Bacterial culture of platelets with large volume delayed sampling

Brandon S. Walker[1], Sandra K. White[2], Ryan A. Metcalf[1,2]^

[1]ARUP Laboratories, Salt Lake City, UT, USA; [2]Department of Pathology, University of Utah, Salt Lake City, UT, USA

Correspondence to: Ryan A. Metcalf, MD, CQA (ASQ). ARUP Laboratories, Salt Lake City, UT, USA; Department of Pathology, University of Utah, 50 N. Medical Drive, Salt Lake City, UT 84132, USA. Email: ryan.metcalf@path.utah.edu.

Comment on: Delage G, Bernier F. Bacterial culture of platelets with the large volume delayed sampling approach: a narrative review. Ann Blood 2021;6:30.

Received: 29 November 2023; Accepted: 05 January 2024; Published online: 19 February 2024.

doi: 10.21037/aob-23-53

View this article at: https://dx.doi.org/10.21037/aob-23-53

We read with interest the article by Delage and Bernier entitled, "Bacterial culture of platelets with the large volume delayed sampling approach: a narrative review" (1). The final paragraph of the review discusses a study that compared the bacterial risk control strategies that employ testing using a simulation approach (2). The simulation study started with the conditional probability that all platelet components were contaminated with bacteria. Delage and Bernier were correct that a range of plausible lag and doubling times were included in the study, and these were weighted equally because we felt there was no synthesized information available at the time to demonstrate otherwise. We wish to clarify, however, their statement about the bacterial inoculum sizes used in our simulation study. It was stated that a single starting inoculum size of 10 colony forming units (CFUs) was used for our study. While we presented summary results for the 10 CFU inoculum size simulation scenarios for simplicity due to the large amounts of data generated by our analysis, we actually evaluated a range of inoculum sizes (1–60 CFU) as stated in the methods section of the paper. These bacterial contamination scenarios and probabilities of exposure can be viewed in the supplemental materials. We made the results of all scenarios available in the supplemental materials so that other authors could evaluate scenarios of interest. When using 60 CFU inoculum sizes, our results did not change.

Recently, we were able to update the practical range of doubling times for the simulation because we performed a meta-analysis of bacterial growth characteristics reported in the literature (3). This allowed us to narrow the doubling time range. We did not revise the lag time range because lag times in published studies generally used inoculum sizes that are likely much larger than what occurs in the real world. These larger inoculum sizes would be expected to artificially shorten lag times. The overall findings and conclusions of the simulation with revised inputs did not change. Additionally, we have also rerun the analysis using the 77 CFU inoculum size noted by the authors (*Table 1*) (4). Again, the overall findings did not change.

The authors also cited a publication that reported growth characteristics of *Staphylococcus epidermidis* where the inoculum size was 10–20 CFU, which was included in the aforementioned meta-analysis (5). This single study involving a single bacterial species had a sample size of 20 and found 75% of lag times were 1–2 days, while 25% were 2–3 days. The authors suggest that perhaps our simulation analysis should not have weighted lag times equally based on these data. However, we also published a meta-analysis quantifying residual bacterial detection rates after initial cultures of platelet components (6). We found the sensitivity of initial culture was just 31%. While many of the included studies performed culture before 48 hours, three studies performed culture on day two (day zero = day of collection) (7-9). The reported sensitivities of day two culture were 21%, 50%, and 100%, respectively. Removing *Cutibacterium acnes*, which is of debated clinical significance, these sensitivities become 41%, 50%, and 100%, respectively. Of

^ ORCID: 0000-0001-6074-7147.

Table 1 Median relative performance ranks and interquartile ranges among bacterial risk control strategies that use testing

Strategy[†]	>0 CFU/mL threshold	10^3 CFU/mL threshold	10^5 CFU/mL threshold
24c-3	9 [9–9]	1 [1–1]	1 [1–1]
24c-d3c-5	5 [3–6]	1 [1–4]	1 [1–1]
24c-d4c-7	2 [2–4]	5 [1–6]	1 [1–7]
24c-r-5	7 [6–7]	3 [1–7]	1 [1–6]
24c-r-7	5 [4–5]	7 [6–7]	5 [2–7]
36c-5	8 [7–8]	1 [1–8]	1 [1–8]
36c-d3c-7	1 [1–2]	3 [1–5]	1 [1–6]
36c-r-7	3 [2–4]	7 [4–8]	5 [1–7]
48c-7	6 [1–7]	9 [4–9]	9 [9–9]

[†], the first number denotes the timing in hours of initial culture (e.g., 48c reflects 48-hour large volume delayed sampling). The last number denotes the expiration in days (e.g., for 48c-7, the expiry is 7 days). Two step strategies also note the day of secondary culture (e.g., d3c) or use of rapid testing (r). CFU, colony forming unit.

note, the study with 100% sensitivity had the smallest sample size at 2,397 platelet components tested. Based on these studies assessing bacterial contamination detected at issue/outdate, we have not elected to revise the contamination scenarios in the simulation analysis at this time.

We appreciate that 48-hour large-volume delayed sampling (LVDS) enhances the detection rate and ability to interdict contaminated platelet components relative to 24-hour primary culture. For bacteria that do not have shorter lag times, risk of false negative culture results along with longer storage periods of 7 days may confer a higher risk versus other strategies outlined in the updated Food and Drug Administration (FDA) guidance. Passive surveillance can miss septic transfusion reaction events and active surveillance approaches could help clarify this question if sample sizes are sufficient to obtain estimates given low overall event rates (10). Alternatively, spiking studies with practical inoculum sizes and adequate sample sizes with a diversity of bacterial species could be used to compare different testing strategies.

Acknowledgments

Funding: None.

Footnote

Provenance and Peer Review: This article was commissioned by the editorial office, *Annals of Blood*. The article did not undergo external peer review.

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://aob.amegroups.com/article/view/10.21037/aob-23-53/coif). R.A.M. serves as an unpaid editorial board member of *Annals of Blood* from September 2023 to August 2025. R.A.M. reports having received speaker's honoraria from Cerus Corporation (manufacturer of pathogen reduction technology) for about three lectures covering his research on risks associated with bacterial contamination of platelet components. Most recent honorarium was about two years ago. The other authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

References

1. Delage G, Bernier F. Bacterial culture of platelets with the large volume delayed sampling approach: a narrative review. Ann Blood 2021;6:30.
2. Walker BS, Schmidt RL, Fisher MA, et al. The comparative safety of bacterial risk control strategies for platelet components: a simulation study. Transfusion 2020;60:1723-31.
3. Walker BS, Schmidt RL, White SK, et al. Meta-analysis of bacterial growth characteristics in platelet components: Refining the inputs of a simulation analysis comparing the relative safety of testing strategies. Transfusion 2023;63:1719-27.
4. Eder AF, Kennedy JM, Dy BA, et al. Limiting and detecting bacterial contamination of apheresis platelets: inlet-line diversion and increased culture volume improve component safety. Transfusion 2009;49:1554-63.
5. Ali H, Greco-Stewart VS, Jacobs MR, et al. Characterization of the growth dynamics and biofilm formation of Staphylococcus epidermidis strains isolated from contaminated platelet units. J Med Microbiol 2014;63:884-91.
6. Walker BS, White SK, Schmidt RL, et al. Residual bacterial detection rates after primary culture as determined by secondary culture and rapid testing in platelet components: A systematic review and meta-analysis. Transfusion 2020;60:2029-37.
7. Dickson M, Dinesh D. Bacterial contamination of platelet concentrates produced in New Zealand. N Z Med J 2013;126:12-21.
8. Brecher ME, Hay SN, Rothenberg SJ. Monitoring of apheresis platelet bacterial contamination with an automated liquid culture system: a university experience. Transfusion 2003;43:974-8.
9. Lee CK, Ho PL, Lee KY, et al. Estimation of bacterial risk in extending the shelf life of PLT concentrates from 5 to 7 days. Transfusion 2003;43:1047-52.
10. 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.

doi: 10.21037/aob-23-53
Cite this article as: Walker BS, White SK, Metcalf RA. Bacterial culture of platelets with large volume delayed sampling. Ann Blood 2024.