

Article Review: A recent article published in TRANSFUSION reported a septic transfusion reaction that occurred in Canada caused by the transfusion of a bacterially contaminated platelet pool to a patient with acute myelogenous leukemia.¹

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The 73-year-old patient received a pool of four-day-old buffy coat-derived platelets transfused for a platelet count of $4 \times 10^9/L$. The product appeared normal when issued from the blood bank. After two-thirds of the platelet product was transfused, the infusion line became obstructed with a fibrous clot, and the transfusion was stopped. A red blood cell (RBC) transfusion was started (hgb 6.4 g/dL). Chills, rigors, nausea, and vomiting occurred after one third of the RBC was infused, which was about two and one-half hours after the platelet transfusion was started. The RBC transfusion was discontinued. The patient was admitted to the hospital. The patient's temperature rose from 36.7°C to 39.3°C by the next morning. After appropriate care, the patient was discharged 11 days after admission. None of the donors had previously provided products implicated in reported transfusion reactions and gave any reason for recent bacteremia (e.g., dental work). Bacterial culture of the patient's peripheral blood, the central venous catheter, and the pooled platelet product grew *Staphylococcus aureus*. The RBC bacterial culture showed no growth.

Subsequent investigations included phenotypic and genetic analyses, which demonstrated that the same *S. aureus* strain had been isolated from the patient samples and the platelet product. The bacterial concentration in the pooled product at the time it was received from the blood collection establishment was approximately 3×10^9 colony-forming units/mL. This concentration is above the level of clinical significance² and can have high levels of *S. aureus* superantigen exotoxins, which are proteins that destroy host cells, disrupt cell metabolism, inhibit immune responsiveness, and generate nutrients required for bacterial growth. Even low levels of superantigens can cause fever and hypotension. The authors report that scanning electron microscopy of a sample from the platelet pool containing visible clots showed bacterial aggregates consisting of staphylococci, platelet debris, and fibrinous material.

It is of interest that the septic reaction associated with the contaminated platelet was delayed in onset by two and one-half hours after the platelet transfusion started. This and even longer delays before the onset of sepsis are common with Gram-positive (GP) organisms and contribute to under-reporting of septic reactions attributable to GP bacterial contamination of platelets.³ The authors speculate that, if a

rapid test for bacterial contamination had been used, it is possible this product would have been interdicted and not transfused.

Buffy coat-derived platelet pools are not a licensed product in the US. The Verax Platelet PGD test was validated for use with whole blood-derived platelets suspended in plasma. Validation studies included testing for *S. aureus*. These studies demonstrated detection by the PGD test at 48 hours after growth was initiated by inoculation of 5 CFU/mL.⁴ In addition, the bacterial concentration in the product implicated in this report was several logs higher than the titer of *S. aureus* determined in studies that established and subsequently confirmed the limit of detection for the Platelet PGD test.⁴

Septic reactions from platelet transfusions continue to occur.^{3,5,6} While *S. aureus* is a major culprit, many organisms have been reported to be involved. The Verax Biomedical Platelet PGD test is FDA-cleared to detect bacteria in leukocyte reduced apheresis platelets (LRAP) suspended in plasma, LRAP suspended in Platelet Additive Solution C and plasma, and pre-storage pools of up to six leukocyte reduced whole blood derived platelets suspended in plasma, within 24 hours prior to platelet transfusion as a safety measure following testing with a growth-based quality control test cleared by the FDA for platelet components. The Platelet PGD test is also cleared for pools of up to six units of leukocyte reduced and non-leukocyte reduced whole blood derived (WBD) platelets suspended in plasma that are pooled within four hours of transfusion as well as single units of WBD platelets. In addition, seven-day expiration is available for apheresis platelets in plasma collected with the Amicus and Trima devices when tested with an FDA cleared safety measure. The PGD test is currently the only technology available in the US to extend platelet expiration to seven days and can detect bacterially contaminated platelets prior to transfusion without altering platelet quantity or quality.

¹ Loza-Correa M, Kou Y, Taha M, et al. Septic transfusion case caused by a platelet pool with visible clotting due to contamination with *Staphylococcus aureus*. *Transfusion* 2017;57:1299-303.

² Jacobs MR, Good CE, Lazarus HM, et al. Relationship between bacterial load, species virulence, and transfusion reaction with transfusion of bacterially contaminated platelets. *Clin Infect Dis* 2008;46:1214-20

³ Hong H, Xiao W, Lazarus HM, et al. Detection of septic transfusion reactions to platelet transfusions by active and passive surveillance. *Blood* 2016;127:496-502

⁴ The Platelet PGD Test. Verax Biomedical Incorporated. Package Insert. Available at: <http://veraxbiomedical.com/pdf/US-PLatelet-PGD-Test-v2.pdf>

⁵ Fatalities reported to FDA following blood collection and transfusion. Annual Summary for Fiscal Year 2015 [Internet]. Silver Spring (MD): Food and Drug Administration; [cited 2016 Sep 1]. Available from: <http://www.fda.gov/downloads/BiologicsBloodVaccines/SafetyAvailability/ReportaProblem/TransfusionDonationFatalities/UCM518148.pdf>

⁶ McDonald CP, Allen J, Roy A, et al. One million and counting: bacterial screening of platelet components by NHSBT, is it an effective risk reduction measure? [abstract 4D-S27-02]. *Vox Sang* 2015;109(Suppl 1):61