Transfusion Reactions

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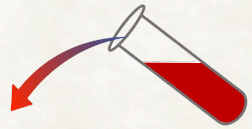
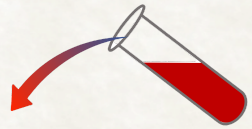


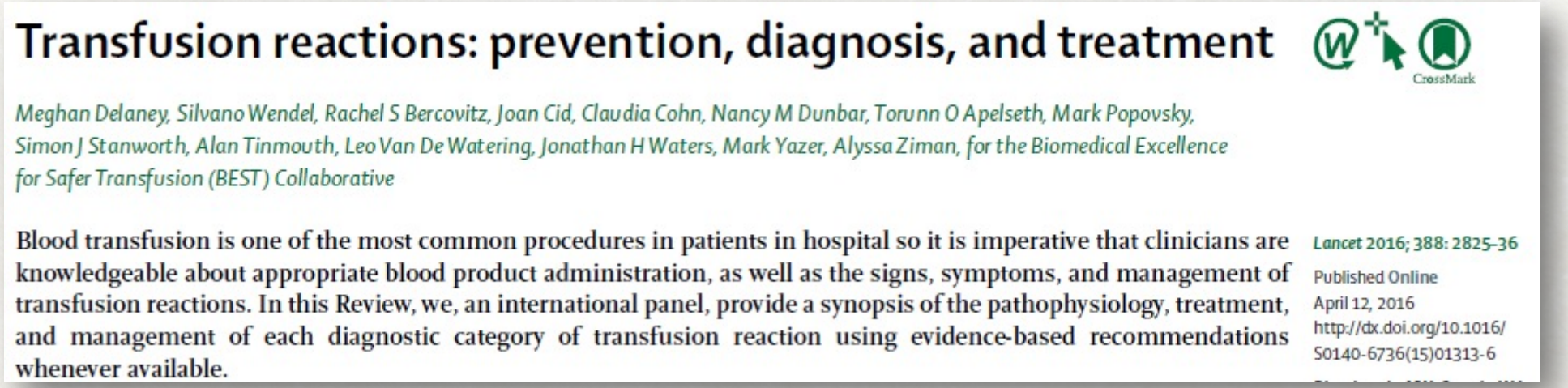
Disclosures

- None

Topics To Cover

1. Transfusion reaction classification
2. Clinical and laboratory work-up of suspected reactions
3. Recommendations for management and prevention





Transfusion reactions: prevention, diagnosis, and treatment

Meghan Delaney, Silvano Wendel, Rachel S Bercovitz, Joan Cid, Claudia Cohn, Nancy M Dunbar, Torunn O Apelseth, Mark Popovsky, Simon J Stanworth, Alan Tinmouth, Leo Van De Watering, Jonathan H Waters, Mark Yazer, Alyssa Ziman, for the Biomedical Excellence for Safer Transfusion (BEST) Collaborative

Blood transfusion is one of the most common procedures in patients in hospital so it is imperative that clinicians are knowledgeable about appropriate blood product administration, as well as the signs, symptoms, and management of transfusion reactions. In this Review, we, an international panel, provide a synopsis of the pathophysiology, treatment, and management of each diagnostic category of transfusion reaction using evidence-based recommendations whenever available.

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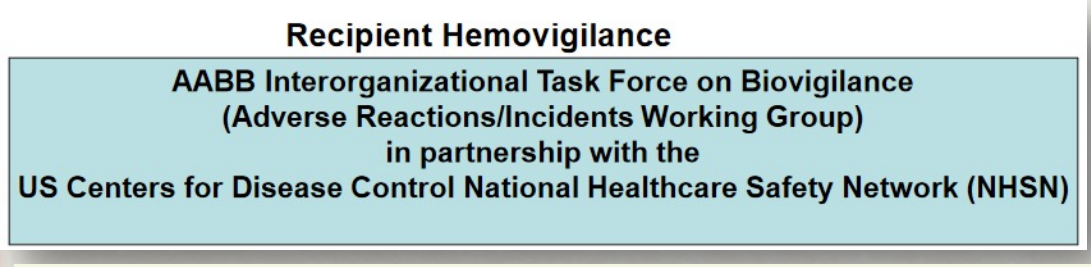
- 2005-2006: Lack of cohesive national surveillance system for transfusion reactions (“hemovigilance”) seen as public health deficiency
  - AABB forms Interorganizational Task Force on Biovigilance
  - Dept. of HHS's Advisory Committee on Blood Safety and Availability (ACBSA) recommends Federal actions to partner with AABB and others to advance US hemovigilance initiatives
- 2009: CDC/AABB partnership pilots Hemovigilance (v1.0) within CDC’s NHSN system
  - Systematic tracking of transfusion reactions
  - Relies on standard, uniform and precise definitions for reporting
    - Harmonized with international definitions (ISBT/IHN)

NHSN Hemovigilance Medical History – 2016
Available from https://www.youtube.com/watch?v=3lklsqeb6A4



US Department of Health Human Services. Biovigilance in the United States: efforts to bridge a critical gap in patient safety and donor health. US Department of Health and Human Services; 2009. Available from https://www.researchgate.net/publication/255703308.

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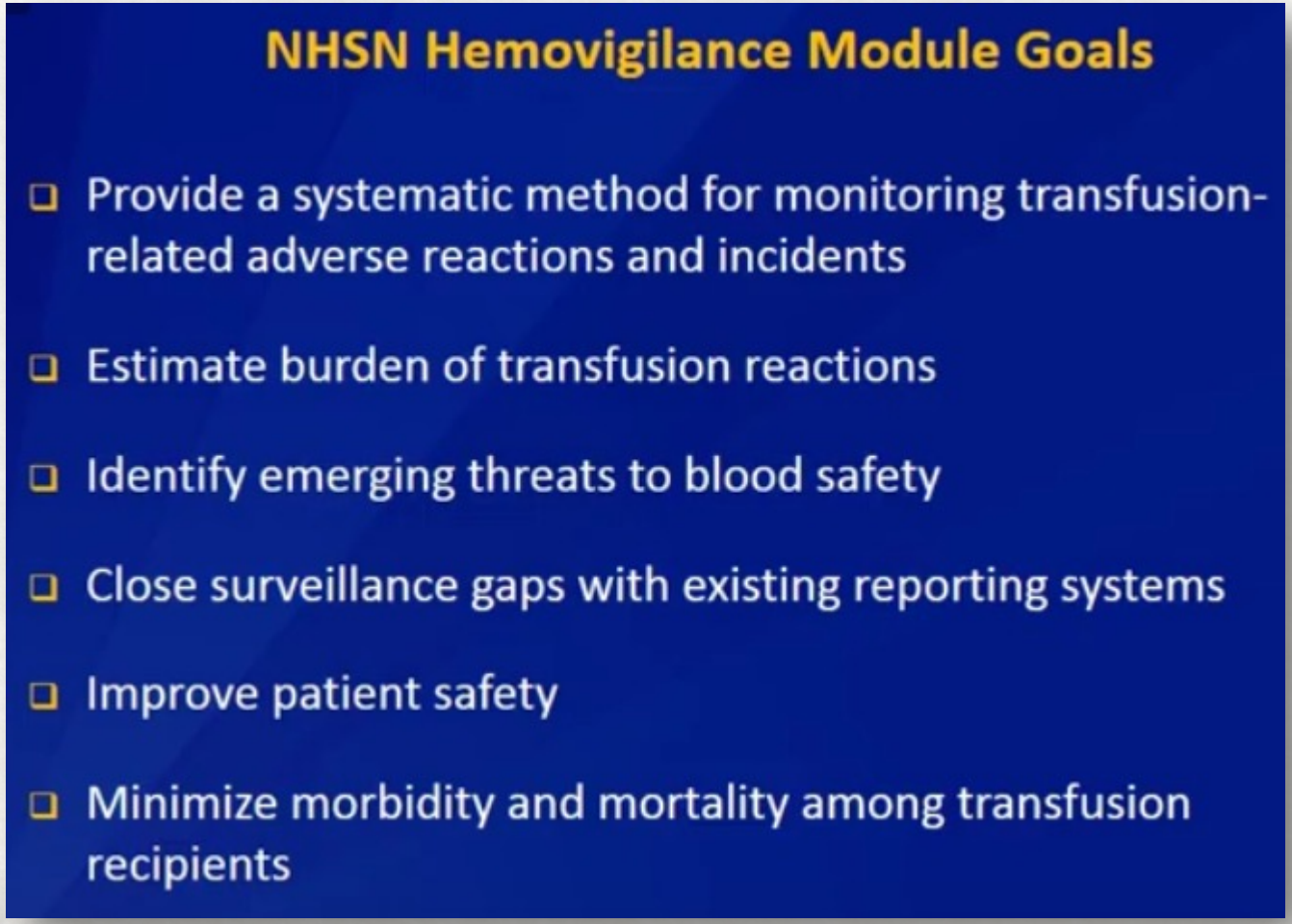
Recipient Hemovigilance

AABB Interorganizational Task Force on Biovigilance
(Adverse Reactions/Incidents Working Group)
in partnership with the
US Centers for Disease Control National Healthcare Safety Network (NHSN)



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Transfusion Reaction Classification

- CDC Hemovigilance
  - Categorizes TRxns by specific case definitions
    - "The surveillance definitions are not intended as clinical diagnostic criteria or to provide treatment guidance."
    - Primary source for FDA classification of fatal TRxns
  - Passive surveillance
  - Participation is voluntary
  - Fulfills regulatory requirement w/ AABB Standards (32nd ed.)
    - 7.3 Classifying Adverse Events
      - "The [Blood Bank/Transfusion Service] shall use nationally recognized classifications for donor and patient adverse events."
  - College of American Pathologist Accreditation Program Standards (2020) – N/A

U.S. Centers for Disease Control and Prevention. The National Healthcare Safety Network (NHSN) Manual: Biovigilance Component v2.6. Atlanta, GA: Division of Healthcare Quality Promotion, National Center for Emerging and Zoonotic Infectious Diseases. Available at: http://www.cdc.gov/nhsn/PDFs/Biovigilance/BV-HV-protocol-current.pdf. Accessed 4/8/2021.

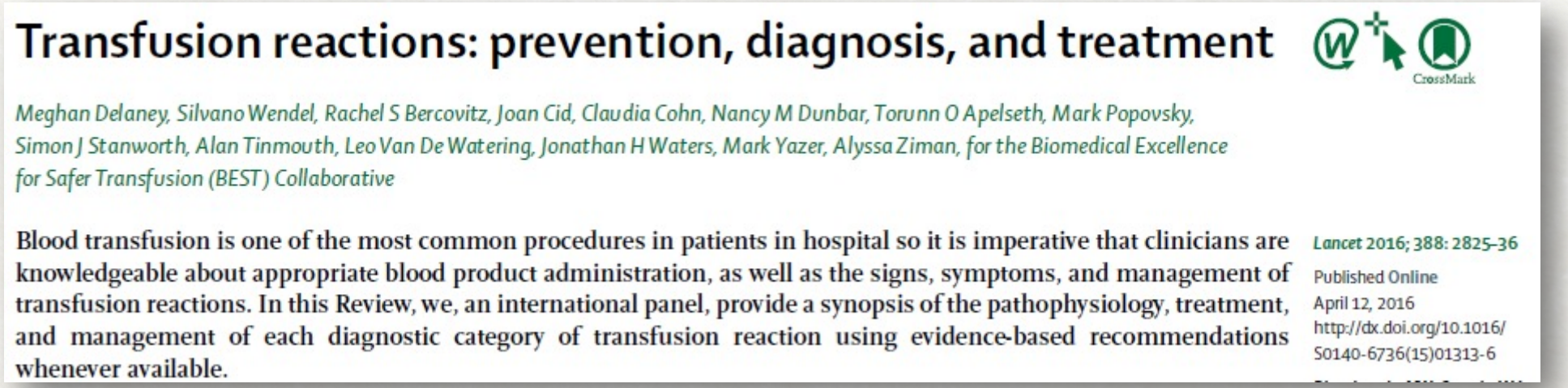
Section 3: Hemovigilance Module Adverse Reactions

Surveillance definitions are distinctly different from clinical definitions. Surveillance definitions are designed to capture data consistently and reliably in order to identify trends and inform quality improvement practices. The surveillance definitions are not intended as clinical diagnostic criteria or to provide treatment guidance.

Defined Adverse Reactions

- Transfusion-associated circulatory overload (TACO)
- Transfusion-related acute lung injury (TRALI)
- Transfusion-associated dyspnea (TAD)
- Allergic reaction (where severity is severe, life threatening, or death)
- Hypotensive transfusion reaction
- Febrile non-hemolytic transfusion reaction (FNHTR)
- Acute hemolytic transfusion reaction (AHTR)
- Delayed hemolytic transfusion reaction (DHTR)
- Delayed serologic transfusion reaction (DSTR)
- Transfusion-associated graft vs. host disease (TAGVHD)
- Post-transfusion purpura (PTP)
- Transfusion-transmitted infection (TTI)

U.S. Centers for Disease Control and Prevention. The National Healthcare Safety Network (NHSN) Manual: Biovigilance Component v2.6. Atlanta, GA: Division of Healthcare Quality Promotion, National Center for Emerging and Zoonotic Infectious Diseases. Available at: http://www.cdc.gov/nhsn/PDFs/Biovigilance/BV-HV-protocol-current.pdf. Accessed 4/8/2021.



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GRADE system

	Description	Methodological quality of supporting evidence	Implications
1A	Strong recommendation, high quality evidence	RCTs without important limitations or overwhelming evidence from observational studies	Strong recommendation, can apply to most patients in most circumstances without reservation
1B	Strong recommendation, moderate quality evidence	RCTs with important limitations (inconsistent results, methodological flaws, indirect, or imprecise) or exceptionally strong evidence from observational studies	Strong recommendation, can apply to most patients in most circumstances without reservation
1C	Strong recommendation, low quality or very low quality evidence	Observational studies or case series	Strong recommendation but might change when higher quality evidence becomes available
2A	Weak recommendation, high quality evidence	RCTs without important limitations or overwhelming evidence from observational studies	Weak recommendation, best action might differ depending on circumstances or patients' or societal values
2B	Weak recommendation, moderate quality evidence	RCTs with important limitations (inconsistent results, methodological flaws, indirect, or imprecise) or exceptionally strong evidence from observational studies	Weak recommendation; best action might differ depending on circumstances or patients' or societal values
2C	Weak recommendation, low quality or very low quality evidence	Observational studies or case series	Very weak recommendations; other alternatives might be equally reasonable

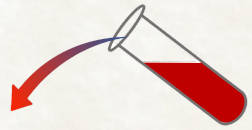
Used from Guyatt et al,[8] with permission. RCT=randomised controlled trial.

Table 2: **Evidence grading system by recommendation**

Delaney M, Wendel S, Bercovitz RS, Cid J, Cohn C, Dunbar NM, Apelseth TO, Popovsky M, Stanworth SJ, Tinmouth A, Van De Watering L, Waters JH, Yazer M, Ziman A; Biomedical Excellence for Safer Transfusion (BEST) Collaborative. Transfusion reactions: prevention, diagnosis, and treatment. Lancet. 2016 Dec 3;388(10061):2825-2836. doi: 10.1016/S0140-6736(15)01313-6. Epub 2016 Apr 12. PMID: 27083327.

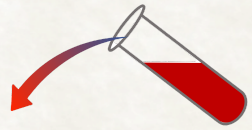
Clinical and laboratory work-up of suspected reactions

Testing
Classification
Prevention



Recognizing Reactions: signs and symptoms

- Fever (at least 1 degree C rise in temperature)
- Chills or rigors
- Respiratory distress
  - Wheezing, dyspnea, cyanosis
- Acute changes in blood pressure
- Abdominal, chest, flank, or back pain
- Skin changes
  - Hives, itching, edema
- Hemoglobinuria
- Nausea/vomiting
- Abnormal bleeding
- Oliguria/anuria

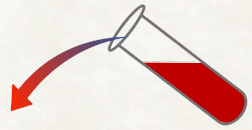


- *I THINK MY PATIENT IS HAVING A TRANSFUSION REACTION…*

  HAS THE TRANSFUSION BEEN STOPPED?

Suspected reaction: Clinical

1. Stop the transfusion
   - Keep line open w/ NS
2. Recheck blood product labeling and patient ID
3. Follow institution's BB policy
   1. At MMC: Product ID tag contains section with instructions:
      - Return remainder of product
      - Send pink top tube (Transfusion Reaction W/U Order in Epic) for:
        - Visual inspection for gross hemoglobinemia
        - DAT (Polyspecific and IgG)
        - Repeat Front type



Suspected reaction: Clinical

Document:

1. TRxn date/time
2. vol transfused
3. s/sx
4. VS
5. mgmt and clinical response
6. specimens that were sent to BB

Suspected reaction: Required Lab w/u

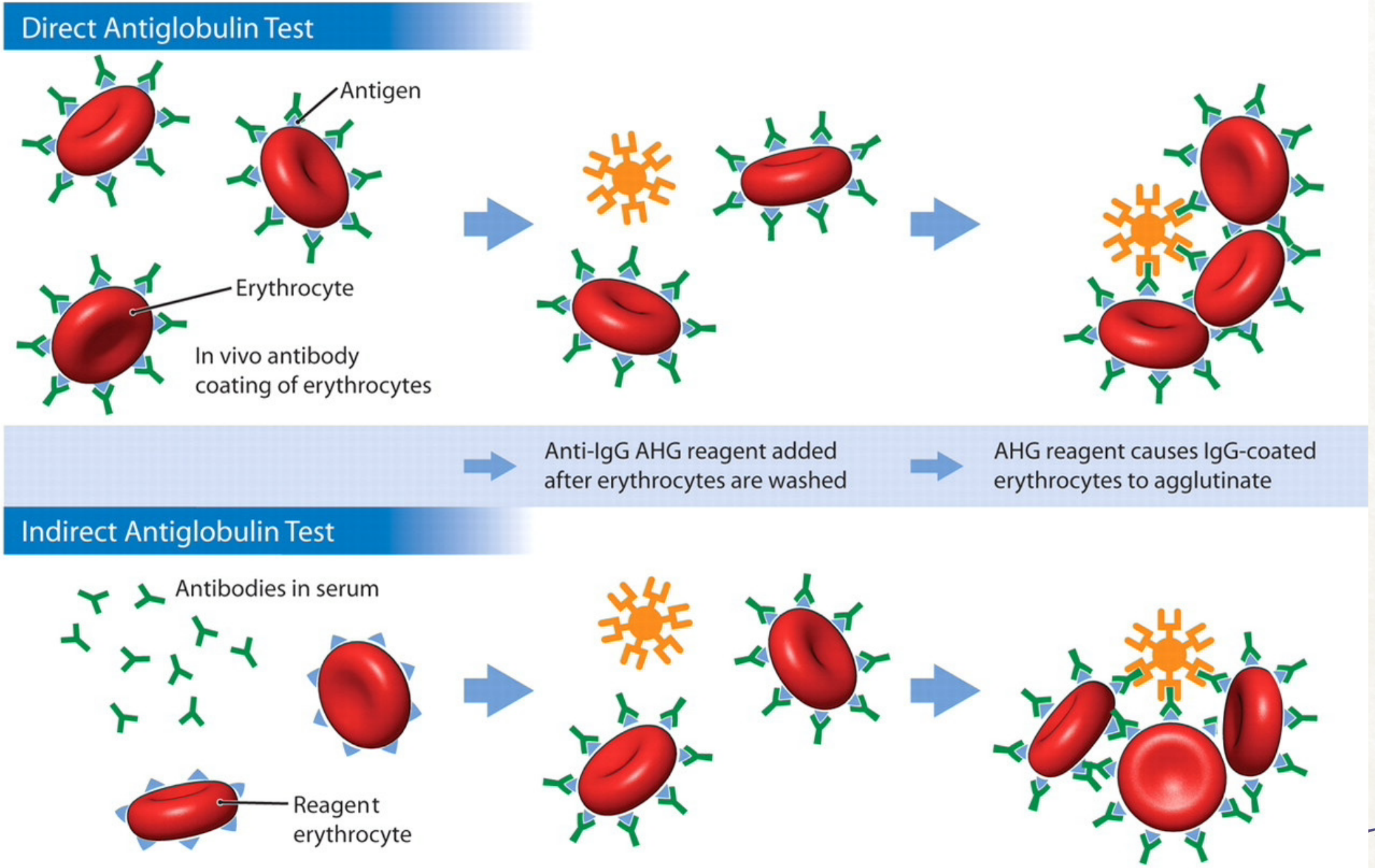
College of American Pathologist Accreditation Program Transfusion Medicine Checklist (2020)

- **TRM.41850 Investigation of Suspected Hemolytic Transfusion Reaction**
- The immediate investigation of a suspected hemolytic transfusion reaction includes all of the following.

1. Examination of patient identification, blood unit labels, and all pre-reaction records for possible errors in patient or blood identification at the bedside and in the laboratory
2. Visual examination of post-reaction and pre-reaction (if available) serum or plasma for evidence of hemolysis
3. ABO and direct antiglobulin test on post-reaction patient (recipient) blood sample

AABB Standards for Blood Banks and Transfusion Services, 32nd Edition

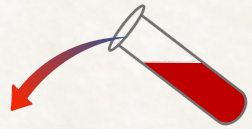
- **7.5.2.1 For suspected hemolytic transfusion reactions the evaluation shall include the following:**
  1) The patient's posttransfusion reaction serum or plasma shall be inspected for evidence of hemolysis. Pretransfusion samples shall be used for comparison.
  2) A repeat ABO group determination shall be performed on the posttransfusion sample.
  3) A direct antiglobulin test shall be performed on the posttransfusion sample. If the result is positive, the most recent pretransfusion sample shall be used for comparison.



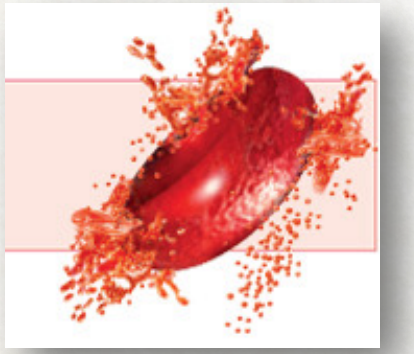
Zarandona JM, Yazer MH. The role of the Coombs test in evaluating hemolysis in adults. CMAJ. 2006 Jan 31;174(3):305-7. doi: 10.1503/cmaj.051489. PMID: 16446468; PMCID: PMC1373708.

Classifying Transfusion Reactions

	Febrile	Afebrile
Acute	Acute Hemolytic Febrile Non-hemolytic Bacterial Contamination TRALI Thermal/mechanical hemolysis	TACO Allergic Pre-medicated FNHTR
Delayed	Delayed hemolytic TA-GVHD	Post-transfusion Purpura Iron overload



Acute Hemolytic Reaction

Presentation 	• Fever/chills in >80% • Pain: back, flank, infusion site or along infusion vein • Sense of “impending doom” or anxiety • Dyspnea • Tachycardia • Hypotension • DIC or bleeding/oozing from IV sites • Hemoglobinuria
Incidence	• 2.2-7.9 per 100,000 units • Fatal AHTR: 1 per 1.8 million units • Products: RBCs, apheresis platelets • Case outcomes: 7% mortality; 22% major morbidity
Pathogenesis	Interaction of pre-formed antibodies to RBC antigens → Complement & phagocyte activation, intravascular hemolysis w/ anaphylatoxin production

Supplement to: Delaney M, Wendel S, Bercovitz RS, et al, for the Biomedical Excellence for Safer Transfusion (BEST) Collaborative. Transfusion reactions: prevention, diagnosis, and treatment. Lancet 2016; published online April 12. http://dx.doi.org/10.1016/S0140-6736(15)01313-6.

Acute Hemolytic Reaction

Management	1. STOP the transfusion 2. Recheck patient and product ID 3. Treat as shock/DIC: Maintain IV access 4. IV fluids: - NS 0.5 – 1 L over 10 min - Lasix 40 mg IVP - maintain urinary output >100 ml/hr (adults) or >1ml/kg/hr 5. AVOID TRANSFUSION until lab workup is complete
Work-Up	• Return product with attached tubing - visual inspection - clerical check • Post-transfusion patient sample - Repeat ABO, Hemolysis check, DAT

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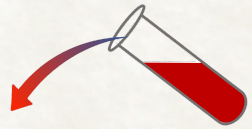

- *Your patient is having a transfusion reaction…*
- *What lab indices might be helpful?*

What results might be expected with an acute hemolytic reaction?

• DAT	+ (or -)
• Cr	↑
• Bilirubin (indirect)	↑
• AST	↑
• LDH	↑
• Haptoglobin	↓
• UA (heme)	↑

- Serial CBCs also indicated
- DIC labs (PT, PTT, Fibrinogen and D-dimer) if high suspicion for intravascular hemolysis or increased bleeding

Acute Hemolytic Reaction

Prevention	1.	Technology/procedures ensuring accurate pt ID • Two person check	Grade 1. 1A
	2.	ABO Confirmation • Two sample policy	2. 1A

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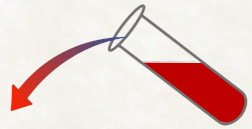

Febrile Nonhemolytic Reaction

Presentation/ Definition
CDC Hemovigilance Module Surveillance Protocol v2.6 www.cdc.gov/nhsn
	• Occurs during or w/in 4 hrs of transfusion cessation &
	  • >1ºC Δ f/ pre- & temp above 38ºC
	  • Or chills/rigors present
	• Clinicolab dx of exclusion

Incidence	• 1-3:100 pre-storage LR RBCs • 1.4:100 apheresis platelets • 11-26:100 post-storage LR (obsolete)
Pathogenesis	• Multifactorial: pyogenic cytokines, recipient HNA or HLA antibodies, biological response modifiers (BRMs)/bioactive lipids, donor HNA or HLA antibodies
Work-Up	Return product with attached tubing - visual inspection - clerical check Post-transfusion patient sample - Repeat ABO, Hemolysis check, DAT

Supplement to: Delaney M, Wendel S, Bercovitz RS, et al, for the Biomedical Excellence for Safer Transfusion (BEST) Collaborative. Transfusion reactions: prevention, diagnosis, and treatment. Lancet 2016; published online April 12. http://dx.doi.org/10.1016/S0140-6736(15)01313-6.

July 7, 2021

Febrile Nonhemolytic Reaction

Management	1. Antipyretics for fever 2. Meperidine for shivering	1. 1A 2. 1C
Prevention	**1. No role for antipyretic prophylaxis[2]** 2. Pre-storage LR 3. Plasma removal 4. Platelet additive solution • FNHTR rate 0.5% → 0.17%	**1. 1A** 2. 1A 3. 2C 4. 1B

"Premedication with antipyretics does not decrease rate of reactions in most patients and should be discouraged (grade 1A)." [2]

1. Supplement to: Delaney M, Wendel S, Bercovitz RS, et al, for the Biomedical Excellence for Safer Transfusion (BEST) Collaborative. Transfusion reactions: prevention, diagnosis, and treatment. Lancet 2016; published online April 12. http://dx.doi.org/10.1016/S0140-6736(15)01313-6.
2. Delaney, Meghan, et al. "Transfusion reactions: prevention, diagnosis, and treatment." The Lancet 388.10061 (2016): 2825-2836.

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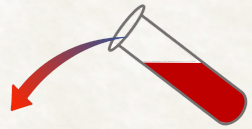

Suspected Septic Transfusion Reaction

Presentation	• May be suspected w/ following s/sx:
	  • Sudden onset temperature increase (>2ºC or >39ºC)
	  • Rigors
	  • Tachycardia
	  • Hypotension
	  • Septic shock
	  • DIC
	  • Nausea/vomiting
	• Requires cx to confirm; d/dx AHTR and FNHTR

Incidence	Apheresis platelets: 9.1-14.3 per 1 million units
	  • 1:5000 (+) culture rate
	RBCs: 5.6 per 10 million units
	  • 1:170,000 (+) culture rate
	Plasma: 2.8 per 10 million units

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Suspected Septic Transfusion Reaction

Pathogenesis	(1) Donor skin - inadequate skin cleansing/disinfection - introduction of skin plug into donor bag, with bacteria hiding in adnexal structures or scarred, pitted skin (2) Asymptomatic/transient donor bacteremia - usually normal GI flora (GNR) (3) Introduction during collection, processing, or transfusion
Work-Up	Return product with attached tubing - visual inspection - clerical check Post-transfusion patient sample - Repeat ABO, Hemolysis check, DAT Product gram stain and culture (alert BB if high suspicion) Culture patient

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Suspected Septic Transfusion Reaction

Definition
CDC Hemovigilance Module Surveillance Protocol v2.6 www.cdc.gov/nhsn
	• Definitive product imputability requires:
	  • Isolation of same pathogen in recipient and product AND
	  • No other potential exposures	

Management	Empiric broad-spectrum antibiotics	1A
Prevention	Donor collection policies: 1. Diversion of first 10-50 mL 2. Bacterial surveillance of platelet units	 1. 1B 2. 1B

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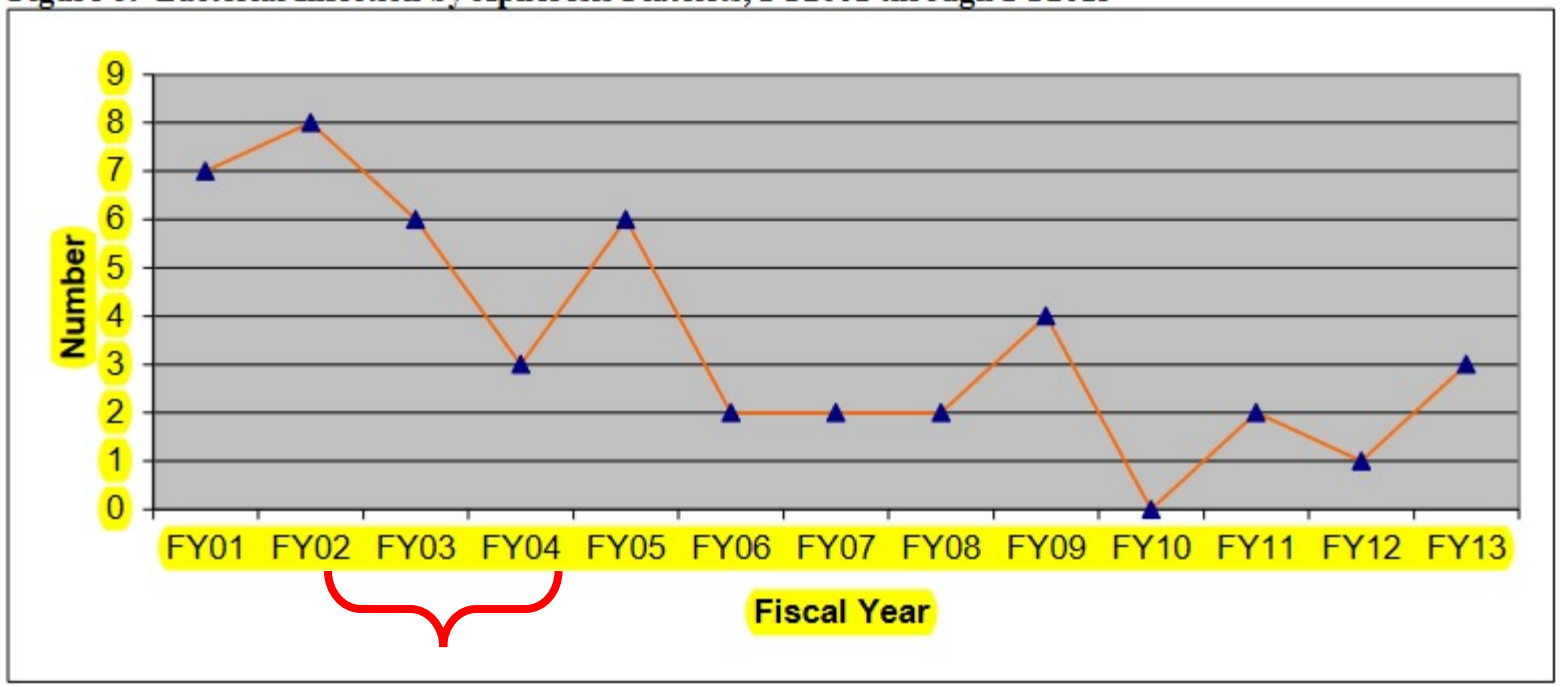
Transfusion Fatalities Reported to FDA

Fatalities Reported to FDA Following Blood Collection and Transfusion Page 11 of 13

Figure 6: Bacterial Infection by Apheresis Platelets, FY2001 through FY2013



- 2002-2004:
  - CAP & AABB issue guidance and update their accreditation standards to require practices that limit contamination
    - Suggested diversion, addressed phlebotomy techniques and recommended surveillance culture
    - Surveillance cx implementation a/w reduction in gram (-) contamination/STR rate in subsequent period

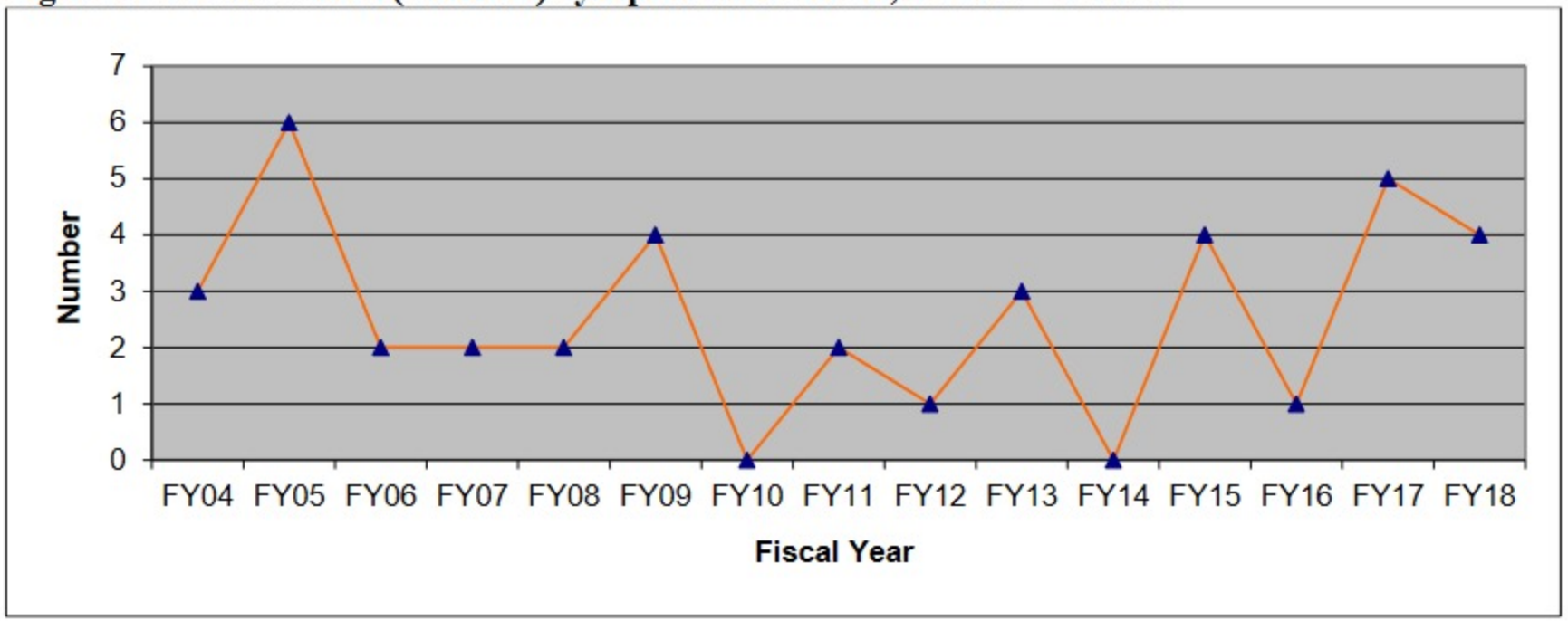
https://olis.leg.state.or.us/liz/2015R1/Downloads/CommitteeMeetingDocument/51408

https://www.aabb.org/docs/default-source/default-document-library/resources/association-bulletins/ab12-04.pdf

Transfusion Fatalities Reported to FDA

Fatalities Reported to FDA Following Blood Collection and Transfusion Annual Summary for FY2018

Figure 6: Contamination (bacterial) by Apheresis Platelets, FY2004 – FY2018



https://www.fda.gov/media/136907/download

Detection of septic transfusion reactions to platelet transfusions by active and passive surveillance

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Key Points

- Bacterial sepsis from contaminated platelet transfusions continues to occur despite recent interventions; additional measures are needed.
- STR to platelet transfusion is frequently not recognized or reported; use of recent AABB criteria showed highest diagnostic sensitivity.

Septic transfusion reactions (STRs) resulting from transfusion of bacterially contaminated platelets are a major hazard of platelet transfusion despite recent interventions. Active and passive surveillance for bacterially contaminated platelets was performed over 7 years (2007-2013) by culture of platelet aliquots at time of transfusion and review of reported transfusion reactions. All platelet units had been cultured 24 hours after collection and released as negative. Five sets of STR criteria were evaluated, including recent AABB criteria; sensitivity and specificity of these criteria, as well as detection by active and passive surveillance, were determined. Twenty of 51 440 platelet units transfused (0.004%; 389 per million) were bacterially contaminated by active surveillance and resulted in 5 STRs occurring 9 to 24 hours posttransfusion; none of these STRs had been reported by passive surveillance. STR occurred only in neutropenic patients transfused with high bacterial loads. A total of 284 transfusion reactions (0.55%) were reported by passive surveillance. None of these patients had received contaminated platelets. However, 6 to 93 (2.1%-32.7%) of these 284 reactions met 1 or more STR criteria, and sensitivity of STR criteria varied from 5.1% to 45.5%. These results document the continued occurrence of bacterial contamination of platelets resulting in STR in neutropenic patients, failure of passive surveillance to detect STR, and lack of specificity of STR criteria. These findings highlight the limitations of reported national STR data based on passive surveillance and the need to implement further measures to address this problem such as secondary testing or use of pathogen reduction technologies. (*Blood*. 2016;127(4):496-502)

Hong, Hong, et al. "Detection of septic transfusion reactions to platelet transfusions by active and passive surveillance." Blood 127.4 (2016): 496-502.

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2019-2020: Citing Hong et al 2016 and the cont'd reporting of fatal STRs w/ current practice, FDA updates its Plt Guidance

Bacterial Risk Control Strategies for Blood Collection Establishments and Transfusion Services to Enhance the Safety and Availability of Platelets for Transfusion

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Guidance for Industry

- Gives options for risk mitigation:
  1. Enhanced bacterial testing
     - Large Volume, Delayed Sampling (LVDS)
       - Sampling requirements for cx changed from former practice of 8 mL @ 24hrs, allowing aerobic cx only, to either:
         - 16 @ 36 using aerobic and anerobic for 5 day storage
         - 16 @ 48 using aerobic and anerobic for 7 day storage
  2. Pathogen Reduction Technology
     - Uses photosensitive nucleic acid cross-linkers (e.g., psoralen) to inactivate infectious agents

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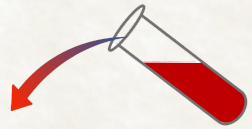
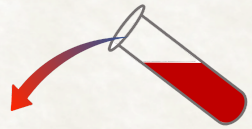
Classifying Transfusion Reactions

	Febrile	Afebrile
Acute	Acute Hemolytic Febrile Non-hemolytic Bacterial Contamination TRALI Thermal/mechanical hemolysis	TACO Allergic Pre-medicated FNHTR
Delayed	Delayed hemolytic TA-GVHD	Post-transfusion Purpura Iron overload



TACO

Clinical Presentation	Acute onset resp s/sx w/in 12 hrs post-transfusion: • dyspnea, tachypnea, decreased O2 sats • Pulm edema on imaging • New/worsened fluid overload signs: crackles, orthopnea, cough, S3, frothy sputum
Incidence	*Uncertain estimates 2/2 underreporting:* 1-8% of transfused recipients, 6% in ICU patients 1.4 per 1,000 units transfused
Pathogenesis	Inability of the recipient's cardiopulmonary system to tolerate the volume or rate of transfusion → pulmonary edema Risk factors: Elderly, h/o ESRD/HD, CHF



TACO Surveillance definitions

Organization	ISBT-IHN-AABB (international consensus) and CDC HM v2.6	Examples www.cdc.gov/nhsn
Surveillance Case Definition	At least 1 required(*) criterion w/ onset w/in 12 hrs, & total of ≥3 criteria	
Resp system*	1. Acute/worsening resp compromise*, OR 2. Acute/worsening pulm edema*	1. dyspnea, tachypnea, decreased O2 sats 2. Imaging, crackles, orthopnea, cough, S3, frothy sputum
CV system	Unexplained CV changes	↑ CVP, Left HF s/sx (new tachycardia, hypertension, widened pulse pressure, JVD, ↑ cardiac silhouette or peripheral edema)
Fluid	Evidence of fluid overload / improvement w/ diuresis	
Biomarkers	Elevated biomarker (e.g., NT-pro-BNP) > 1.5 pretransfusion	

Wiersum-Osselton, Johanna C., et al. "Revised international surveillance case definition of transfusion-associated circulatory overload: a classification agreement validation study." The Lancet Haematology (2019).

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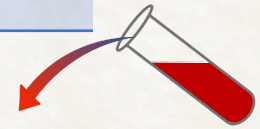
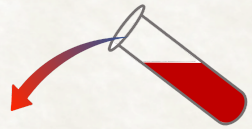


TACO

Management	Diuretics & supportive care	
Prevention	1. Slow infusion rate	1. 2C
	2. Avoid concurrent crystalloids	2. 2C
	3. Monitor VS closely	3. 2C

Supplement to: Delaney M, Wendel S, Bercovitz RS, et al, for the Biomedical Excellence for Safer Transfusion (BEST) Collaborative. Transfusion reactions: prevention, diagnosis, and treatment. Lancet 2016; published online April 12. http://dx.doi.org/10.1016/S0140-6736(15)01313-6.



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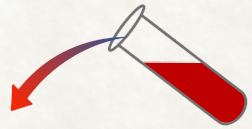


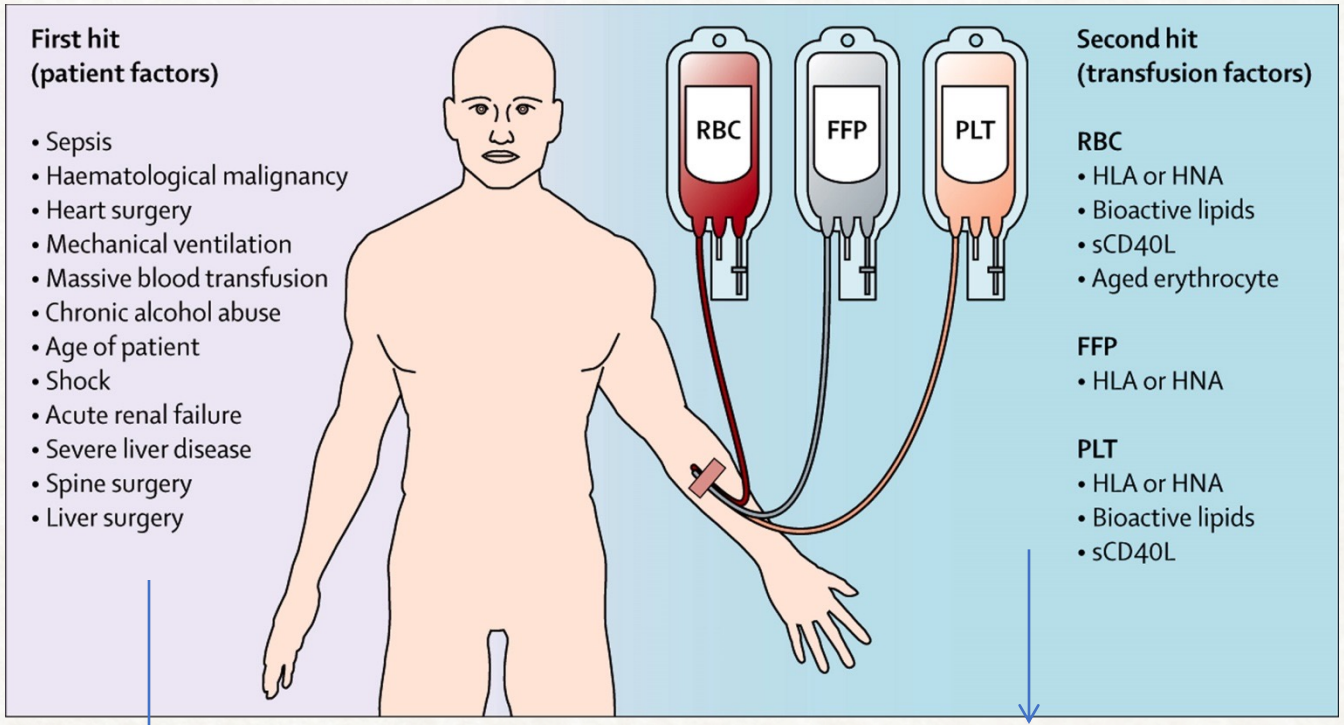
TRALI

Clinical Presentation	• **Hypoxemia**: in an intubated patient this could manifest as a change in oxygenation or increased oxygen requirements (100 percent, by definition) • **Pulmonary infiltrates on chest radiography** (100 percent, by definition; the cardiac silhouette is classically normal) • If previously intubated, pink frothy airway secretions from the endotracheal tube (56 percent) • Fever (33 percent) • Hypotension (32 percent) • Cyanosis (25 percent)
Incidence (post risk mitigation)	Plasma: 0.4 per 100,000 Apheresis platelets: 1 per 100,000 RBC: 0.5 per 100,000

Van Stein, Daniëlle, et al. "Transfusion-related acute lung injury reports in the Netherlands: an observational study." Transfusion 50.1 (2010): 213-220.

TRALI

Pathogenesis



Primes Neutrophils

Transfusion factors activates neutrophil
Pulmonary capillary leak and edema

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TRALI Surveillance definitions

Organization	CDC Hemovigilance Module Surveillance Protocol v2.6 www.cdc.gov/nhsn	Delphi panel of experts (international)

Surveillance Dx criteria	Must meet all criteria:
	• ALI w/in 6 hrs
	• Hypoxemia, either by:
	  • PaO2/FiO2 ≤300
	  • SaO2 <90% on RA
	  • Other clinical evidence
	• Bilateral infiltrates on imaging
	• No evidence of pre-existing ALI
	• No left atrial hypertension/TACO
		TRALI Type I – No ARDS risks
		• W/in 6 hrs:
		1. Acute onset
		2. Hypoxemia, either by:
		1. PaO2/FiO2 ≤300
		2. SaO2 <90% on RA
		3. Bilateral pulm edema on imaging
		4. No left atrial hypertension
		TRALI Type II – pts w/ ARDS/risks but who experience:
		1. Acute hypoxemia (defined above) post transfusion
		2. Despite stable resp status 12hrs prior to transfusion

Vlaar APJ, Toy P, Fung M, et al. A consensus redefinition of transfusion-related acute lung injury. Transfusion 2019; 59(7):2465-2476. https://onlinelibrary.wiley.com/doi/full/10.1111/trf.15311

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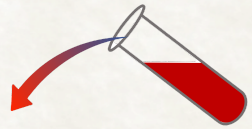


TABLE 4. ARDS risk factors according to the Berlin definition (with slight modification due to consideration of the transfusion setting)*

Direct
Pneumonia
Aspiration of gastric contents
Inhalational injury
Pulmonary contusion
Pulmonary vasculitis
Drowning
Indirect
Nonpulmonary sepsis
Major trauma†
Pancreatitis
Severe burns
Noncardiogenic shock*
Drug overdose

* Multiple (massive) transfusion is included in the Berlin definition of ARDS risk factors; however, we have removed it from this list because we recommend that ARDS occurring during or within 6 hours after multiple transfusions be classified as TRALI, provided no other ARDS risk factors (as listed in this table) are present. One example of a case scenario of multiple (massive) transfusion that fits the criteria for TRALI Type I is acute gastrointestinal bleeding without trauma or any other ARDS risk factors.

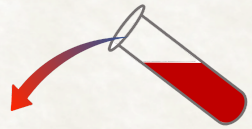
† Major trauma is defined as multiple fractures (two or more major long bones, an unstable pelvic fracture, or one major long bone and a major pelvic fracture).[20] An alternate definition proposed by the Panel is an injury severity score of greater than 15.

Vlaar APJ, Toy P, Fung M, et al. A consensus redefinition of transfusion-related acute lung injury. Transfusion 2019; 59(7):2465-2476. https://onlinelibrary.wiley.com/doi/full/10.1111/trf.15311

TRALI D/dx Surveillance definitions

Organization	Delphi panel of experts (international)
Surveillance Dx criteria for other entities in the d/dx	• TRALI/TACO cannot be distinguished: Findings compatible w/ TRALI and w/ TACO and/or lack of data to establish LAH status • ARDS: Pts who have risk factors for ARDS and deteriorate as a result of them (unrelated to transfusion / pt already deteriorating)

Vlaar APJ, Toy P, Fung M, et al. A consensus redefinition of transfusion-related acute lung injury. Transfusion 2019; 59(7):2465-2476. https://onlinelibrary.wiley.com/doi/full/10.1111/trf.15311



TRALI

Work-Up	Return product with attached tubing - visual inspection - clerical check Post-transfusion patient sample - Repeat ABO, Hemolysis check, DAT Patient (and donor) testing may be performed: - HLA/HNA typing and antibody testing *(in 30% of cases no antibody is found)*
Management	Supportive (1A) ECMO (2C)
Prevention	Platelet additive solutions (2C) Washed cellular products (2C) Screening & selecting blood donors (2C)

Supplement to: Delaney M, Wendel S, Bercovitz RS, et al, for the Biomedical Excellence for Safer Transfusion (BEST) Collaborative. Transfusion reactions: prevention, diagnosis, and treatment. Lancet 2016; published online April 12. http://dx.doi.org/10.1016/S0140-6736(15)01313-6.

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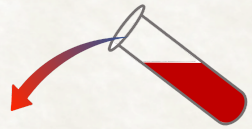

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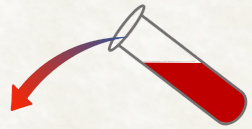
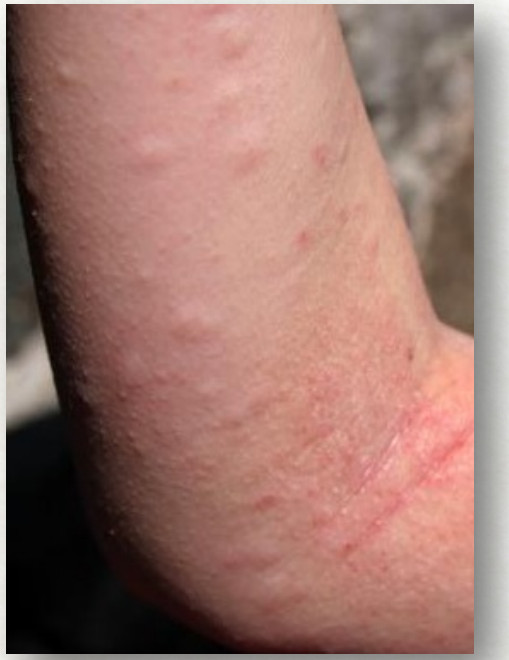


Allergic Transfusion Reactions



Within four hours of transfusion

CDC Hemovigilance Module Surveillance Protocol v2.6
www.cdc.gov/nhsn

Mild

- Urticarial, itching, erythema

Moderate

- Mucosal involvement: Edema/erythema of conjunctiva, periorbital, lips, tongue, uvula, bradycardia, hypotension
- Angioedema

Severe

- Anaphylactic
- Respiratory : laryngeal (tightness in the throat, dysphagia, dysphonia, hoarseness, stridor) or pulmonary (dyspnea, cough, wheezing/bronchospasm, hypoxemia)
- Cardiovascular/CNS: hypotension, syncope, collapse, incontinence
- Gastrointestinal: abdominal pain, vomiting

Allergic Transfusion Reactions

Incidence[1]	• Overall: 112.2 per 100,000 units • RBCs: 53.6 per 100,000 units • Platelets: 302 per 100,000 units • Plasma: 105.7 per 100,000 units • Cryoprecipitate: 4.8 per 100,000 units • Granulocytes: Unknown • Anaphylaxis: 8 per 100,000 units
Pathogenesis	1) Recipient/donor pre-formed IgE against donor/recipient antigens (bidirectional) causes degranulation of recipient mast cells/basophils 2) Anaphylactic: same as (1), w/ serum protein deficiencies occ implicated: • ?IgA deficiency w/ anti-IgA in recipient (***phenomenon disputed***[2-4]) • Haptoglobin deficiency

1. Supplement to: Delaney M, Wendel S, Bercovitz RS, et al, for the Biomedical Excellence for Safer Transfusion (BEST) Collaborative. Transfusion reactions: prevention, diagnosis, and treatment. Lancet 2016; published online April 12. http://dx.doi.org/10.1016/S0140-6736(15)01313-6.
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Allergic Transfusion Reactions

Work-Up for moderate-to-severe reactions	Return product with attached tubing - visual inspection - clerical check Post-transfusion patient sample - Repeat ABO, Hemolysis check, DAT For anaphylaxis, consider w/u for serum protein deficiencies (IgA, haptoglobin) and other allergens (e.g., drugs, latex)

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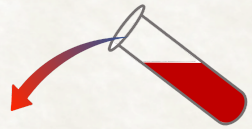

Allergic Transfusion Reactions

Management	• STOP the transfusion • Administer H_1 antihistamine (e.g., diphenhydramine 25 to 50 mg, PO or IV) (1A) - *If purely urticarial and vital signs stable*, may resume transfusion if reaction responds to treatment • Moderate reaction: - Add corticosteroids (hydrocortisone 100 mg IV, prednisone 50 mg PO or methylprednisolone 125 mg IV) (1C)

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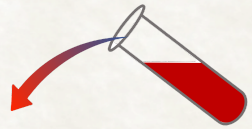

Allergic Transfusion Reactions

Management

- Severe/Anaphylactic:
  - Epinephrine, 0.01 mg/kg of a 1:1000 (1 mg/mL) solution, to a maximum of 0.5 mg (adult) or 0.3 mg (child) (1A)
  - Airway maintenance and High-flow (>8-10L via face mask) supplemental O2 (1C)
  - rapid 0.5-2L bolus resuscitation of hypotension with crystalloid solution (0.9% saline) (1C)
  - Recumbent position if tolerated
  - Adjuncts: antihistamine (H1 and H2), albuterol 2.5 to 5 mg/3mL (adult), 2.5 mg/3mL (child), Hydrocortisone 200 mg (adult) maximum 100 mg (child) or Methylprednisolone 50–100 mg (adult), 1 mg/kg, maximum 50 mg (child) (1C)

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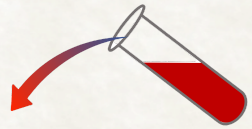

Allergic Transfusion Reactions

Prevention	Usually an idiosyncratic interaction between recipient and specific donor proteins that cannot be identified
	• **In patients with no history of reaction or only previous *mild* allergic reactions, pre-medication with antihistamines and/or glucocorticoids is <u>NOT</u> indicated** (2C)
	• Severe or repeat moderate reactions:
	  • Supernatant removal or wash (1C)
	  • or platelet additive solution (1C)
	  • pre-medicate w/ antihistamines (2C)

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Allergic Transfusion Reactions

Prevention	Anaphylactic • Discuss w/ allergist/immunologist and Transfusion Medicine (1C) • Administer transfusion in clinical area with direct observation and resuscitation capabilities (2C) • Washed/plasma-reduced cellular components (2C) • Premedication w/ antihistamine (2C)

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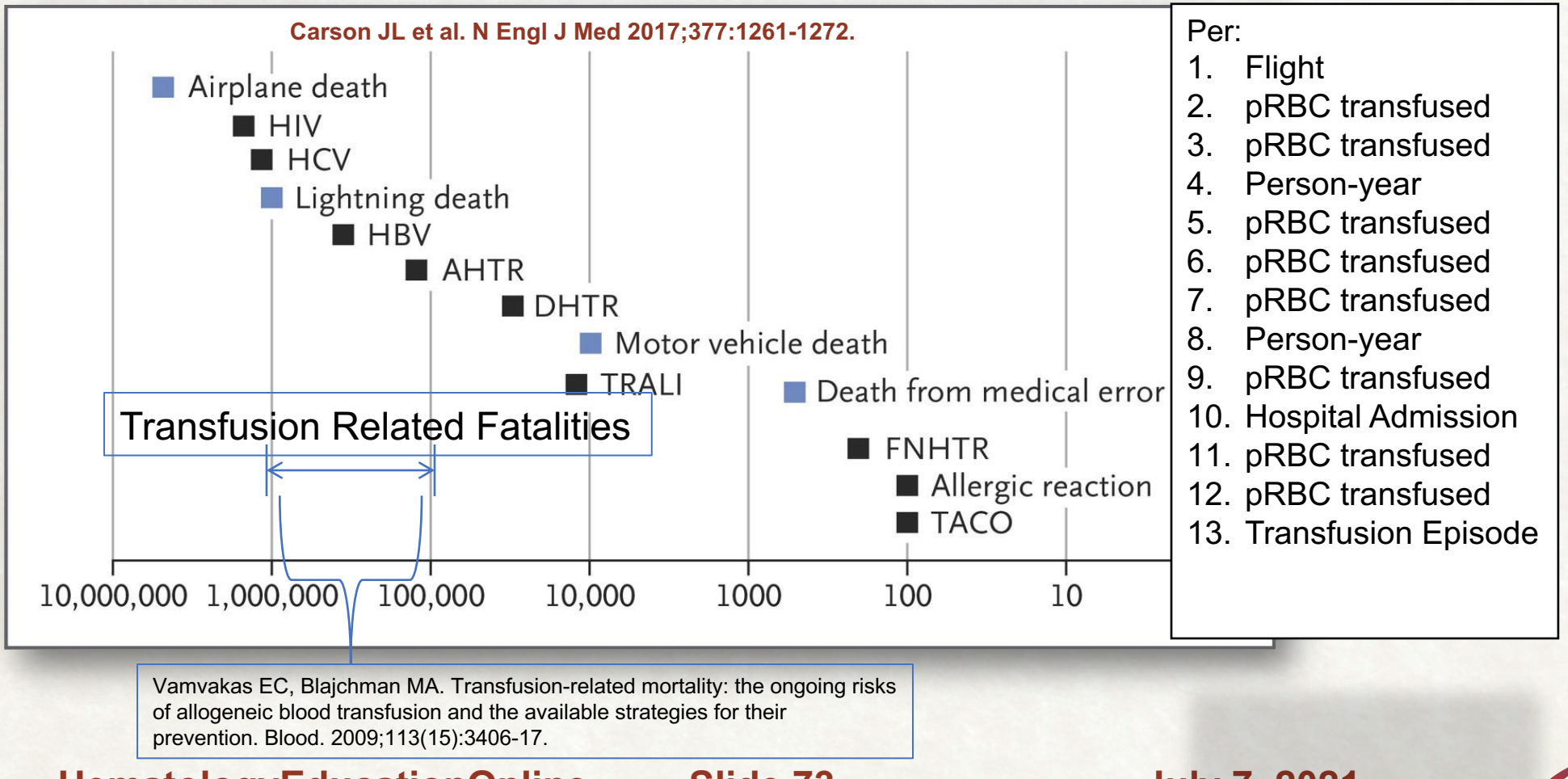
Infectious and Noninfectious Adverse Effects of Red-Cell Transfusions as Compared with Other, Unrelated Risks



Per:
1. Flight
2. pRBC transfused
3. pRBC transfused
4. Person-year
5. pRBC transfused
6. pRBC transfused
7. pRBC transfused
8. Person-year
9. pRBC transfused
10. Hospital Admission
11. pRBC transfused
12. pRBC transfused
13. Transfusion Episode

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Additional References

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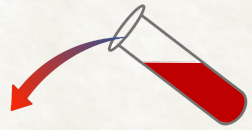

Thank you

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