



Transfusion Associated Acute Lung Injury (TRALI)

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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



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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.



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History of TRALI

A horizontal timeline arrow pointing right, with five blue circles representing key events. The text is as follows:

- 1951** Dr Bernard described a transfusion (trxn) related phenomena where main feature was a non-cardiogenic, pulmonary edema.
- 1967** Dr Asbaugh et al, described an acute respiratory distress syndrome
- 1980**, Popovsky et al, introduce TRALI as a distinct clinical entity
- 2004** Canadian Consensus Conference-define TRALI
- 2005** NHLBI-define TRALI

Logos for IMMUCOR and Learn are at the bottom.

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

Two side-by-side chest X-rays showing bilateral infiltrates.

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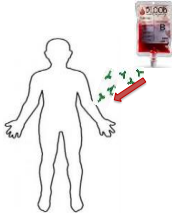
Pathogenesis of TRALI

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

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Immune Mediated: HLA/HNA antibodies

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



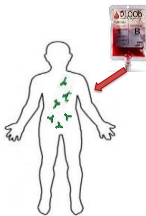
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Immune Mediated: HLA/HNA antibodies

- Antibody originates in the recipient (10%)



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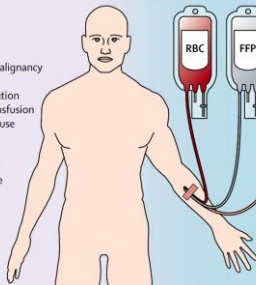
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Immune Mediated: Two-hit model

First hit (patient factors)

- Sepsis
- Haematological malignancy
- Heart surgery
- Mechanical ventilation
- Massive blood transfusion
- Chronic alcohol abuse
- Age of patient
- Shock
- Acute renal failure
- Severe liver disease
- Spine surgery
- Liver surgery



Second hit (transfusion factors)

- RBC**
- HLA or HNA
 - Bioactive lipids
 - sCD40L
 - Aged erythrocyte
- FFP**
- HLA or HNA
- PLT**
- HLA or HNA
 - Bioactive lipids
 - sCD40L

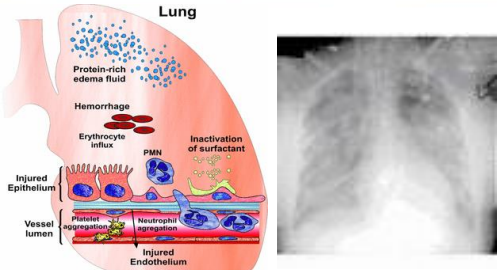
Dr Alexander Pj Viar, MD, Nicole P Juffermans, MD Lancet: Volume 382, No. 9896, p984-994, 14 September 2013

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Pathogenesis of TRALI



The diagram illustrates the pathogenesis of TRALI in the lung. It shows a cross-section of a blood vessel with an injured endothelium. Platelets and neutrophils aggregate on the injured endothelium, leading to vessel lumen obstruction. This causes hemorrhage and erythrocyte influx into the lung tissue. Protein-rich edema fluid also accumulates in the lung. Additionally, there is inactivation of surfactant. A chest X-ray to the right shows bilateral infiltrates, characteristic of TRALI. Logos for IMMUCOR and Learn are present at the bottom.

Pathogenesis- Non-Immune

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

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

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



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Most Common Symptoms

	TRALI	TACO	Anaphylaxis	Sepsis
x- usually present /- occasionally present O-local				
onset	<6 hrs			
hypoxemia	x	x		
respiratory distress/ failure	x		x	/
Hypotension	x		x	x
Hypertension	/	x		
fever	x			x
pulmonary edema	x	x	o	
chills			x	x
dyspnea	x	x	x	
cyanosis	x	x	x	
headache		x		
urticaria			x	
bronchospasm			x	


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- ### Treatment for TRALI
- Intensive respiratory support.
 - supplemental oxygen
 - mechanical respirator
 - Intensive circulatory support.
 - Pressors
 - Corticosteroids
 - Diuretic
- 
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- ### 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
- 
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Why Is This Such A Big Deal?

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



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Reported Data from FDA Website

Figure 1: Transfusion-Related Fatalities by Complication, FY2009 through FY2013

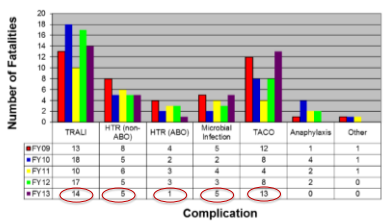


Figure 1: FY09 TRALI 13 HTR(non-ABO) 8 HTR(ABO) 4 Microbial Infection 5 TACO 12 Anaphylaxis 1 Other 1
 FY10 TRALI 18 HTR(non-ABO) 5 HTR(ABO) 2 Microbial Infection 2 TACO 8 Anaphylaxis 4 Other 1
 FY11 TRALI 10 HTR(non-ABO) 6 HTR(ABO) 3 Microbial Infection 4 TACO 4 Anaphylaxis 2 Other 1
 FY12 TRALI 17 HTR(non-ABO) 5 HTR(ABO) 3 Microbial Infection 3 TACO 8 Anaphylaxis 2 Other 0
 FY13 TRALI 14 HTR(non-ABO) 5 HTR(ABO) 1 Microbial Infection 5 TACO 13 Anaphylaxis 0 Other 0



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Finding Our Way to Less HLA

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






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Prevalence of HLA Antibody




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



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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



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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.



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

Additional AABB and CAP Standards

<ul style="list-style-type: none"> • Processes to evaluate • Lab policies to evaluate and report • Notification of blood supplier • Plan to reduce risk of TRALI • Track the frequency of TRALI 	<p>AABB</p> <ul style="list-style-type: none"> • 7.4.2 • 7.4.2.2 • 7.4.2.3 • 7.4.2.4 	<p>CAP</p> <ul style="list-style-type: none"> • TRM41700 to TRM42185 • TRM 42050 • TRM 42100 • TRM.42110
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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


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
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


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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



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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)



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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.



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