



Advancing Transfusion and
Cellular Therapies Worldwide

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To: AABB Members

From: Graham Sher, MD, PhD—President

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Re: Clinical Recognition and Investigation of Suspected Bacterial Contamination of Platelets

Summary

The AABB Transfusion Transmitted Diseases Bacterial Contamination Work Group has developed this bulletin to provide guidance on the recognition of suspected reactions to bacterially contaminated platelets and the steps recommended to minimize patient harm. This bulletin supplements Association Bulletin #12-04, “Recommendations to Address Residual Risk of Bacterial Contamination of Platelets,” published in October 2012. The 2012 bulletin contained several recommendations including one to focus on improved recognition and monitoring of septic transfusion reactions (STRs) of all platelet components.

Association Bulletins, which are approved for distribution by the AABB Board of Directors, may include announcements of standards or requirements for accreditation, recommendations on emerging trends or best practices, and/or pertinent information. This bulletin contains information and recommendations for clinical recognition and investigation of suspected bacterial contamination of platelets. No new standards are proposed.

Background

Bacterial contamination of platelets has been and continues to be a leading infectious risk of transfusion therapy. Unfortunately, this finding is either unknown, under-appreciated or under-recognized by many clinicians and other healthcare providers caring for patients receiving platelets. The increasing use of platelets that are tested for bacterial contamination early in the storage period—such as apheresis or pre-pooled stored platelets—has greatly reduced the frequency of gram-negative bacterial sepsis. However, many instances of gram-positive bacterial contamination are neither interdicted nor recognized, and septic reactions and deaths continue to be reported. Further compounding the problem is that an initially tested apheresis collection is often split into 2 or 3 separate units, each of which may be bacterially contaminated, transfused to different patients, and cause variable clinical outcomes. It is therefore recommended that suspected

patient transfusion reactions to platelets, as defined below, trigger an immediate review for the possibility of sepsis, and possible recall of all units derived from the primary collection. It is estimated that after early screening for bacteria, about 1/2,000 to 1/3,000 platelet transfusions are still contaminated with bacteria, primarily coagulase-negative *Staphylococcus* species, and that the risk of serious STRs leading to morbidity and mortality continues.

The purpose of this document is to provide transfusion service medical directors with guidance on the recognition of suspected reactions to bacterially contaminated platelets and the steps recommended to minimize patient harm. Transfusion service medical directors are encouraged to bring this document to the attention of the hospital Transfusion Committee for education and dissemination throughout the hospital clinical staff and incorporation of these recommendations into the institution's policies.

Clinical Criteria for Investigation of Suspected Bacterial Contamination

Caregivers should be vigilant for signs and symptoms of reactions resulting from bacterial contamination of platelet products. Bacterial contamination should be suspected and an investigation initiated if the criteria for a transfusion reaction described below appear during or within 24 hours after the end of transfusion. Caregivers noting these STR criteria should immediately notify not only clinicians caring for the patient but also the transfusion service. Reactions starting beyond 6 hours after completion of transfusion are known to occur and expert clinical judgment is required to recognize the potential link and to intervene.

Although the definition of a septic transfusion reaction is likely set by facility policy, two representative examples are provided below.

1) Fever defined as temperature ≥ 38 C (100.4 F) with a rise of ≥ 1 C (1.8 F) from the pre-transfusion 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. Fever may not occur in immunosuppressed or neutropenic patients, particularly in patients pre-medicated with antipyretic and antihistaminic agents before transfusion. In particular, syncope or hypotension in the absence of other features of

sepsis have been reported in patients transfused with bacterially contaminated platelets. These findings may be delayed for up to 24 hours.

Bedside Actions

Rapid recognition of sepsis and initiation of clinical support of the patient are critically important to survival. Septic reactions should be treated aggressively. If sepsis is suspected and/or the above criteria are met facilities should:

- Immediately stop the transfusion.
- Provide fluids, pharmacologic support of blood pressure, and support for organ failure according to guidelines of the “Surviving Sepsis Campaign.”¹
- Notify the transfusion service and return the blood product container(s) to the transfusion service per facility policy.
- Immediately draw blood samples from the patient for culturing—preferably in two sets of aerobic and anaerobic bottles—irrespective of whether the patient is already receiving antibiotic therapy.

Laboratory Management—Transfusion Service/Microbiology

Quick responses from laboratory staff and good communication between various laboratory services will enable quarantine of additional, relevant, co-components.

Initial Actions

- Immediately search transfusion service inventory for any co-components (defined as all blood components prepared from the same donation) and place any such units found into quarantine to prevent distribution.
- Immediately contact the collection facility that provided the index component (defined as the blood component that triggered the reaction work-up) to evaluate the need for a broader inventory search for co-components so these can be quarantined.
- Test returned product for bacterial contamination as noted below under “Laboratory Methodology.”

Follow-up Actions

- When all test and culture results are available and the investigation is complete, discard all co-components if any result for any component is positive. [Note: a process to allow release of rare units from quarantine when negative results are obtained is acceptable.]

Laboratory Testing

Testing should be performed on the index component involved in the suspected STR. This testing should include direct stain and culture, may involve optional use of available rapid assays, and can be adapted according to facility policies. If the index component bag is not available for testing, a

residual sample from the index component prepared **at time of issue** may be used for testing. Note that segments made at the time of production by the supplier should **NOT** be used.

The microbiology laboratory should save all bacterial isolates from the recipient of a potentially contaminated blood component and from implicated components in anticipation of further analysis to establish the relatedness of bacteria isolated from these two sources.

Direct Stain and Culture on Component

All work should be performed in a Class II Biological Safety Cabinet. Samples should be obtained using aseptic technique from the index component using a needle and syringe. Quarantined co-components should be tested using the same procedures used for the index component.

For direct stain:

- A slide for direct examination by staining (e.g., Gram's or acridine orange stain) should be prepared for immediate assessment on a direct smear of the product or on a cytospin preparation.
- The sensitivity of direct Gram's stain is 10^5 to 10^6 CFU/mL; that of acridine orange is 10^4 to 10^5 CFU/mL.

For culture:

- If insufficient volume is present in the component bag, add 10 to 20 mL of sterile broth to the component bag and mix thoroughly before sampling.
- Test using plate culture and blood culture bottles as follows²:
 - Plate culture: Inoculate 0.1-mL volumes onto blood and chocolate agar plates for incubation in CO₂ and onto an anaerobic blood agar plate for incubation under anaerobic conditions. Examine plates every 24 hours and incubate for a minimum of 5 days.
 - Blood culture: Inoculate one aerobic and one anaerobic bottle (minimum volume of 1.0 mL) of the blood culture system in use at the institution. Follow the manufacturer's instructions for the system in use and incubate bottles for a minimum of 5 days.
- Work up any positive cultures according to laboratory procedures, including determination of antimicrobial susceptibility.
- Retain the index component at 4 C should repeat testing be required.
- Preserve any bacterial isolates recovered at -70 C for additional studies.
- Sensitivity of plate culture is around 10^1 to 10^2 CFU/mL and of blood culture bottles is around 1 CFU/mL. Septic transfusion reactions are typically associated with bacterial loads of $>10^5$ CFU/mL.

Patient Blood Cultures

- The bacterial species, and its antimicrobial susceptibility, from any positive blood culture obtained following a suspected STR should be noted and compared with any bacterial isolates obtained from culture of the index component.
- Preserve any bacterial isolates recovered at -70 C for additional studies.

Rapid Assays

- Available FDA-approved rapid assays, e.g., Platelet PGD Test System (Verax Biomedical, Marlborough, MA) and BacTx Bacterial Detection Kit for Platelets (Immunetics, Boston, MA), can also be performed to provide information in addition to direct staining for early detection of bacterial contamination.

Interpretation of Tests Performed Due to Suspected Reaction

Units are interpreted as bacterially contaminated if at least one of the following conditions is met:

- The initial Gram's stain is positive and/or culture yields a bacterial species with the same Gram's stain characteristics, e.g., gram-positive cocci in clusters found on Gram's stain and *Staphylococcus aureus* obtained by culture.
- The same bacterial species with the same susceptibility is recovered from platelet specimens from both plate culture and blood culture bottle(s).
- The same bacterial species with the same susceptibility or other test of identity (e.g., RFLP and sequencing) is recovered from culture of the platelet specimen and from blood culture obtained from the patient during or shortly after the transfusion.

Result Reporting

- Any positive results, including direct stains, rapid assays, and cultures, which are indicative of bacterial contamination, should be communicated immediately by the microbiology laboratory to the transfusion service with as much detail as available, and updated as additional results are generated.
- The transfusion service should immediately notify the clinical team and transfusion service medical director of any positive result, including direct stains, rapid assays, and culture results indicative of bacterial contamination, and follow up with the identification of the bacterial isolate and its antimicrobial susceptibility as soon as these results are available.
- The transfusion service should forward all results, including direct stains, rapid assays, and culture results indicative of bacterial contamination, to the donor center supplying the implicated blood product to facilitate identification and quarantine of co-components, and donor evaluation if required. To facilitate timely release and return to inventory of co-components that have been quarantined it is important that negative results also be forwarded to the donor center.
- State and Federal reporting requirements must be followed by the microbiology laboratory, transfusion service, or blood center.

Blood Center Actions

- If the index component is found to be bacterially contaminated:
 - Co-components still present at the center should be quarantined and cultured prior to discard.
 - Co-components issued to other institutions should be recalled and quarantined, if not transfused, and should be cultured prior to discard if returned to the blood center.
 - These co-components should be cultured using the methods described above to establish relatedness of any bacteria isolates to the index component.
- If the culture on the index component is negative, or is not performed due to an inadequate sample, the blood center medical director should assess the need for further action with co-components. See Initial Actions.
- The occurrence of transfusion reactions should be determined for co-components issued to other institutions and transfused.

Key Steps

In summary, in order to recognize and provide a timely response to suspected STRs and to protect other patients from receiving contaminated co-components, the following steps are recommended.

A. Clinical Service or Patient Care Professionals

- 1) Recognize a potential septic reaction.
- 2) Immediately stop the transfusion.
- 3) Support patient as indicated—STRs can lead to a precipitous clinical decline in the patient.
- 4) Obtain blood cultures from the patient.
- 5) Return the platelet bag/component to the transfusion service or laboratory for investigation.
- 6) Alert the patient's physician.

B. Transfusion Service and Microbiology Laboratory

- 1) Gain control of and quarantine co-components.
- 2) Test suspected component for bacterial contamination.
- 3) Notify supplying blood center of all findings.

C. Blood Centers

- 1) Gain control of, quarantine, and investigate co-components.
- 2) Determine appropriate disposition of co-components.
- 3) Facilitate reporting relevant to transfused co-components.

References

1. Dellinger RP, Levy MM, Rhodes A, et al. Surviving Sepsis Campaign: International guidelines for management of severe sepsis and septic shock: 2012. Crit Care Med 2013; 41:580-637.
2. Williams PP. Culture of blood bank products, Section 13.13. In: Clinical microbiology procedures handbook, 3rd ed. Washington, DC: ASM Press, 2007.