voice-mail: 240-402-9160
  - E-mail: fatalities2@fda.hhs.gov
  - Fax: 301-595-1304

### Potential TRALI Mitigation Strategies

- Screening for HLA and or HNA antibody
  - All donors
  - Only female donors
  - Donors with history of exposure
- Defer all donors based on history of transfusion or pregnancy
- Defer all female donors
Strategies Reduce Incidence of TRALI

- **TRANSFUSION** 2015;55:164-175. Müller et al.
- Male-only donor for plasma containing products
  - Significant reduction of TRALI
  - Reduction in 30-day mortality
  - Benefits “at-risk” patient populations most

Strategies Reduce Incidence of TRALI

- Four year study at UCSF and Mayo Clinic
  - Decrease of 68% in risk of TRALI reactions with the implementation of male only (Mayo) and female never pregnant / male only plasma (UCSF)

Summary

- TRALI is primary cause of trxn related death
- 90% of TRALI cases are immune mediated
- 33% of People exposed to HLA form Abys
- 10% of donations contain HLA Abys
- Studies have shown mitigation strategies are effective in reducing the rate and effect of TRALI
- Accreditation organizations are requiring the implementation of mitigation strategies.