

Septic Reactions from Apheresis Platelets

What have we learned from 10 years of hemovigilance?

Anne Eder, MD PhD

Adjunct Associate Professor

Georgetown University School of Medicine

Chief, Blood Services Section, Dept Transfusion Medicine

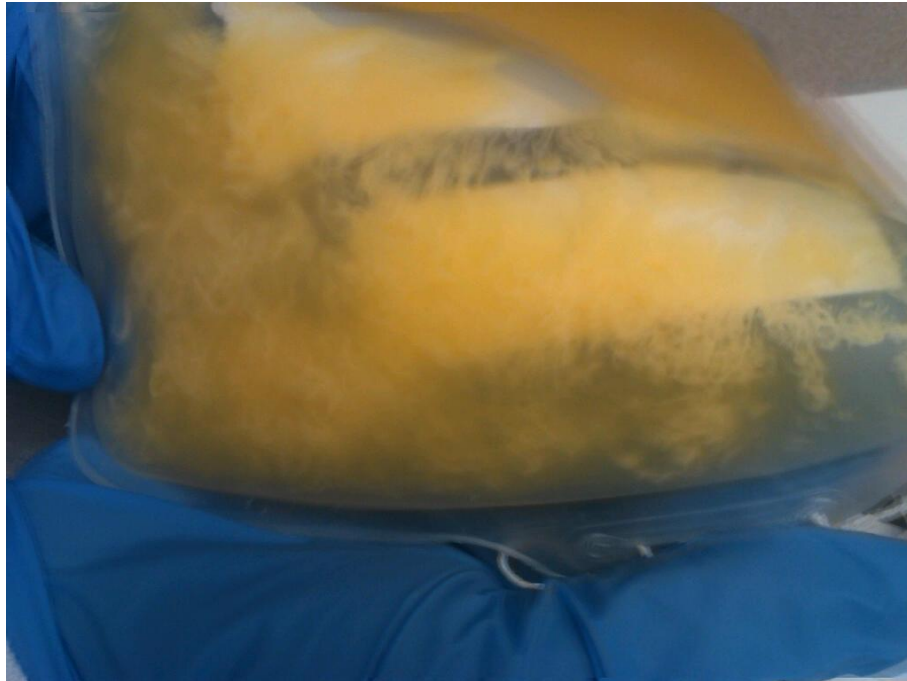
Clinical Center, National Institutes of Health

Disclosures

- No relevant financial relationships with commercial interests to disclose. No commercial support was received for this activity.
- The opinions expressed are my own and not those of the US government or American Red Cross

Septic Transfusion Reactions

American Red Cross Hemovigilance, 2004 - 2014



Onset within 4 h of transfusion

Any of the following clinical signs

- Fever $\geq 39^{\circ}\text{C}$ (102.2°F) or change of $\geq 2^{\circ}\text{C}$ (3.6°F)
- Rigors
- BP increase or decrease ≥ 30 mmHg
- Tachycardia ≥ 120 bpm or change in HR \uparrow or $\downarrow \geq 40$ bpm

- Cultures of residual product and patient with identical isolates (**definite**) OR
- Culture of residual product (not lab contamination) (**probable**)

Hemovigilance definitions reflect the *final classification* of definite and probable cases, not the triggers for investigation. Any change in condition or suspicion for sepsis after transfusion should be reported and investigated.

Eder et al. *Transfusion*, 2014;54:857-862

Investigate Suspected Sepsis after Transfusion

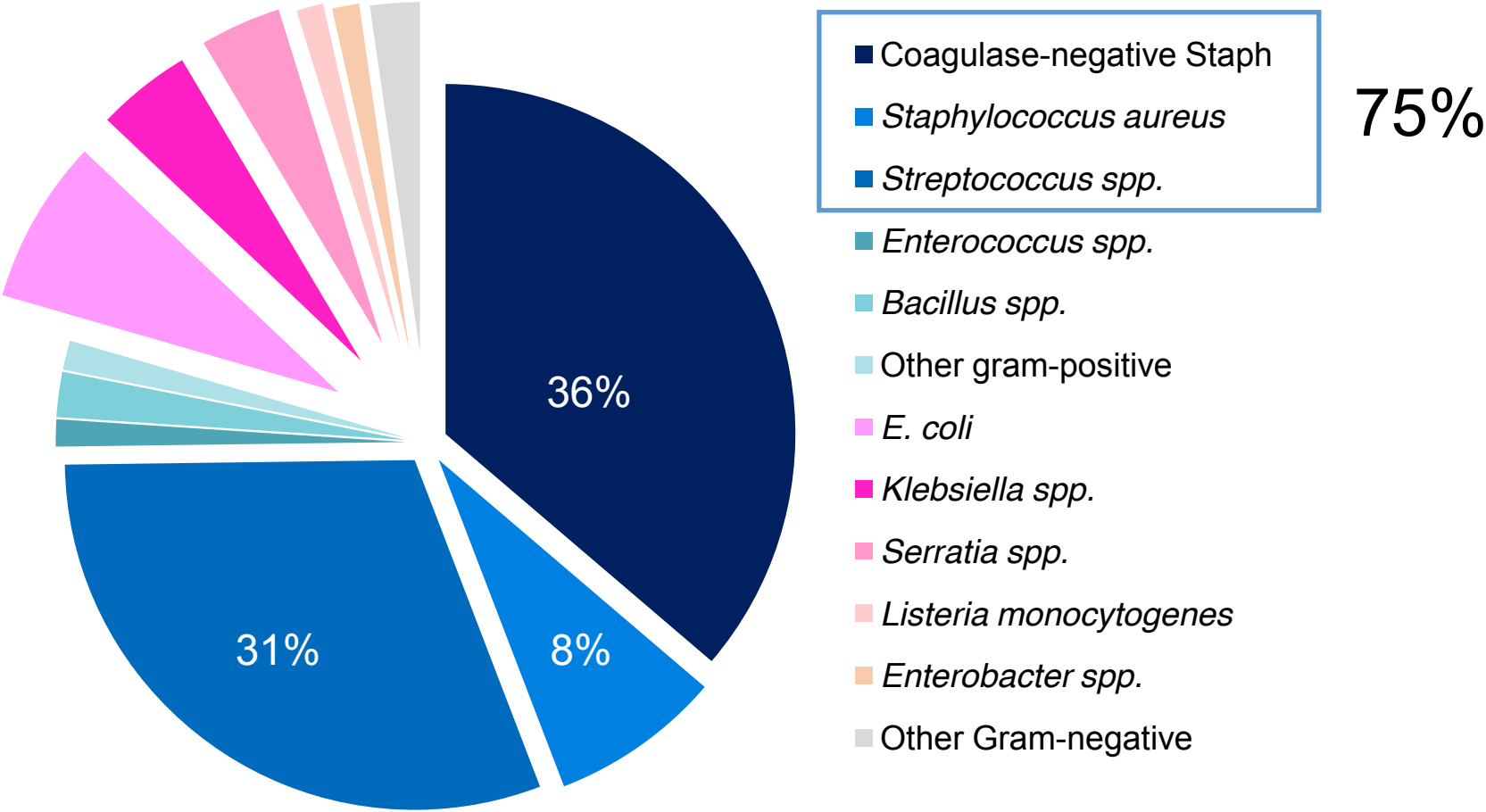
Clinical triggers for investigation

1. Fever defined as temperature $\geq 38^{\circ}\text{C}$ (100.4°F) with a rise of $\geq 1^{\circ}\text{C}$ (1.8°F) from the pretransfusion value PLUS any of the following signs and symptoms:
 - Rigors
 - Hypotension
 - Shock
 - Tachycardia (rise of >40 beats/minute from pre-transfusion value)
 - Dyspnea
 - Nausea/vomiting
2. Any change in clinical condition leading to a suspicion of sepsis, even in the absence of fever or other typical signs and symptoms of sepsis.

BacT Confirmed-Positive Aph Plt Donations

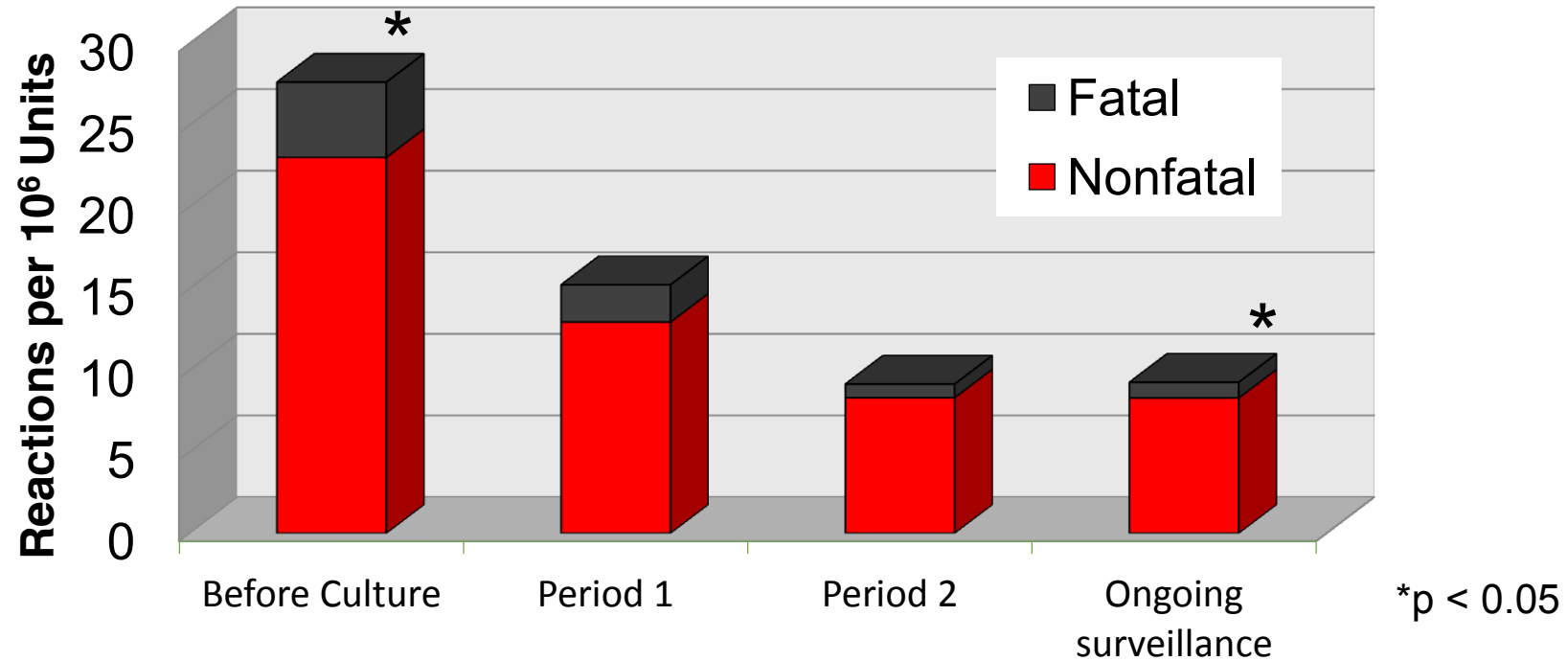
March 1, 2004 to December 31, 2014

960 Confirmed-positive cultures (4.7 million Aph Plt Donations)



Septic Transfusion Reactions, APLTs

American Red Cross Hemovigilance, 2004 - 2014



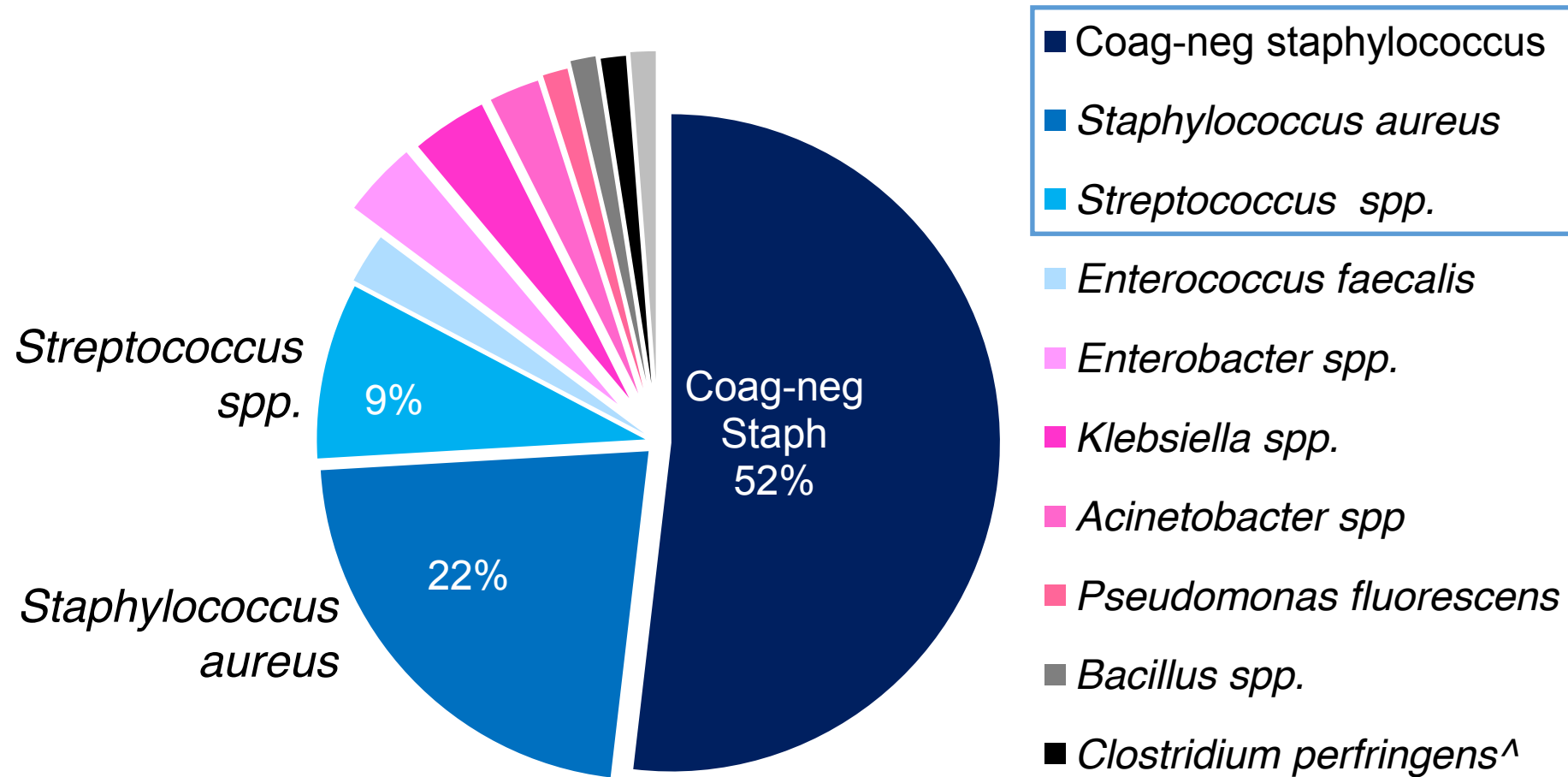
Culture Volume	NA	4 mL	8 mL	8 mL
Diversion	NA	39%	100%	100%
Septic RATE	1:36,000	1:66,000	1:109,000	1:108,000



American Red Cross

Eder et al, *Transfusion* 2009,49:1554 (Period 1 & 2);
Eder et al. *Transfusion*, 2014;54:857-862

Implicated Bacteria in STRs



March 1, 2004 to December 31, 2014
> 8 million distributed Apheresis Platelets

Eder et al. *Transfusion*, 2014;54:857-862



**American
Red Cross**

Delayed Septic Reactions

- Active surveillance = plate cultures (100 uL) before transfusion; retrospective chart review
- 7 year period; 20 of 51,440 platelet units had positive cultures;
- 5 reactions/sxs identified; 4 confirmed, all delayed onset (>9hrs)

Table 3. Clinical presentations of patients with confirmed STR

Case no.	Age, y/sex	Diagnosis	In/out patient	Onset, h	Presentation	Severity
63	56/M	MM PBSCT	Out	24	Hypotension syncope	Moderate
68	62/M	AML BMT	In	12	Cardiac arrest multiorgan failure	Fatal
70	78/M	NHL	Out	9	Fever (39.5°C), rigors	Life-threatening
72*	22/F	AA	Out	18	Hypotension	Moderate
76	7/M	ALL	Out	16	Fever (39.5°C), rigors	Severe

AA, aplastic anemia; ALL, acute lymphoblastic leukemia; AML, acute myeloid leukemia; BMT, bone marrow transplant; MM, multiple myeloma; NHL, non-Hodgkin lymphoma; PBSCT, peripheral blood stem cell transplant.

*Posttransfusion blood culture was negative.

Hong et al. Blood 2016;127: ePub Ahead of Print

FDA Draft Guidance

Bacterial Detection Testing, December 2014

Blood Collectors:

- Primary testing (apheresis platelets and prestorage pools, single units whole blood platelets)
- Additional Considerations for Blood Centers
 - Secondary testing, Day 4 and Day 5 platelets

Transfusion Services:

- Primary testing platelet components, if not done by blood center
- Additional Considerations for Transfusion Services
 - Inventory management to minimize day 4 and 5 transfusions
 - Secondary (rapid) testing on day 4 or 5
 - Secondary (culture) testing on day 4 for transfusion on day 5
 - Recommendations for testing required for 7 day storage, when cleared by FDA

<http://www.fda.gov/downloads/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/Blood/UCM425952.pdf>

Summary

- Bacterial sepsis after apheresis platelets is the leading infectious risks associated with blood component transfusion in the US
- The current residual risk of sepsis after apheresis platelet transfusion is ~1:108,000 distributed components based on reporting to the Red Cross
 - All apheresis platelet components implicated in septic transfusion reactions have been from prestorage culture-negative donations
- **Clinical recognition and immediate reporting of suspected transfusion reactions to transfusion service and blood supplier is essential to intercept other contaminated units from same donation**