

Hemovigilance Definitions of Transfusion Reactions: Case Studies



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Disclosures

- I have no relevant financial relationships to disclose.

Learning Objectives

- Describe the evolving history of hemovigilance-based transfusion reaction definition
- Summarize the clinical utility and benefit of establishing a harmonized classification schema
- Review at least 3 transfusion reaction cases and their classification according to current hemovigilance definitions

Hemovigilance

- *'hema'*: blood *'vigilans'*: watchful
- Surveillance procedures for collection of errors and adverse events
- Blood donation → → → Recipient transfusion



- Goal: Improve donor and patient safety

<http://bloodcenter.org/learn/faq/blood-donation/some-common-faq-asking-questions-that-require-a-blood-transfusion>
<http://redcross.org/learn/faq/blood-donation/some-common-faq-asking-questions-that-require-a-blood-transfusion>

Historical background


- 1993: first hemovigilance system in Japan
- 1994: France *nationwide* hemovigilance system
- 1995: hemovigilance became governed by legal requirements set in EU Directives
- 1998: European Hemovigilance Network
- 2009: International Hemovigilance Network (IHN)

RIP de Vries et al. Vox Sanguinis (2011) 100, 60-67
Hemovigilance: An effective tool for improving transfusion safety-2012-Edited by RIP de Vries and J-C Faber

Hemovigilance in the US

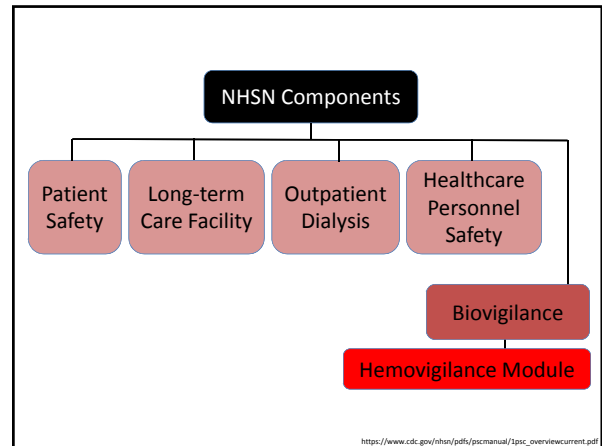
- 2006: Dept. of HHS's Advisory Committee on Blood Safety and Availability (ACBSA) recommended a national surveillance system to monitor blood product recipient outcome
- AABB: *'Inter-organizational Task Force on Biovigilance'*
 - Chose CDC's **National Healthcare Safety Network (NHSN)** as the national surveillance system for blood system event tracking

NHSN



- Secure, Internet-based surveillance system
 - Integrates patient and healthcare personnel safety surveillance systems managed by:
 - Division of Healthcare Quality Promotion (DHQP)
 - Covers some reporting programs operated by CMS
 - Used by some US states for mandatory reporting of HAI (Healthcare-associated infections)

https://www.cdc.gov/nhsn/pdfs/pscmanual/1psc_overviewcurrent.pdf



National Healthcare Safety Network (NHSN)

Blood Safety Surveillance

Resources for NHSN Users

- Facility Enrollment or Component Activation
- Training
- Protocol** ←
- Data Collection Forms
- Supporting Material
- Quick Reference Guides
- Analysis Resources
- Electronic Reporting
- FAQs

<https://www.cdc.gov/nhsn/acute-care-hospital/bio-hemo/index.html>

Facility Enrollment or Component Activation

Training


Protocol

- NHSN Manual: Biovigilance Component Protocol January 2017 ←
- Guidelines and procedures for monitoring hemovigilance.

Table of Contents:

- Section 1: Hemovigilance Module Surveillance Overview
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 - Adverse Reaction Case Classification Criteria Tables
 - Transfusion-associated circulatory overload (TACO)
 - Transfusion-related acute lung injury (TRALI)
 - Transfusion-associated sepsis (TASIS)
 - Allergic reaction
 - Haemolytic transfusion reaction
 - Extravascular hemolytic transfusion reaction (EVTFR)
 - Acute hemolytic transfusion reaction (AHTR)
 - Delayed hemolytic transfusion reaction (DHTR)
 - Transfusion-associated graft-versus-host disease (TA-GVHD)
 - Post-transfusion purpura (PTP)
 - Transfusion-transmitted infection (TTI)
- Other/Unknown
- Adverse Reaction Glossary

<https://www.cdc.gov/nhsn/acute-care-hospital/bio-hemo/index.html>



NHSN Biovigilance Component
Hemovigilance Module Surveillance Protocol v2.4
www.cdc.gov/nhsn

National Healthcare Safety Network Biovigilance Component Hemovigilance Module Surveillance Protocol

<https://www.cdc.gov/nhsn/pdfs/biovigilance/bv-hv-protocol-current.pdf>

Hemovigilance Module Surveillance Protocol

- March 2009: version 1.0 released
 - Pilot year, 9 facilities
- June 2010: version 1.1
- Currently: version 2.4 (Jan 2017)
- 2 main components:
 - Adverse Reactions
 - Incidents

Hemovigilance Module: Adverse Reactions

v1.0 (March 2009) v2.4 (January 2017)

<ol style="list-style-type: none"> 1. Allergic reaction 2. Hemolytic transfusion reaction <li style="padding-left: 20px;">A. Acute hemolytic transfusion reaction (AHTR) 3. Delayed hemolytic transfusion reaction (DHTR) 4. Delayed serologic transfusion reaction (DSTR) 5. Hypotensive transfusion reaction 6. Febrile non hemolytic transfusion reaction (FNHTR) 7. Post transfusion purpura (PTP) 8. Transfusion associated circulatory overload (TACO) 9. Transfusion associated dyspnea (TAD) 10. Transfusion associated – graft vs. host disease (GVHD) 11. Transfusion-related acute lung injury (TRALI) 12. Infection 	<ol style="list-style-type: none"> 1. Transfusion-associated circulatory overload (TACO) 2. Transfusion-related acute lung injury (TRALI) <li style="padding-left: 20px;">A. Transfusion-associated dyspnea (TAD) 3. Allergic reaction 4. Hypotensive transfusion reaction 5. Febrile non-hemolytic transfusion reaction (FNHTR) 6. Acute hemolytic transfusion reaction (AHTR) 7. Delayed hemolytic transfusion reaction (DHTR) 8. Delayed serologic transfusion reaction (DSTR) 9. Transfusion-associated graft vs. host disease (TAGVHD) 10. Post transfusion purpura (PTP) 11. Transfusion-transmitted infection (TTI) 12. Other or Unknown
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Hemovigilance Module: Adverse Reactions

- Case Definition
 - Signs/symptoms and laboratory and/or radiographic data supportive of diagnosis of a specific reaction
- Severity
- Imputability
 - Strength of the relationship between transfusion and the reaction

NHSN Biovigilance Component
 Hemovigilance Module Surveillance Protocol v2.4
 www.cdc.gov/nhsn

Version History

Version	Release Date	Summary of Revisions
1.0	March 2009	First version publicly released.
1.1	June 2010	Revised background and text in main body of document. Revised case definition criterion based on VIG recommendations, pilot responses, and CDC recommendations. Updated FNHTR definition to allow reaction without documented fever. Defined hypotension for infants and small children. Clarified TAGVHD probable and possible criteria.
1.2	July 2010	Corrected definition of hypoxemia in glossary of terms.
1.3	June 2011	Added version number and version history summary. Summarized introduction and background sections for brevity. Reorganized surveillance methods section for ease of use. Clarified reporting of "approved deviation" incidents. Clarified use of "other" in adverse reaction reporting. Clarified use of "doubtful" or "ruled out" in adverse reaction reporting. Added denominator summary options to list of available analysis reports. Replaced < and > signs with appropriate text for. Added "cessation of" to time frame requirements in case definitions. NEW probable case definition category for allergic reaction reporting. Updated adult hypotensive reaction case definition to align with updated IBSB definition. NEW possible imputability category for DHTR. DELETED possible case definition category for hypotensive reaction. NEW probable imputability category for PTP reaction. Updated and clarified imputability categories for TAGVHD reaction. DELETED possible case definition category for TRALI. Simplified imputability criteria for TTI. Clarified case definition and imputability criteria for all adverse reactions.

Hemovigilance Module v1.0-v1.3

9. Transfusion-related acute lung injury (TRALI) – Acute hypoxemia with PaO₂/fraction of inspired oxygen (FIO₂) ratio of 300 mm Hg or less combined with chest x-ray showing bilateral infiltrates in the absence of left atrial hypertension (i.e., circulatory overload). There is abrupt onset in association with transfusion.

Case Definition Criteria	Laboratory/Radiology	Grade (Severity)	Relationship to Transfusion (Imputability)
Signs & Symptoms Definitive: NO evidence of acute lung injury (ALI) prior to transfusion AND Acute onset of ALI during or within 6 hours of transfusion AND Hypoxemia defined by: • PaO ₂ / FIO ₂ ≤ 300 mm Hg OR • Oxygen saturation is < 90% on room air OR • Other clinical evidence AND NO evidence of left atrial hypertension (i.e. circulatory overload) AND NO temporal relationship to an alternative risk factor for ALI during or within 6 hours of completion of transfusion.	Laboratory/Radiology Definitive: Bilateral infiltrates on chest radiograph	Use grades as provided in Appendix C.	If protocol criterion = Definitive then relationship is Definitive If protocol criterion = Possible then relationship is Possible

Hemovigilance Module v2.0-v2.4

Transfusion-related acute lung injury (TRALI)

Case Definition	Severity	Imputability
Definitive: NO evidence of acute lung injury (ALI) prior to transfusion AND ALI onset during or within 6 hours of cessation of transfusion AND Hypoxemia defined by any of these methods: • PaO ₂ /FIO ₂ less than or equal to 300 mm Hg • Oxygen saturation less than 90% on room air • Other clinical evidence AND Radiographic evidence of bilateral infiltrates AND No evidence of left atrial hypertension (i.e., circulatory overload)	Non-severe: Medical intervention (e.g. symptomatic treatment) is required but lack of such would not result in permanent damage or impairment of a bodily function. Severe: Inpatient hospitalization or prolongation of hospitalization is directly attributable to the adverse reaction, persistent or significant disability or incapacity of the patient occurs as a result of the reaction, or a medical or surgical intervention is necessary to preclude permanent damage or impairment of a body function.	Definitive: There are no alternative risk factors for ALI present. Probable: N/A Possible: There is evidence of other causes for acute lung injury such as: Direct Lung Injury • Aspiration • Pneumonia • Toxic inhalation • Lung contusion • Near drowning Indirect Lung Injury • Severe sepsis • Shock • Multiple trauma • Burn injury • Acute pancreatitis • Cardio/respiratory bypass

Highlight of some changes...

- June 2010 (v1.1): allowed reactions *without* documented fever to be classified as **'Definitive'** FNHTR
- Jan 2013 (v 2.0): added a separate case definition table for **'Other and Unknown'** reactions
- Aug 2013 (v2.1)- **'Possible'** case definitions added to:
 - FNHTR
 - Hypotensive reaction
 - Acute Hemolytic Transfusion Reaction (AHTR)
 - Delayed Hemolytic Transfusion Reaction (DHTR)

Advantages

- Uniform, standardized classification of transfusion reactions
- Facilitate research
- Benchmark against other institution's data
- Better understanding of rare reactions

UCSF Practice

- Clinical consult note for every reaction → EMR
- Nov 2011
 - NHSN: only 'Case definition' criteria used
- August 2013
 - NHSN: Case definition, Severity and Imputability

UCSF MEDICAL CENTER
DEPARTMENT OF LABORATORY MEDICINE
DIVISION OF TRANSFUSION MEDICINE
TRANSFUSION REACTION WORKUP

Patient Name: _____
MRN: _____
DOB: _____
Gender: _____
Hospital: _____

Date of transfusion reaction: _____
Time of transfusion reaction: _____
Product ID: _____

Chief complaint: _____

History: The patient is a _____-year-old, blood type _____ gender with a history of _____. On date at time, after premedication with _____, amount (ml) of donor blood type product type was transfused over time. At time with approximately amount (ml) of the unit remaining, the patient developed _____. These symptoms resolved with administration of _____. Throughout the transfusion there was no evidence of respiratory compromise and the patient's vital signs were stable. The patient has been transfused previously on multiple occasions without incident.

Laboratory Evaluation: The empty/partially transfused bag was returned to the blood bank for work-up of a possible transfusion reaction. There is no evidence of clerical error. The post-transfusion specimen showed no evidence of visual hemolysis. DAT was negative in the post-transfusion specimen in the polyspecific phase. (Mild allergic: "The post-transfusion specimen visual hemolysis check and DAT are not indicated since this is a mild allergic reaction.")

Pre and post-transfusion vital signs:

	Pre	Post
Temp (°C):		
BP (mmHg):		
HR:		
RR:		
O2 sat (%):		

Impression:
Transfusion-associated adverse reaction*: CHOOSE FROM CATEGORIES LISTED AT THE END

Case definition:	Definitive	Probable	Possible	N/A		
Severity:	Non-severe	Severe	Life-threatening	Death	Not determined	
Imputability:	Definite	Probable	Possible	Doubtful	Ruled out	Not determined

ENTER YOUR INTERPRETATION HERE

*The case definition, severity and imputability of the transfusion-associated adverse reaction are in accordance with the National Healthcare Safety Network (NHSN) Hemovigilance Module Surveillance Protocol v.2.4 (<http://www.cdc.gov/nhsn/PDFs/Biovigilance/BV-HV-protocol-current.pdf>).

Recommendation:

This case was discussed with _____ on _____.
This evaluation was undertaken at the request of the clinical service.
I have personally worked-up this case.
Resident/Fellow: _____ MDP#: _____

NHSN Transfusion-associated adverse reactions to choose from:

[Link to the ICD-10 code mapping to TR codes](#)

Mild Allergic Transfusion Reaction [TR33, _____ enter ICD-10 code for outpatients]

Severe Allergic Transfusion Reaction [TR34, _____ enter ICD-10 code for outpatients]

Febrile Non-Hemolytic Transfusion Reaction (FNHTR) [TR32, _____ enter ICD-10 code for outpatients]

Transfusion Related Acute Lung Injury (TRALI) [TR28, _____ enter ICD-10 code for outpatients]

Transfusion Associated Circulatory Overload (TACO) [TR35, _____ enter ICD-10 code for outpatients]

Transfusion Associated Dyspnea (TAD) [TR36, _____ enter ICD-10 code for outpatients]

Hypotensive Transfusion Reaction [TR41, _____ enter ICD-10 code for outpatients]

Post-Transfusion Purpura (PTP) [TR37, _____ enter ICD-10 code for outpatients]

Transfusion Associated Graft vs Host Disease (TA-GVHD) [TR42, _____ enter ICD-10 code for outpatients]

Acute Hemolytic Transfusion Reaction (AHTR) [TR38, _____ enter ICD-10 code for outpatients]

Delayed Hemolytic Transfusion Reaction (DHTR) [TR39, _____ enter ICD-10 code for outpatients]

Delayed Serologic Transfusion Reaction (DSTR) [TR40, _____ enter ICD-10 code for outpatients]

Other Transfusion Reaction [TR30, _____ enter ICD-10 code for outpatients]

Unknown Transfusion Reaction [TR31, _____ enter ICD-10 code for outpatients]



Case Studies

Case #1

- An O-positive 10 y/o male with sickle cell anemia presents for his monthly outpatient RBC transfusion. 1 unit of O-positive leukoreduced, HbS-neg RBC was transfused uneventfully over ~2 hours. He is observed for about an hour, and just when he is about to be discharged home, his mother notices 2 hives on his neck. The hives resolve 30 minutes after administering diphenhydramine.

	Pre	15 min	Post	Reaction
Temp (°C)	36.8	36.7	36.7	36.9
Blood Pressure (mmHg)	110/65	115/70	112/68	118/70
Pulse Rate (/min)	75	78	80	76
Respiratory Rate (/min)	18	18	18	18
O2 Saturation (%)	100	100	100	100

- No other rash/flushing
- No itching
- No respiratory distress
- No edema/angioedema/swelling
- No medications administered during this visit



Allergic Reaction	
Case Definition	?
Severity	?
Imputability	?

Allergic Reaction	
Case Definition	Probable
Severity	?
Imputability	?

Case Definition
Definitive: 2 or more of the following occurring during or within 4 hours of cessation of transfusion:
 • Conjunctival edema
 • Edema of lips, tongue and uvula
 • Erythema and edema of the periorbital area
 • Generalized flushing
 • Hypotension
 • Localized angioedema
 • Maculopapular rash
 • Pruritus (itching)
 • Respiratory distress; bronchospasm
 • Urticaria (hives)

Probable: ANY 1 of the following occurring during or within 4 hours of cessation of transfusion:
 • Conjunctival edema
 • Edema of lips, tongue and uvula
 • Erythema and edema of the periorbital area
 • Localized angioedema
 • Maculopapular rash
 • Pruritus (itching)
 • Urticaria (hives)

Allergic Reaction	
Case Definition	Probable
Severity	Non-severe
Imputability	?

Severity
Severe, Life-threatening, Death: Involves respiratory and/or cardiovascular systems and presents like an anaphylactic reaction. There is anaphylaxis when, in addition to mucocutaneous symptoms, there are airway symptoms, hypotension, or associated symptoms like hypotonia and syncope. The respiratory signs and symptoms may be laryngeal (tightness in the throat, dysphagia, dysphonia, hoarseness, stridor) or pulmonary (dyspnea, cough, wheezing, bronchospasm, hypoxemia). Such a reaction usually occurs during or shortly after cessation of transfusion.

Death should be used if death is possibly, probably or definitely related to transfusion. If the patient died of a cause other than the transfusion, the severity of the reaction should be graded as appropriate given the clinical circumstances related to the reaction.

Not Determined: The severity of the adverse reaction is unknown or not stated.

OPTIONAL

Non-severe: There is no immediate risk to the life of the patient, and the patient responds quickly to symptomatic treatment.

Allergic Reaction	
Case Definition	Probable
Severity	Non-severe
Imputability	Definite

Imputability
Definite:
Occurs during or within 2 hours of cessation of transfusion
AND
No other evidence of environmental, drug or dietary risks.
Probable:
Occurs during or within 2 hours of cessation of transfusion
AND
There are other potential causes present that could explain symptoms, but transfusion is the most likely cause.
Possible:
Occurs 2 - 4 hours after cessation of transfusion
OR
Other present causes are most likely, but transfusion cannot be ruled out.

Case #2

- An A-positive 50 y/o female who is undergoing chemotherapy for Acute Myelogenous Leukemia (AML). She is pancytopenic and transfusion dependent. Her platelet count is 7000/ μ L, so she is transfused with a unit of O-positive apheresis platelets. 15 minutes into the transfusion, she develops a fever to 38.2°C. Transfusion is stopped, and blood bank notified.

	Pre	15 min
Temp (°C)	37.4	38.2
Blood Pressure (mmHg)	120/70	125/75
Pulse Rate (/min)	85	95
Respiratory Rate (/min)	18	19
O2 Saturation (%)	100	100

- 0.8°C increase in temperature (<1°C)
- No chills or rigors
- No respiratory distress
- No hypotension, hematuria, back/chest pain
- No clinical suspicion of hemolysis

Transfusion Service Work Up

- Clerical check: OK
- Post-transfusion sample:
 - Visual hemolysis check: Negative
 - ABO/Rh: Same as pre-transfusion (A-positive)
 - DAT: Negative



Febrile Reactions

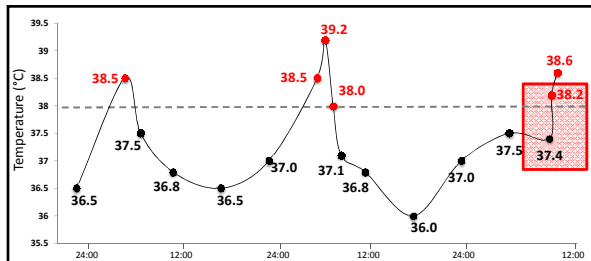
- Febrile Non-hemolytic Transfusion Reaction (FNHTR)
- Septic Reaction
- Hemolytic Reaction
- TRALI

Febrile Reactions

- Febrile Non-hemolytic Transfusion Reaction (FNHTR)
- Septic Reaction
- ~~Hemolytic Reaction~~
- TRALI

Febrile Reactions

- Febrile Non-hemolytic Transfusion Reaction (FNHTR)
- Septic Reaction
- ~~Hemolytic Reaction~~
- ~~TRALI~~



- Patient had been spiking fever before reaction
- Known *S. aureus* bacteremia pre-transfusion
- Temperature further increased to 38.6°C (1 hr after stopping transfusion)

Febrile Reactions

- Febrile Non-hemolytic Transfusion Reaction (FNHTR)
- Septic Reaction
- ~~Hemolytic Reaction~~ (DAT negative)
- ~~TRALI~~ (no respiratory symptoms)

Febrile Reactions

- Febrile Non-hemolytic Transfusion Reaction (FNHTR)
- ~~Septic Reaction~~
- ~~Hemolytic Reaction~~ (DAT negative)
- ~~TRALI~~ (no respiratory symptoms)

Febrile Non-hemolytic Transfusion Reaction	
Case Definition	?
Severity	?
Imputability	?

	Pre	15 min (Post)	
Temp (°C)	37.4	38.2	+0.8C (<1C)

Febrile Non-hemolytic Transfusion Reaction	
Case Definition	Possible
Severity	?
Imputability	?

Case Definition

Definitive:
Occurs during or within 4 hours of cessation of transfusion
AND EITHER
Fever (greater than or equal to 38°C/100.4°F oral and a change of at least 1°C/1.8°F) from pre-transfusion value
OR
Chills/rigors are present.

Probable:
N/A

OPTIONAL

Possible:
FNHTR is suspected, but reported symptoms and/or available information are not sufficient to meet the criteria defined above. Other, more specific adverse reaction definitions do not apply.

	Pre	15 min (Post)	1 hr Post
Temp (°C)	37.4	38.2	38.6

+1.2C (>1C) within 4 hrs

Febrile Non-hemolytic Transfusion Reaction	
Case Definition	Definitive
Severity	?
Imputability	?

Case Definition

Definitive:
Occurs during or within 4 hours of cessation of transfusion
AND EITHER
Fever (greater than or equal to 38°C/100.4°F oral and a change of at least 1°C/1.8°F) from pre-transfusion value
OR
Chills/rigors are present.

Probable:
N/A

OPTIONAL

Possible:
FNHTR is suspected, but reported symptoms and/or available information are not sufficient to meet the criteria defined above. Other, more specific adverse reaction definitions do not apply.

	Pre	15 min (Post)
Temp (°C)	37.4	38.2

Febrile Non-hemolytic Transfusion Reaction	
Case Definition	Definitive
Severity	Non-severe
Imputability	?

Severity

Non-severe:
Medical intervention (e.g. symptomatic treatment) is required but lack of such would not result in permanent damage or impairment of a bodily function.

Severe:
Inpatient hospitalization or prolongation of hospitalization is directly attributable to the adverse reaction, persistent or significant disability or incapacity of the patient occurs as a result of the reaction, or a medical or surgical intervention is necessary to preclude permanent damage or impairment of a body function.

Life-threatening:
Major intervention required following the transfusion (e.g. vasopressors, intubation, transfer to intensive care) to prevent death.

Death:
The recipient died as a result of the adverse transfusion reaction. Death should be used if death is possibly, probably or definitely related to transfusion. If the patient died of a cause other than the transfusion, the severity of the reaction should be graded as appropriate given the clinical circumstances related to the reaction.

Not Determined:
The severity of the adverse reaction is unknown or not stated.

	Pre	15 min (Post)	1 hr Post
Temp (°C)	37.4	38.2	38.6

Febrile Non-hemolytic Transfusion Reaction	
Case Definition	Definitive
Severity	Non-severe
Imputability	Possible

Imputability

Definite:
Patient has no other conditions that could explain signs/symptoms.

Probable:
There are other potential causes present that could explain signs/symptoms, but transfusion is the most likely cause.

Possible:
Other present causes are most likely, but transfusion cannot be ruled out.

OPTIONAL

Doubtful:
Evidence is clearly in favor of a cause other than the transfusion, but transfusion cannot be excluded.

Ruled Out:
There is conclusive evidence beyond reasonable doubt of a cause other than the transfusion.

Not Determined:
The relationship between the adverse reaction and the transfusion is unknown or not stated.

Case #3

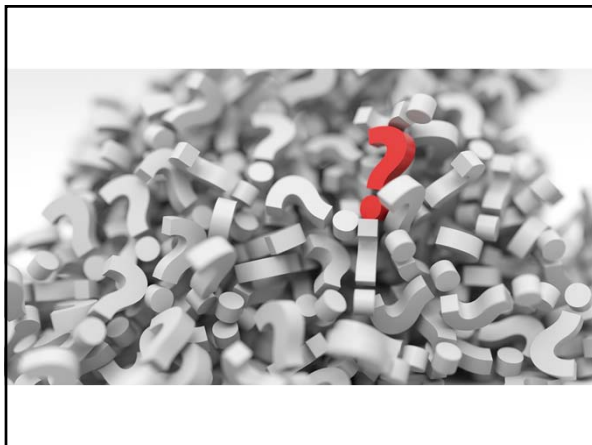
- A 55 y/o female with ovarian cancer undergoing chemotherapy is scheduled to receive an RBC transfusion in the clinic. One hr/~150 mL into the transfusion, she complains of shortness of breath (SOB) and chest tightness. Transfusion is terminated and blood bank notified.

	Pre	15 min	Post (1 hr)
Temp (°C)	36.6	36.8	37.0
Blood Pressure (mmHg)	120/70	118/72	117/68
Pulse Rate (/min)	85	90	88
Respiratory Rate (/min)	15	17	24
O2 Saturation (%)	100	100	95

- Clinical findings/physical exam:
 - Mild wheezing
 - No rash/hives or itching
 - No edema/angioedema (eyelid/lip/tongue)
 - No peripheral edema
 - No elevated jugular venous pressure (JVP)

- History of mild dyspnea over last few weeks
- Chest X-ray (post-reaction):
 - No pulmonary edema (similar to 3 wks prior)
- Brain natriuretic peptide (BNP):
 - 29 (normal < 82 pg/mL)
- ECHO from 3 wks before showed normal cardiac function

- ### Outcome
- Supplemental O2
 - IV diphenhydramine
 - SOB, wheezing and hypoxia resolved ~1 hr later
 - Discharged home in stable condition



- ### Respiratory Distress
- Severe allergic reaction
 - Transfusion-related acute lung injury (TRALI)
 - Transfusion-associated circulatory overload (TACO)

Allergic Reaction

Case Definition

Definitive:
2 or more of the following occurring during or within 4 hours of cessation of transfusion:

- Conjunctival edema
- Edema of lips, tongue and uvula
- Erythema and edema of the periorbital area
- Generalized flushing
- Hypotension
- Localized angioedema
- Maculopapular rash
- Pruritus (itching)
- **Respiratory distress; bronchospasm**
- Urticaria (hives)

Probable:
ANY 1 of the following occurring during or within 4 hours of cessation of transfusion:

- Conjunctival edema
- Edema of lips, tongue and uvula
- Erythema and edema of the periorbital area
- Localized angioedema
- Maculopapular rash
- Pruritus (itching)
- Urticaria (hives)

OPTIONAL

Possible:
N/A

- ### Respiratory Distress
- Severe allergic reaction
 - Transfusion-related acute lung injury (TRALI)
 - Transfusion-associated circulatory overload (TACO)

Respiratory Distress

- ~~Severe allergic reaction~~
- Transfusion-related acute lung injury (TRALI)
- Transfusion-associated circulatory overload (TACO)

TRALI

Case Definition
Definitive: NO evidence of acute lung injury (ALI) prior to transfusion
AND ALI onset during or within 6 hours of cessation of transfusion
AND Hypoxemia defined by any of these methods: <ul style="list-style-type: none"> • PaO₂/FIO₂ less than or equal to 300 mm Hg • Oxygen saturation less than 90% on room air • Other clinical evidence
AND Radiographic evidence of bilateral infiltrates
AND No evidence of left atrial hypertension (i.e., circulatory overload)
Probable: N/A
Possible: N/A

O2 sat=95%

Respiratory Distress

- ~~Severe allergic reaction~~
- Transfusion-related acute lung injury (TRALI)
- Transfusion-associated circulatory overload (TACO)

Respiratory Distress

- ~~Severe allergic reaction~~
- ~~Transfusion-related acute lung injury (TRALI)~~
- Transfusion-associated circulatory overload (TACO)

TACO

Case Definition
Definitive: New onset or exacerbation of 3 or more of the following within 6 hours of cessation of transfusion: <ul style="list-style-type: none"> • Acute respiratory distress (dyspnea, orthopnea, cough) • Elevated brain natriuretic peptide (BNP) • Elevated central venous pressure (CVP) • Evidence of left heart failure • Evidence of positive fluid balance • Radiographic evidence of pulmonary edema
Probable: N/A
Possible: N/A

Respiratory Distress

- ~~Severe allergic reaction~~
- ~~Transfusion-related acute lung injury (TRALI)~~
- Transfusion-associated circulatory overload (TACO)

Respiratory Distress

- Severe allergic reaction
- Transfusion-related acute lung injury (TRALI)
- Transfusion-associated circulatory overload (TACO)

Transfusion-associated dyspnea (TAD)	
Case Definition	Definitive
Severity	?
Imputability	?

Case Definition

Definitive: Acute respiratory distress occurring within 24 hours of cessation of transfusion **AND** Allergic reaction, TACO, and TRALI definitions are not applicable.

Probable: N/A

Possible: N/A

Transfusion-associated dyspnea (TAD)	
Case Definition	Definitive
Severity	Non-severe
Imputability	?

Severity

Non-severe: Medical intervention (e.g. symptomatic treatment) is required but lack of such would not result in permanent damage or impairment of a bodily function.

Severe: Inpatient hospitalization or prolongation of hospitalization is directly attributable to the adverse reaction, persistent or significant disability or incapacity of the patient occurs as a result of the reaction, or a medical or surgical intervention is necessary to preclude permanent damage or impairment of a bodily function.

Life-threatening: Major intervention required following the transfusion (e.g. vasopressors, intubation, transfer to intensive care) to prevent death.

Death: The recipient died as a result of the adverse transfusion reaction. Death should be used if death is possibly, probably or definitely related to transfusion. If the patient died of a cause other than the transfusion, the severity of the reaction should be graded as appropriate given the clinical circumstances related to the reaction.

Not Determined: The severity of the adverse reaction is unknown or not stated.

Transfusion-associated dyspnea (TAD)	
Case Definition	Definitive
Severity	Non-severe
Imputability	Probable

Imputability

Definite: Patient has no other conditions that could explain symptoms.

Probable: There are other potential causes that could explain symptoms, but transfusion is the most likely cause.

Possible: Other present causes are most likely, but transfusion cannot be ruled out.

OPTIONAL

Doubtful: Evidence is clearly in favor of a cause other than the transfusion, but transfusion cannot be excluded.

Ruled Out: There is conclusive evidence beyond reasonable doubt of a cause other than the transfusion.

Not Determined: The relationship between the adverse reaction and the transfusion is unknown or not stated.

Case #4

- A 35 y/o O-positive male with factor V deficiency is scheduled for surgery. His physician orders 4 FFPs to correct his coagulopathy prior to the procedure. After the first 2 FFPs are transfused over 1 hr, the nurse notices he has become hypotensive/tachycardic. Patient feels weak, but otherwise has no other complaints. Transfusion is stopped and blood bank notified.

1 st FFP:			
	Pre	15 min	Post
Temp (°C)	36.6	36.8	37.0
Blood Pressure (mmHg)	125/75	122/73	122/70
Pulse Rate (/min)	85	90	88
Respiratory Rate (/min)	15	17	16
O2 Saturation (%)	100	100	100

2 nd FFP:			
	Pre	15 min	Post
Temp (°C)	37.0	36.8	37.1
Blood Pressure (mmHg)	122/70	115/60	80/50
Pulse Rate (/min)	88	94	112
Respiratory Rate (/min)	16	17	20
O2 Saturation (%)	100	100	100

Transfusion Service Work Up

- Clerical check: OK
- Post-transfusion sample:
 - Visual hemolysis check: negative
 - Repeat ABO: matches patient’s known ABO (O-positive)
 - DAT: negative
- Patient’s vitals returned to baseline ~10 minutes after stopping transfusion and infusing 1 liter normal saline bolus



Hypotension

- Severe allergic reaction
- TRALI
- Septic reaction
- Hemolytic reaction

Allergic Reaction

Case Definition
Definitive: 2 or more of the following occurring during or within 4 hours of cessation of transfusion: <ul style="list-style-type: none"> • Conjunctival edema • Edema of lips, tongue and uvula • Erythema and edema of the periorbital area • Generalized flushing • Hypotension • Localized angioedema • Maculopapular rash • Pruritus (itching) • Respiratory distress; bronchospasm • Urticaria (hives)
Probable: ANY 1 of the following occurring during or within 4 hours of cessation of transfusion: <ul style="list-style-type: none"> • Conjunctival edema • Edema of lips, tongue and uvula • Erythema and edema of the periorbital area • Localized angioedema • Maculopapular rash • Pruritus (itching) • Urticaria (hives)
OPTIONAL
Possible: N/A

Hypotension

- Allergic reaction
- TRALI
- Septic reaction
- Hemolytic reaction

TRALI

Case Definition
Definitive: NO evidence of acute lung injury (ALI) prior to transfusion AND ALI onset during or within 6 hours of cessation of transfusion AND Hypoxemia defined by any of these methods: <ul style="list-style-type: none"> • PaO₂/FIO₂ less than or equal to 300 mm Hg • Oxygen saturation less than 90% on room air • Other clinical evidence AND Radiographic evidence of bilateral infiltrates AND No evidence of left atrial hypertension (i.e., circulatory overload)
Probable: N/A
Possible: N/A

Hypotension

- Allergic reaction
- TRALI
- Septic reaction
- Hemolytic reaction

Hypotension

- Allergic reaction
- TRALI
- Septic reaction
- Hemolytic reaction

Hypotension

- Allergic reaction
- TRALI
- Septic reaction
- Hemolytic reaction

	Pre	15 min	Post
Blood Pressure (mmHg)	122/70	115/60	80/50

Hypotensive transfusion reaction	
Case Definition	Definitive
Severity	?
Imputability	?

Case Definition
Definitive: All other adverse reactions presenting with hypotension are excluded
AND Hypotension occurs during or within 1 hour after cessation of transfusion.

- **Adults (16 years and older):** Drop in systolic BP of greater than or equal to 30 mmHg and systolic BP less than or equal to 80 mmHg.
- **Infants, children and adolescents (1 year to less than 16 years old):** Greater than 25% drop in systolic BP from baseline (e.g., drop in systolic BP of 120mmHg to below 90mmHg).
- **Neonates and small infants (less than 1 year old OR any age and less than 12 kg body weight):** Greater than 25% drop in baseline value using whichever measurement is being recorded (e.g., mean BP).

Probable:
N/A

OPTIONAL

Possible: Hypotension occurs, does not meet the criteria above. Other, more specific, reaction definitions do not apply.

Hypotensive transfusion reaction	
Case Definition	Definitive
Severity	Non-severe
Imputability	?

Severity
Non-severe: The recipient required no more than discontinuation of transfusion and symptom management and no long-term morbidity resulted from the reaction.
Severe: Inpatient hospitalization or prolongation of hospitalization is directly attributable to hypotension, or hypotension led directly to long-term morbidity (e.g., brain damage)
AND Vasopressors were not required.
Life-threatening: The recipient required vasopressors.
Death: The recipient died as a result of the adverse transfusion reaction. Death should be used if death is possibly, probably or definitely related to transfusion. If the patient died of a cause other than the transfusion, the severity of the reaction should be graded as appropriate given the clinical circumstances related to the reaction.
Not Determined: The severity of the adverse reaction is unknown or not stated.

Hypotensive transfusion reaction	
Case Definition	Definitive
Severity	Non-severe
Imputability	Probable

Imputability
Definitive: Occurs less than 15 minutes after the start of the transfusion
AND Responds rapidly (i.e., within 10 minutes) to cessation of transfusion and supportive treatment.
AND The patient has no other conditions that could explain hypotension.
Probable: Occurs between 15 minutes after start and 1 hour after cessation of transfusion
OR The patient does not respond rapidly to cessation of transfusion and supportive treatment
OR There are other potential causes present that could explain hypotension, but transfusion is the most likely cause.
Possible: Other conditions that could readily explain hypotension are present.

OPTIONAL

Doubtful: Evidence is clearly in favor of a cause other than the transfusion, but transfusion cannot be excluded.
Ruled Out: There is conclusive evidence beyond reasonable doubt of a cause other than the transfusion.
Not Determined: The relationship between the adverse reaction and the transfusion is unknown or not stated.

