Large Volume Delayed Sampling Protocol: Review of Report from Canadian Blood Services

Paul D. Mintz, M.D., Chief Medical Officer, Verax Biomedical Incorporated

Investigators from Canadian Blood Services recently published results obtained from a large volume, delayed sampling (LVDS) protocol implemented in August 2017.[1]

The method uses a 16mL sample from each apheresis component or pool taken at least 36 hours after collection (from the mother bag for apheresis platelets) which is split into aerobe and anaerobe cultures that are held for six hours before component release with expiration seven days after collection.

From August 2017 to December 2019, a total of 223,156 buffy coat-derived platelet pools and 39,725 apheresis platelet units were screened during routine testing. Additionally, results from 2,356 cultures performed after outdate on apheresis platelets (most 8 days post-collection) are reported. The authors also present the protocol's impact on outdate rates.

The confirmed positive rates for the pools and apheresis units were 0.09% and 0.04% respectively. As in the UK, more than 70% of confirmed positives were strict anaerobes the majority of which are of rare clinical significance following transfusion of contaminated components.[2]

For apheresis components, there were 16 true positives from the 36-hour cultures (rate 1:2,483). Among the apheresis outdate cultures, there were two positive results (*Streptococcus mitis* and *Corynebacterium pseudodiphtheriticum*) for a false-negative rate of 1:1,178. Therefore, the sensitivity of this LVDS testing strategy was only 32%. Jacobs and colleagues noted PGD testing detected bacterial contamination in 1:3,069 components following a negative 8mL primary culture (aerobic only) of 27,620 platelets in the US.[3] This study has been cited by the FDA as demonstrating the inadequacy of this primary culture protocol. The current authors report an even higher false-negative rate.

The authors acknowledge that the FDA and Héma-Québec protocols involving a minimum sampling hold time of 48 hours after blood collection and an additional 12 hours after sampling could be more effective in identifying bacterially contaminated platelets. However, a validation study they performed showed that *S. epidermidis* could be missed when present at very low concentrations even with sampling after 48-hours post-collection. Further, they note a 48-hour hold would reduce effective component shelf-life.

There was one nonfatal septic transfusion reaction implicating a 7-day old pool contaminated with *Staphylococcus epidermidis* for a rate of approximately one in 350 000 platelet doses since Canadian Blood Services extended shelf-life to seven days.

The authors claim septic reactions were reduced threefold by their protocol. However, since they report only a single such reaction since implementation, the reader must conclude there were only 3 septic reactions during a comparable period previously. They acknowledge they have not proven either this threefold reduction in the rate of reactions nor provided proof of overall improved safety. "Since septic reactions are rare, many years of observation are necessary to confidently conclude that the frequency of reactions has truly decreased, and a larger data set is needed to analyze the risk of missed bacterial detection during routine (platelet) screening at Canadian Blood Services." They also acknowledge their

passive reporting system results in septic transfusion reactions not being routinely recognized and, even when recognized, not always investigated.[4]

Outdate rates during the use of the protocol were reduced by just 31% from 18.9% to 13.1%. This is in contrast to the 74% reduction observed on average by hospital users of the PGD Test to extend dating to seven days.[5]

The authors correctly conclude that a longer surveillance period will be necessary to assess the value of anaerobic cultures and also residual safety risk resulting from implementation of their LVDS protocol.

1. Ramirez-Arcos S, Evans S, McIntyre T, et al. Extension of platelet shelf life with an improved bacterial testing algorithm. Transfusion. 2020;1–11. https://doi.org/10.1111/trf.16112

2. Mcdonald C, Allen J, Brailsford S, et al. Bacterial screening of platelet components by National Health Service Blood and Transplant, an effective risk reduction measure. Transfusion. 2017;57:1122–1131.

3. Jacobs, MR, Smith, D, Heaton, WA, et al. Detection of bacterial contamination in prestorage culture-negative apheresis platelets on day of issue with the Pan Genera Detection test, Transfusion, 2011;51:2573-2582.

4. Kundrapu S, Srivastava S, Good CE, Lazarus HM, Maitta RW, Jacobs MR. Bacterial contamination and septic transfusion reaction rates associated with platelet components before and after introduction of primary culture: experience at a US Academic Medical Center 1991 through 2017. Transfusion 2020;60:974–985.

5. Mintz PD, Sanders JR. Seven-day platelet storage: Outdate reduction and cost savings. Ann Clin Lab Sci;2020;50:404-407.