Transfusion-related Acute Lung Injury

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HAEMONETICS®

Early Synonyms for TRALI

- Leukoagglutinin Reaction
- Pulmonary hypersensitivity reaction
- Non-cardiogenic pulmonary edema
- Adult respiratory distress syndrome
- Allergic pulmonary edema

What is TRALI?

- Acute respiratory distress
- Hypoxemia (severe)
- Hypotension (moderate)
- Acute pulmonary edema
- Fever (1-2°C elevation),
- 1-2 hours of transfusion of plasma- containing blood products

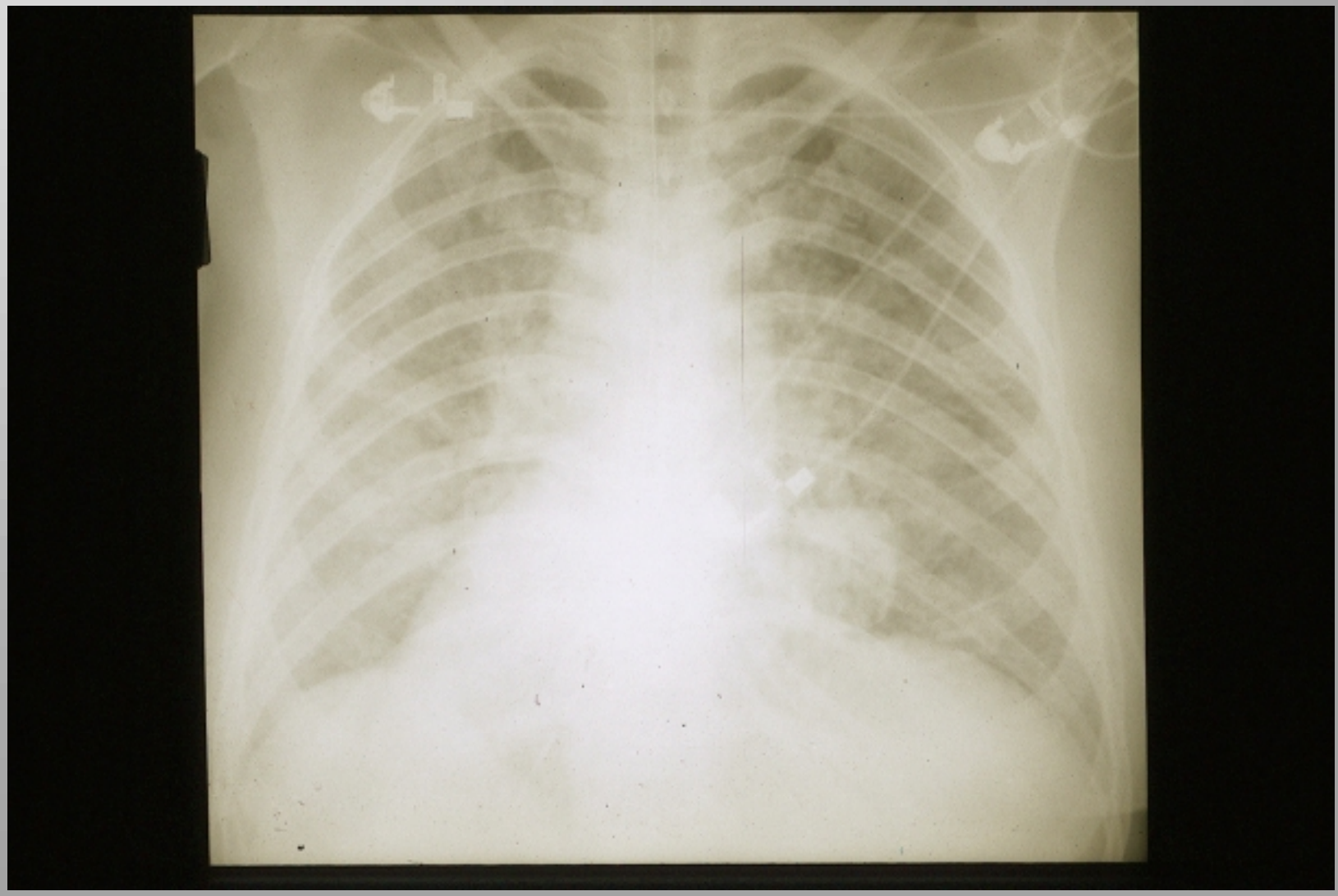
What is TRALI?

Predominant presenting symptoms (N=46)

Sign/Symptoms	%
Respiratory distress	76
Hypotension	15
Hypertension	15

[Popovsky & Haley, Immunohemotology 2000;16]

What is TRALI?



Differential Diagnosis

- Anaphylactic transfusion reaction
- Circulatory overload
- Bacterial contamination
- Cardiac failure

Who Is At Risk?

- No common thread
- Male:female ratio is about 1:1
- Patients have ranged from very young to very old
- No common underlying diagnosis

Implicated Blood Products

- Whole blood
- FFP
- RBC (all anticoagulant/preservatives)
- Granulocytes (by apheresis)
- Cryoprecipitate
- Platelet concentrate
- Plateletpheresis
- IVIG (rare)

What is the frequency of TRALI?

Incidence:

- **Unknown**
- **Mayo Clinic Study 1:5000 plasma – containing transfusions**

[Popovsky & Moore, Transfusion 1985]

What is the frequency of TRALI?

Underdiagnosed:

>240 cases published or reported

- 0.32% of severe respiratory reactions to random donor platelets (46/14,602 transfusions). [Clarke et al, Blood 1994]
- More frequent among patients with hematological disease and cardiac disease
- Average age of platelets 4.5 days

What is the frequency of TRALI?

Underdiagnosed (cont.):

Cooperman and Price, 1970:

- 40 patients with pulmonary edema in the operating setting
- 50% of cases were due to circulatory overload/ unknown causes

What is Clinical Outcome? Morbidity (N=36)

Morbidity		
Required oxygen support	36	100
Required mechanical ventilation	26	72
Pulmonary infiltrates		
Rapid resolution (≤ 96 hrs)	29	81
Slow resolution (> 7 days)	6	17
Mortality	2	6
Long-term sequelae	0	

Popovsky & Moore, Transfusion 1985;25]

Popovsky & Haley, 2000 (2000): 13% died

Mortality

FDA data on deaths from transfusion,1990-1998.

	Rank	Cases	%
Hemolytic transfusion reactions	#1	161	50%
TRALI	#3	29	9%

Mortality (cont.)

SHOT 2000 Annual Report

- 18 cases
- Major morbidity: 12
- Death: 6
- 2nd most common cause of death

Pathogenesis

HLA Class I / Granulocyte Antibodies

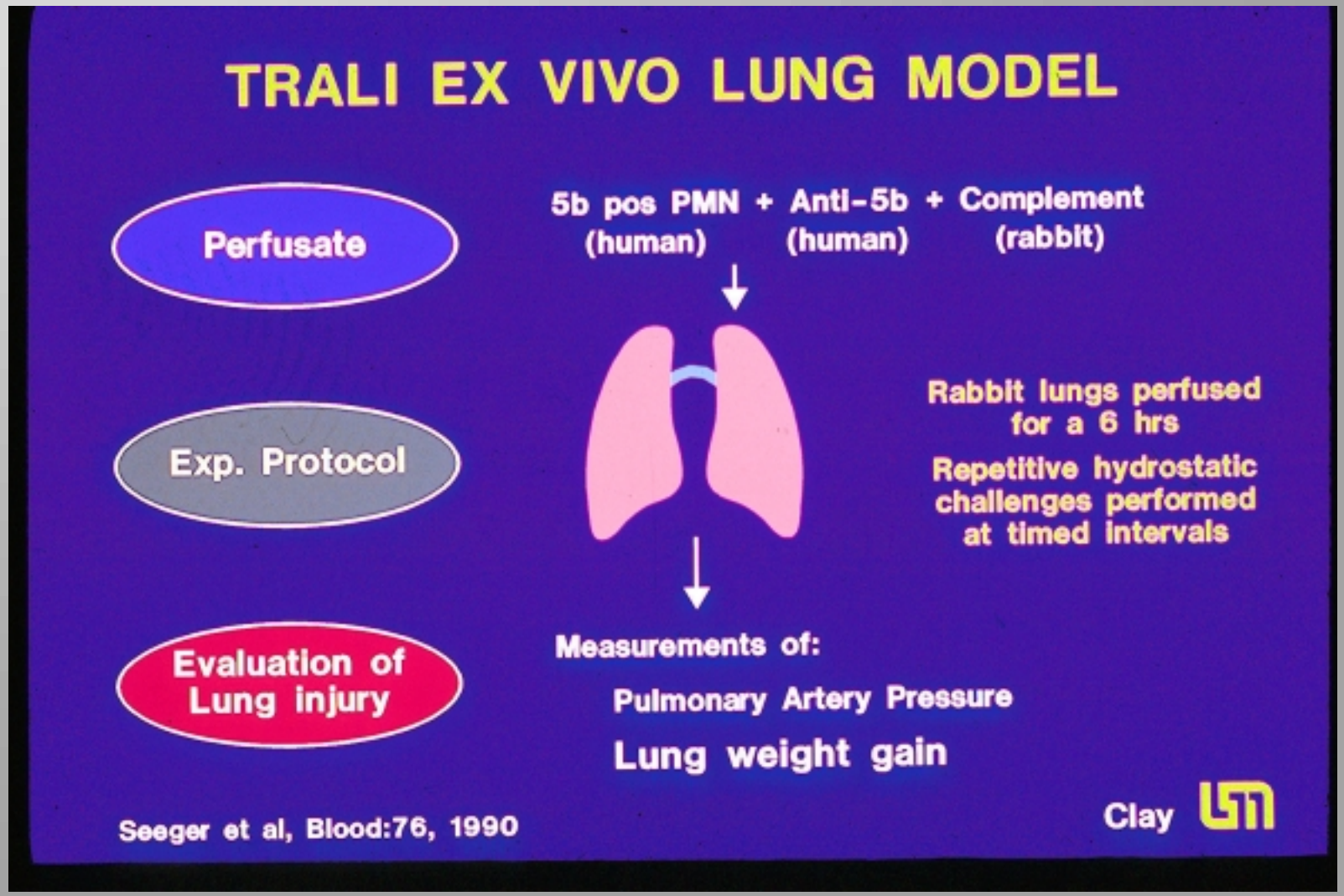
- Precise mechanism is unknown
- Donor HLA or granulocyte-specific antibodies (anti-NB2, -NA2, -5b): 60-85% of cases
- HLA antibody/antigen correspondence: 50% of cases
- Antibodies activate complement

Pathogenesis (2)

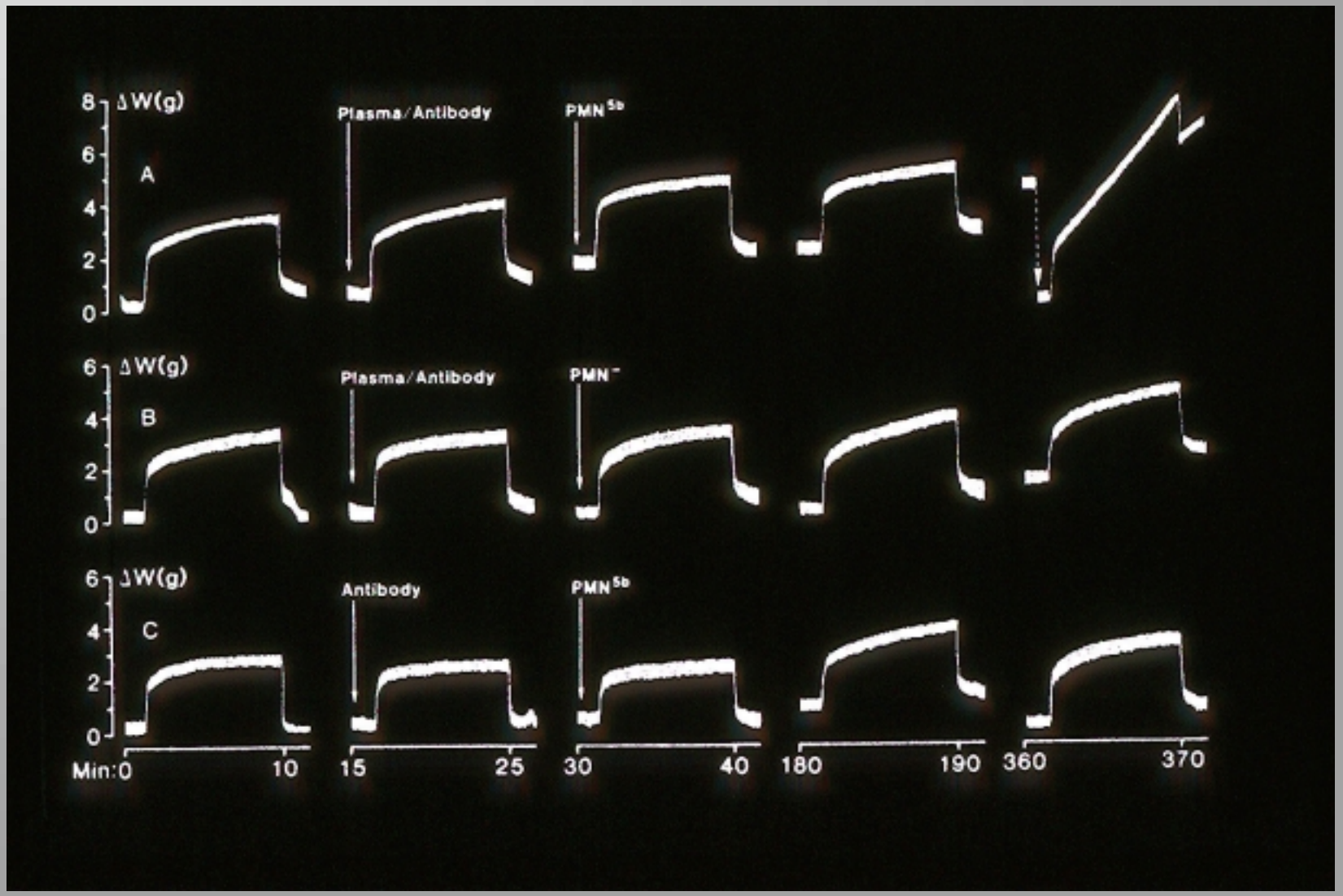
HLA Class I / Granulocyte Antibodies

- C5a promotes neutrophil aggregation/sequestration in microvasculature of lung
- There is margination of neutrophils in pulmonary microvasculature
- Activated neutrophils release proteases, superoxide radicals: results in endothelial cell injury → pulmonary edema

Pathogenesis (3)



Pathogenesis (4)



Pathogenesis (5)

Implicated Antibodies

	HLA	Granulocyte	Total
Donor	28%	41%	50%
Recipient	7%	4%	11%
Total			61%

[Popovsky & Haley, 2000]

Pathogenesis (6)

Role of Multiparous donor plasma

- Prospective, randomized study
- 102 ICU patients receiving ≥ 2 units FFP
- Multiparous (≥ 3 pregnancies) donors vs. controls
- 5 patients had clinical reactions → 1 TRALI
  - Donor was multiparous
- ↓ PaO_2/FiO_2 ($p < 0.05$) in multiparous-donor vs. control plasma

(Palfi et al, Transfusion 2001:41)

Pathogenesis (7)

HLA Class II antibodies:

3 cases that were negative for Class I/granulocyte antibodies

(Kopko et al, 1999 & 2000)

Pathogenesis (8)

Alternative hypothesis (Silleman et al)

- **May combine the antibody model with the cytokine model**
- **Underlying disease→ endogenous cytokines**
- **Infusion of granulocyte/HLA antibodies or biologically active lipids**
- **Granulocyte activation → endothelial damage**

Prevention Research

- Identify at risk recipients:
  - ✓ Prospective
  - ✓ Multicenter Studies
- Role of leukodepletion
- Educate clinicians

Regulatory Recommendations

- Quarantine untransfused components traced to implicated donors
- Defer donors previously implicated from future plateletpheresis donations
- Divert plasma-containing components from future donations (whole blood) by implicated donors → RBC / washed RBC only

Conclusion

- **TRALI is an under-diagnosed, serious problem**
- **Represents a spectrum of lung injury (NCPE → ARDS)**