Pulmonary Complications of Transfusion: Changes and Challenges

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Disclosures

Slide 12

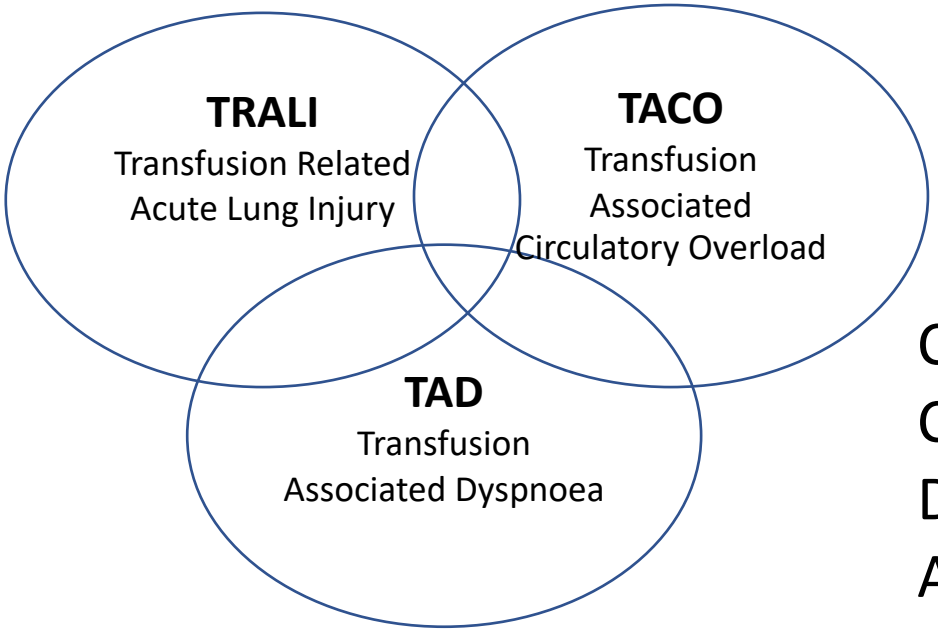
Red Cell Dosage Calculator

https://rcdcalculator.co.uk/

No personal commercial or financial interest

- Highlights from this year's SHOT report
- New definitions for TACO and TRALI published
- Challenges in categorisation of cases
- Future challenges

The Pulmonary Complications of Transfusion



Can co-exist
Could represent a spectrum
Difficult to differentiate
All limited by incomplete data

	Death definitely related	Death probably related	Death possibly related	Major morbidity
Delayed transfusion		2	6	
Overtransfusion			1	
FAHR				60
HTR		2		4
IBCT-WCT (clinical)				1
IBCT-WCT (laboratory)				2
IBCT-SRNM (laboratory)				1
UCT				3
TACO		2	3	36
TAD			2	1
TRALI		1		
TTI		1		1
Total	**0**	**8**	**12**	**109**

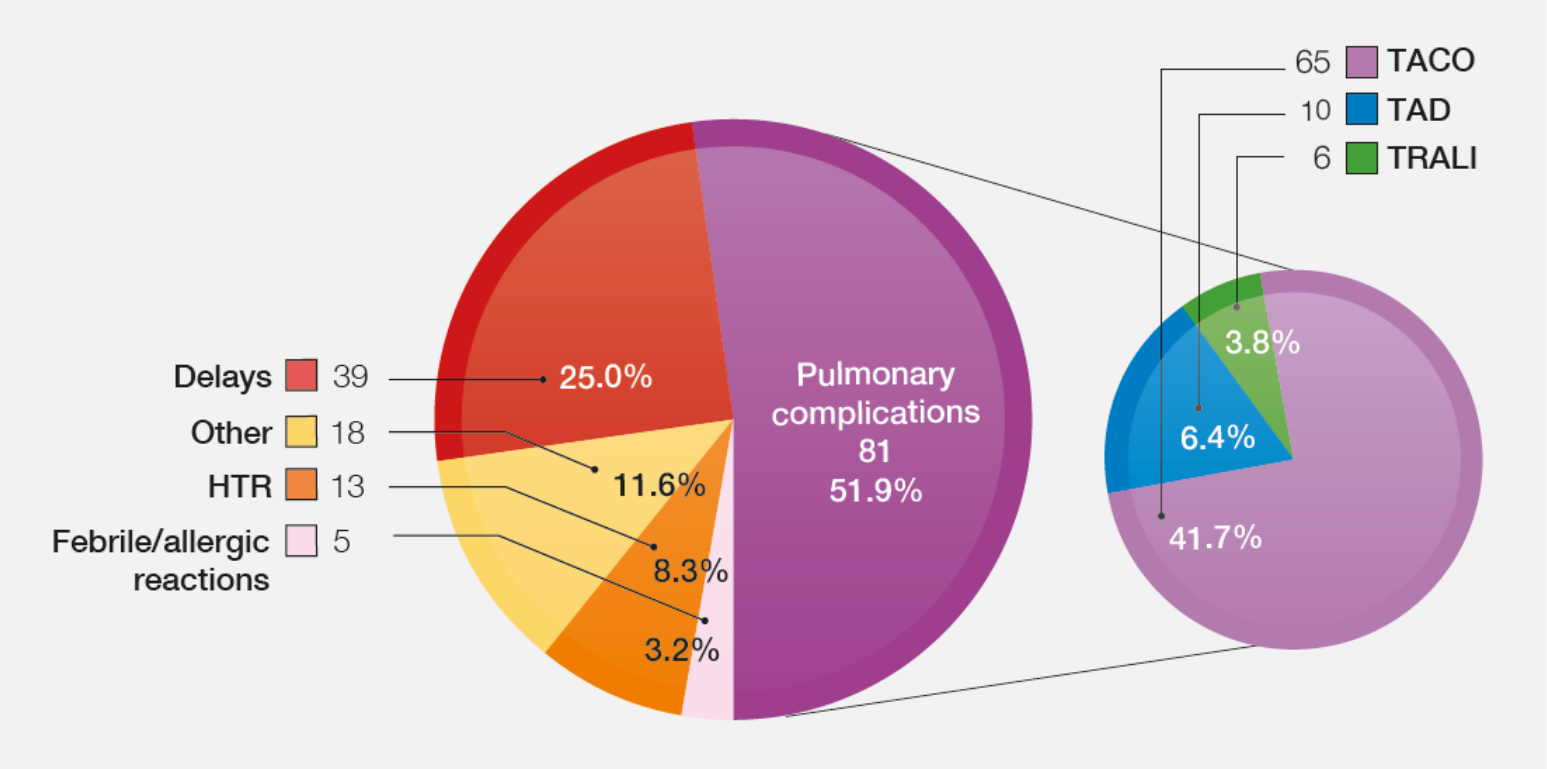


Figure 3.3: Transfusion-related deaths 2010 to 2018 n=156

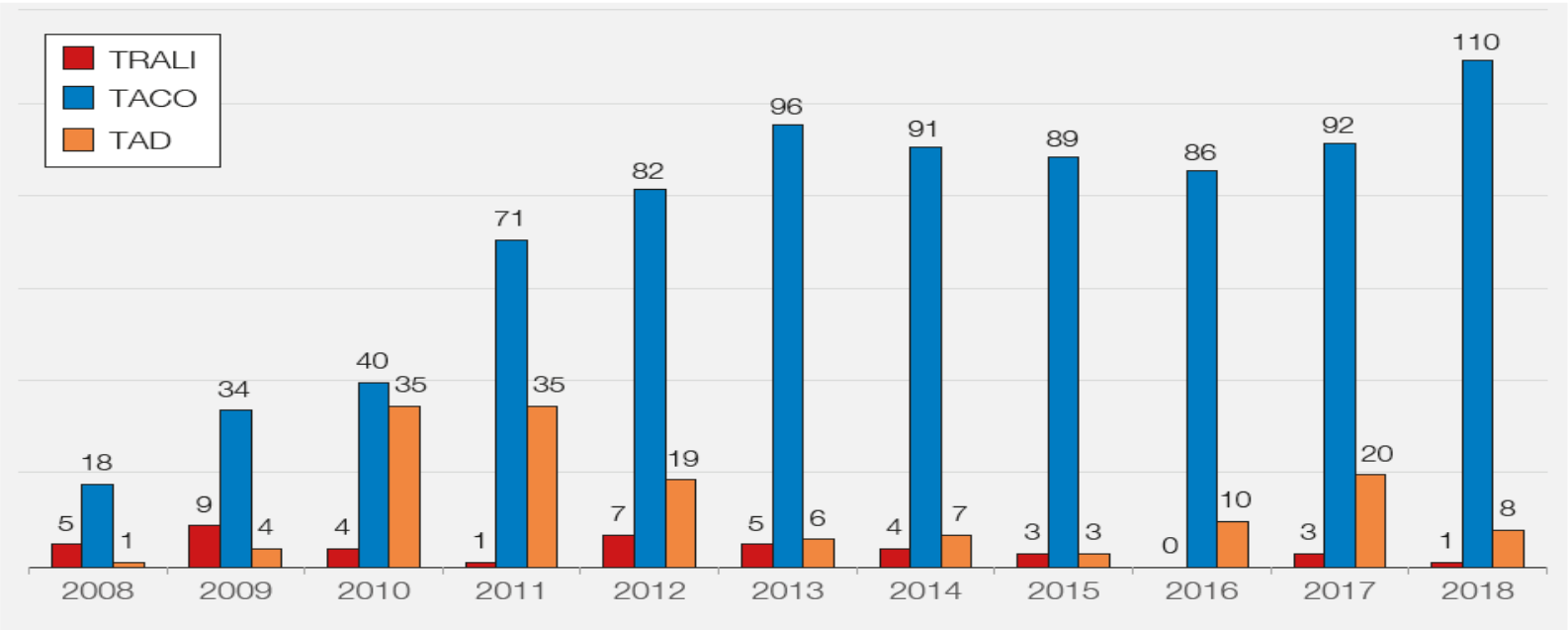


Figure 17.1: Reports of pulmonary complications by year 2008-2018

2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	
24	47	79	107	108	107	102	95	96	115	119	TOTAL

TACO Checklist → TACO NCA

Revised international surveillance case definition of transfusion-associated circulatory overload: a classification agreement validation study

Johanna C Wiersum-Osselton, Barbee Whitaker, Sharran Grey, Kevin Land, Gabriela Perez, Srijana Rajbhandary, Chester Andrzejewski Jr, Paula Bolton-Maggs, Harriet Lucero, Philippe Renaudier, Pierre Robillard, Matilde Santos, Martin Schipperus

www.thelancet.com/haematology **Published online May 9, 2019** **http://dx.doi.org/10.1016/S2352-3026(19)30080-8**

Standardisation: Internationally consistent surveillance and reporting

2011 ISBT definition – highly likely/probable cases not meeting definition
2017 – 2018: iterative validation process
Final adopted version: 76% positive agreement; 37% negative agreement
Not effective in distinguishing between pulmonary complication categories

Patients classified with TACO (surveillance diagnosis) should exhibit at least one required criterion* with onset during or up to 12 hours after transfusion (SHOT continues to accept cases up to 24 hours), and a total of 3 or more criteria i.e. *A and/or B, and total of at least 3 (A to E)

* **Required criteria** (A and/or B)

A. Acute or worsening respiratory compromise and/or

B. Evidence of acute or worsening pulmonary oedema based on:

- clinical physical examination, and/or
- radiographic chest imaging and/or other non-invasive assessment of cardiac function

Additional criteria

C. Evidence for cardiovascular system changes not explained by the patient's underlying medical condition, including development of tachycardia, hypertension, jugular venous distension, enlarged cardiac silhouette and/or peripheral oedema

D. Evidence of fluid overload including any of the following: a positive fluid balance; clinical improvement following diuresis

E. Supportive result of a relevant biomarker, e.g. an increase of B-type natriuretic peptide levels (BNP) or N-terminal-pro brain natriuretic peptide) NT-pro BNP to greater than 1.5 times the pre-transfusion value

BNP regulates blood pressure. Raised in Left Atrial Hypertension
Can it be performed by your Biochemistry Dept?

SHOT Serious Hazards of Transfusion

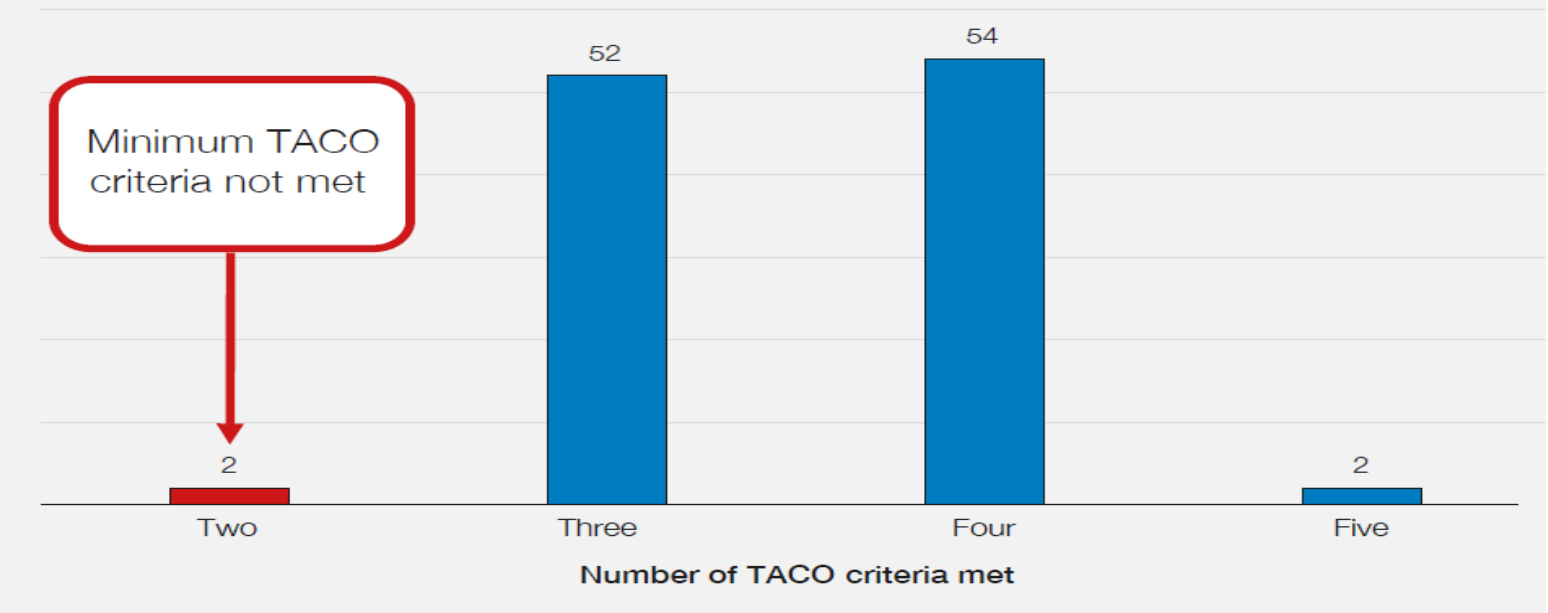


Figure 17b.2: Analysis of reports by the revised surveillance diagnosis criteria (number of criteria versus number of accepted cases)

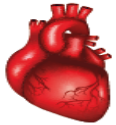
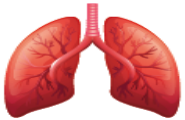
Both: <u>No vital sign observations or fluid balance</u>

1. Worsened after diuretic (renal failure), aortic stenosis and hypoalbulinaemia
2. No response to diuretic. ACS complicated the clinical picture and +++fluids

Recommendation

- A formal pre-transfusion risk assessment for transfusion-associated circulatory overload (TACO) should be undertaken whenever possible (especially if older than 50 years or weighing less than 50kg), as TACO is the most commonly reported cause of transfusion-related mortality and major morbidity

Action: All staff authorising transfusion

TACO Checklist	Red cell transfusion for non-bleeding patients	If 'yes' to any of the
	Does the patient have a diagnosis of 'heart failure' congestive cardiac failure (CCF), severe aortic stenosis, or moderate to severe left ventricular dysfunction? Is the patient on a regular diuretic? Does the patient have severe anaemia?	1 • R…
	Is the patient known to have pulmonary oedema? Does the patient have respiratory symptoms of undiagnosed caus…	…be resolved?
	Is the fluid balance clinic… positive? Is the patient on … been in the pas… Is there any peri… Does the patient … Does the patient h… impairment?	…y weight dosing for red …cially if low body weight) …ase one unit (red cells) and …ew symptoms of anaemia Measure the fluid balance • Consider giving a prophylactic diuretic • Monitor the vital signs closely, including oxygen saturation

…rusion …klist

Due to the differences in ad… neonatal physiology, babies may have a different risk for TACO. Calculate … dose by weight and observe the notes above.

IS SEVERE ANAEMIA AN INDEPENDENT RISK FACTOR FOR TACO? CASE BASED DISCUSSIONS BASED ON TACO REPORTS TO SHOT, THE UNITED KINGDOM HAEMOVIGILANCE SCHEME

S Narayan[1], S Grey[2], P Bolton-Maggs[3] and D Poles[4]

Recommendation

- Use weight-adjusted red cell dosing to guide the appropriate number of units required, for all non-bleeding adult patients, ideally using tools which also highlight inappropriate transfusion (Grey et al. 2018, National Comparative Audit, 2017)

Action: All staff authorising transfusion

The data continues to show TACO in non-bleeding patients where the volume of red cells was in excess of that calculated for their body weight and target haemoglobin (see Case 17b.2). Weight-adjusted red cell dosing for non-bleeding patients remains a recommendation.

Red Cell Dosage Calculator

https://rcdcalculator.co.uk/

Weight adjusted red cell dosing is usual practice in paediatrics and neonates – this patient group is still at risk due to dosing errors

4 cases – 2 due to volume/dosing errors in neonates (one death)

Definition:

Transfusion-related acute lung injury (TRALI) is defined as acute dyspnoea with hypoxia and bilateral pulmonary infiltrates during or within 6 hours of transfusion, in the absence of circulatory overload or other likely causes, or in the presence of human leucocyte antigen (HLA) or human neutrophil antigen (HNA) antibodies cognate with the recipient.

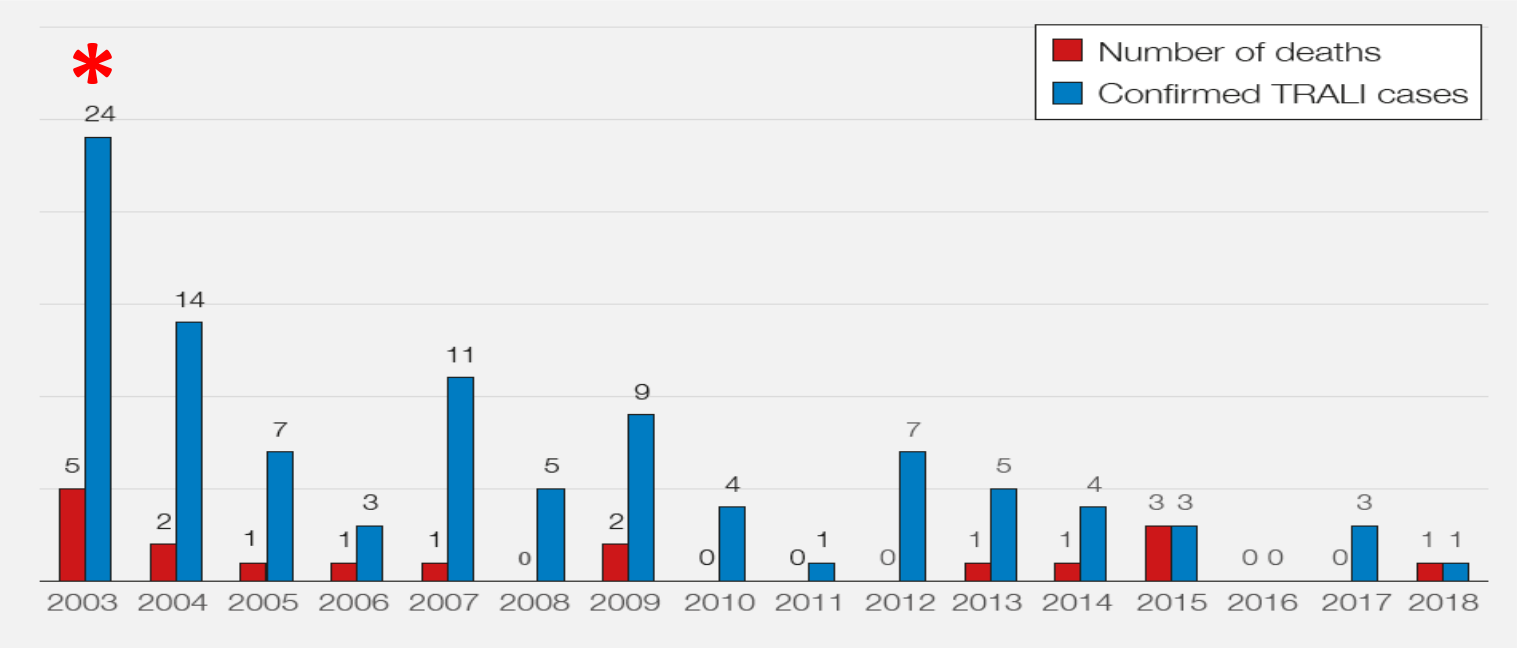


Figure 17a.1: Number of confirmed TRALI cases and deaths at least possibly related to TRALI by year of report

Table 17a.1: Revised SHOT criteria for assessment of TRALI cases

Classification	Definition	Mapping to Canadian Consensus definition
Highly likely	Cases with a convincing clinical picture and positive serology	TRALI +positive serology
Probable	Cases with positive serology but other coexisting morbidity which could independently cause acute lung injury or fluid overload	Possible TRALI (pTRALI) +positive serology
Equivocal	Cases with positive serology in the clear presence of lung injury due to other causes or fluid overload	Not TRALI [excluded because of other morbidity but meets positive criteria]+positive serology
Antibody-negative TRALI	Cases with a convincing clinical picture where serology is not available or negative	TRALI + absent or negative serology
Unlikely - reclassify as TAD	Cases where the picture and serology was not supportive of the diagnosis. These cases are transferred to TAD	pTRALI or not TRALI + negative or absent serology

Deaths n=1

Case 17a.1: Antibody-negative TRALI - post mortem diagnosis without serology

Donor HLA/HNA antibody criterion in important from a HV perspective as this monitors the effectiveness of risk-reduction measures

The classification still allows reporting of non-antibody mediated TRALI

A consensus redefinition of transfusion-related acute lung injury

Alexander P.J. Vlaar,[1,2] Pearl Toy,[3] Mark Fung,[5] Mark R. Looney,[4] Nicole P. Juffermans,[1,2] Juergen Bux,[6] Paula Bolton-Maggs,[7] Anna L. Peters,[8] Christopher C. Silliman,[9] Daryl J. Kor,[10] and Steve Kleinman[11]

TRANSFUSION 2019;59;2465–2476

New insights into pathogenesis prompted revision of the 2004 consensus definition
Expert panel – Delphi method

Proposes:

TRALI Type I – no risk factor for ARDS
TRALI Type II – risk factor for ARDS/mild pre-existing ARDS
A clinical diagnosis not requiring detection of cognate HLA/HNA antibodies
Recommends adoption into HV systems for standardisation

TRALI Differentiation (New Definition)

Acute onset hypoxemia and pulmonary oedema within 6 hours of transfusion			
Pulmonary complication	**ARDS risk factors present**	**ARDS stability**	**LAH**
TRALI Type I	NO	-	No evidence of/not significant
TRALI Type II	YES	Pre-existing/stable	No evidence of/not significant
ARDS	YES	Deteriorating over past 12 hours	No evidence of/not significant
TACO/TRALI	Clinically compatible with TACO and TRALI May co-exist		Lack of data
TACO			Present
TAD	Temporal association with transfusion, not meeting other criteria		

Modified from tables 2 and 7: A consensus re-definition of TRALI
TRANSFUSION 2019;59;2465–2476

LAH = Left Atrial Hypertension
Authors recommend objective assessment (echocardiogram/invasive monitoring)

Challenge of Distinguishing TACO and TRALI

- What is the driver of lung oedema?

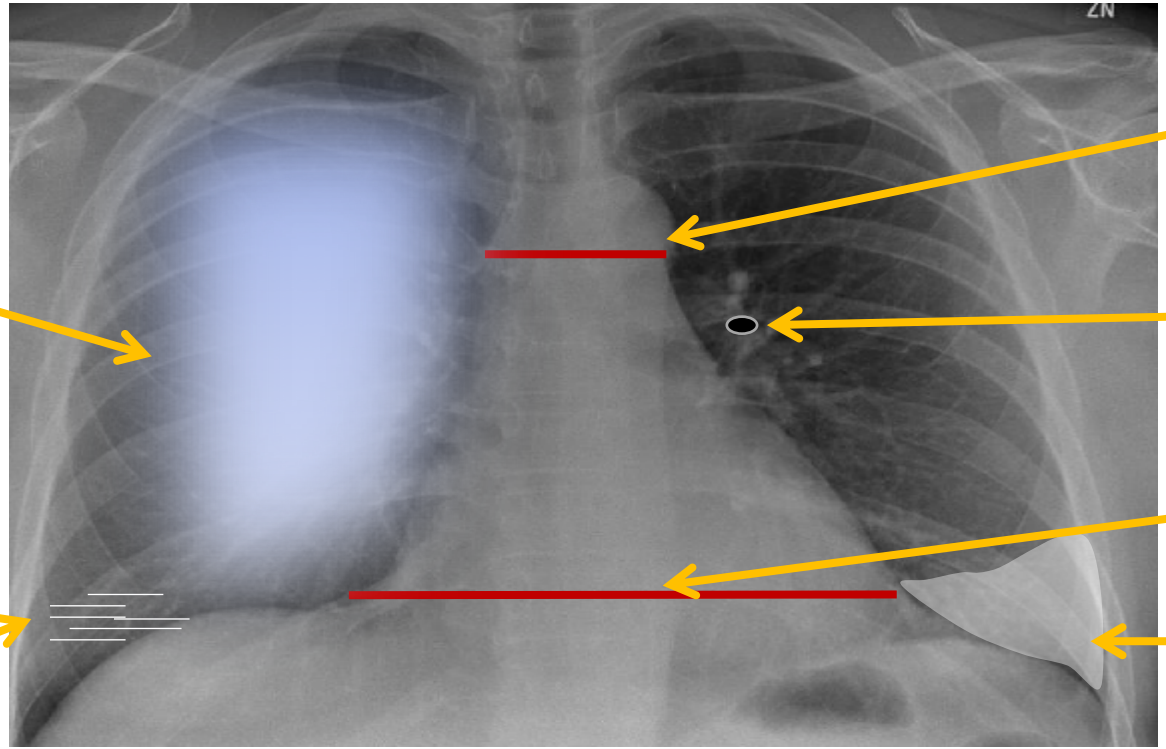
- Inflammatory – increased capillary permeability (TRALI, ARDS). 2-Hit theory (1 patient-related; 2 transfusion-related)

- Hydrostatic – increased capillary hydrostatic pressure (CHF, TACO). Often not proportionate to volume transfused.

Normal PA CXR annotated for Illustration.
Reproduced with patient consent.

Limitations of Chest Imaging

Features are not TACO-specific



pulmonary oedema (TACO and TRALI)

Hydrostatic (TACO) and Inflammatory (TRALI) cannot be distinguished

Kerley B lines (TACO)

widened vascular pedicle (TACO)

Peri-bronchial cuffing (TACO)

enlarged cardiac silhouette (TACO)

pleural fluid (TACO)

Issues with Demonstrating LAH

- Incomplete/unavailable data (9.1% had echo; 2.7% had NT-Pro BNP performed) 2018 SHOT Report

- May not need to be performed to clinically manage patient

- NT-Pro BNP is a surrogate for LAH but has limitations Klanderman et al, 2019 – systematic review of biomarkers in TACO
  - Normal BNP excludes TACO
  - >1.5x rise supports TACO (often raised pre-transfusion)
  - Unreliable in critically ill
  - Other biomarkers require further investigation

Other Issues

- Co-morbidities and concurrent diagnoses both complicate the evaluation and may contribute to the reaction
- Fluid balance not well recorded. Positive FB a risk for both TACO and TRALI
- Response to diuretics not well recorded (esp. volume of diuresis) and may be impaired by renal failure
- Unanticipated change in CV status can occur in TRALI and TACO (though hypotension more common in TRALI)
- Fever can occur in TACO (≈30%) and TRALI (suggesting TACO may also have an inflammatory component) SHOT 2017 report, Parmar et al (2016)
- Blood not the only cause of CO – iatrogenic fluids and co-morbidities (imputability)

TAD

- **24hrs, NOT TRALI/TACO/Allergic/underlying condition**
- 8 cases (2 deaths, 1 major morbidity)
- 6 cases came from TACO and TRALI
- 5 reported as TAD transferred to TRALI and FAHR
- Important repository for building case series
- Lack of data from reporter → TAD category
- Likely affected by revisions TRALI and TACO definitions

Prophylactic diuretics

HV reporting implications (TRALI definition)

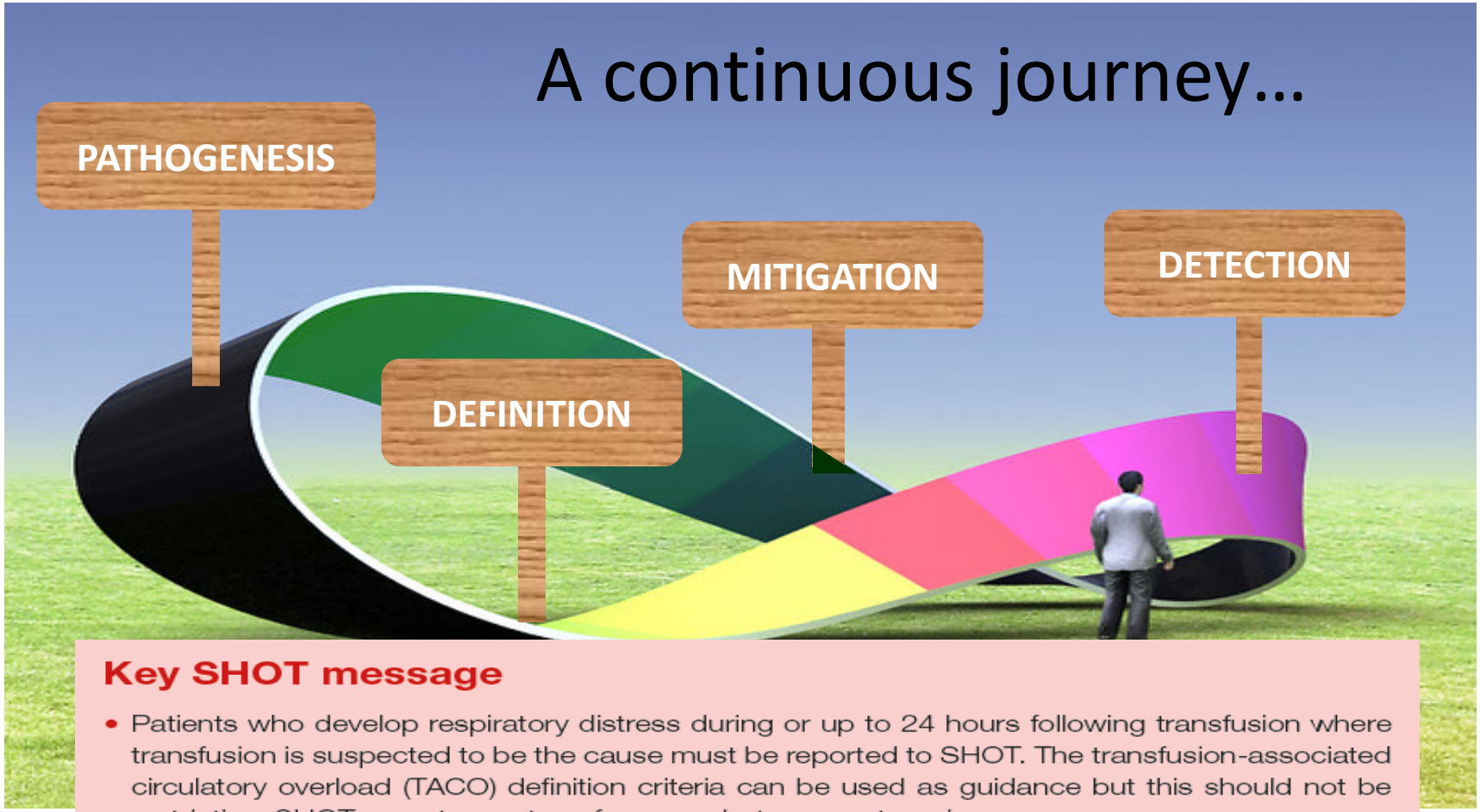
Pathophysiology of pulmonary complications

Unanswered Questions

Effectiveness of risk controls

Biomarkers

A continuous journey…



Key SHOT message

- Patients who develop respiratory distress during or up to 24 hours following transfusion where transfusion is suspected to be the cause must be reported to SHOT. The transfusion-associated circulatory overload (TACO) definition criteria can be used as guidance but this should not be restrictive. SHOT experts can transfer cases between categories

Acknowledgements

- The SHOT team
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