ImpactLife Blood Bulletin
America's Blood Centers It's About Life

Today's Platelet Products — Not Your Grandfather's Platelets

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Key Points

- There are a number of platelet products available to treat a variety of patient needs.
- Cold stored platelets are most appropriate for the bleeding patient, while the other products may be used prophylactically to prevent bleeding.
- Apheresis platelets offer the advantage of antigen matching to treat the refractory patient.

Introduction: The introduction of plastic blood bags in the 1960s came at the same time that hematologic diseases were beginning to be treated with chemotherapy. Chemotherapy damaged the patient's megakaryocytes and platelet levels became low enough to make the patient susceptible to hemorrhage. Platelet concentrates (PC) produced from whole blood (WB) collections could sustain patients until their platelet count recovered.[1] Room temperature (RT) stored platelets are associated with a higher risk of sepsis and related fatality than any other transfusable blood component.[2] While requirements for methods to detect bacteria in platelets have been in place for many years, the United States (U.S.) Food and Drug Administration (FDA) has recently provided guidance to mitigate the risk of bacterial contamination of platelets.[2]

Apheresis Platelets: Apheresis platelet products are prepared from a single donor collection using an automated instrument. An apheresis platelet donation from a single donor can yield one to three full-dose platelet products, with each dose manufactured to contain a minimum of 3×10^{11} platelets. Platelets are transported at 20-24 C and are stored in a gas-permeable plastic bag at 20-24 C with continuous gentle agitation. The shelf life is five to seven days depending on the bacterial mitigation strategy employed, i.e., large volume delayed sampling, day of transfusion secondary point of release testing, or pathogen reduction (PR) technology.[3] The disadvantage of apheresis platelet production is the limited pool of donors relative to the wider availability of WB donors. Utilizing exclusively apheresis platelet donors places a limitation on the supply of platelet products to meet patient transfusion needs.[3] The advantage of an apheresis platelet collection system is the additional types of platelet products that can be produced. They can be suspended in 100 percent donor plasma or alternatively, a portion of donor plasma (typically ~65 percent) can be replaced with a platelet additive solution (PAS). PAS platelets offer the benefit of reduced incidence of allergic transfusion reactions as well as a reduced amount of incompatible plasma transfused to ABO-incompatible recipients.[3]

The INTERCEPT Blood System (Cerus Corp) is a PR technology currently approved in the U.S. for apheresis platelets and plasma products. INTERCEPT platelets are treated with the photoactive compound amotosalen and ultraviolet A (UVA) light illumination to irreversibly cross-link nucleic acids, inactivating bacteria and key protozoan and viral pathogens including cytomegalovirus (CMV). In addition to mitigating risk of transfusion-transmitted infection, the treatment process inactivates lymphocytes, thus eliminating risk of transfusion-associated graft versus host disease (TA-GVHD) without need for irradiation. For patients with alloimmune refractory thrombocytopenia, an apheresis platelet product from a donor negative for specific human leukocyte antigens (HLA) or human platelet antigens (HPA) can be provided. These antigen negative platelet products are supplied by blood centers that perform specialized testing and maintain a database of genotyped/phenotyped platelet donors.

Whole Blood Derived Platelets: Whole blood derived platelets, also referred to as "random donor platelets" or PCs are platelets prepared from individual units of WB by centrifugation. They contain at least 5.5×10^{10} platelets and comprise 5.9 percent of the total platelets distributed.[4, 5,6] For neonates and young patients, the smaller platelet content of a PC provides the advantage of not having to divide or aliquot an apheresis platelet unit for transfusion. PCs may be pooled to increase the therapeutic dose or individually transfused. Pooling of PCs can be performed by the blood collection organization (BCO) or the hospital transfusion service. Pooled platelets prepared in an open system have an expiration of four hours, while a closed system of pooling maintaining component sterility does not compromise the expiration time.[4] A pool of four to six PCs is roughly equivalent to an apheresis platelet unit, which is the standard dose for adults. Prestorage pooling by the BCO of PCs prepared from platelet-rich plasma simplifies bacterial detection of the platelet product without compromising effectiveness based on a randomized trial demonstrating noninferiority compared to PCs stored individually.[5] In contrast to apheresis platelets, there is sufficient contamination of red blood

cells (RBCs) in PCs to cause Rh(D) sensitization such that Rh Immune Globulin must be considered if Rh-positive PCs are provided to Rh negative individuals.[7,8]

In contrast to the platelet-rich plasma method in the U.S., many international BCOs prepare prestorage pools of buffy coat platelets (BCPs).[9,10] BCPs are prepared by a method of centrifugation which allows platelets from the WB donation to be manufactured within 24 hours of collection. BCPs from four donations are then pooled together using either PAS or male donor plasma. This is followed by a second centrifugation and leukoreduction to produce a pooled BCP in a closed system, which is done during the manufacturing process at the BCO and maintains a five day outdate.

Given the ongoing challenges of widespread platelet shortages, there has been a groundswell of interest in considering BCP production in the U.S., since implementation would offer an additional source of platelets with the potential to significantly reduce platelet shortages.[11] Conversion to BCPs would require addressing significant regulatory barriers with the FDA, as well as the cost to convert the manufacturing infrastructure, careful planning, and communication in partnership with all stakeholders. The process would require several years and include a feasibility study to prepare data to submit to the FDA. Other factors to take into account may include consideration of whether a seven-day PR BCP can be licensed and produced in the U.S.

Cold Stored Platelets: Cold stored platelets (CSP) may have two major advantages when compared to conventional room temperature stored units. Storage in the cold (1-6 C) reduces the risk of bacterial growth which could allow for a shelf-life that extends well beyond a five- or seven-day outdate of RT stored platelets. An ongoing randomized clinical trial, the CHIlled Platelet Study (CHIPS), is currently testing the safety and efficacy of cold stored platelets stored up to 21 days. The extended shelf-life would allow for increased availability and decreased wastage of platelet units. While the advantage of increased safety from bacterial contamination is intuitive, the efficacy of CSP is less clear. Storing platelets in the cold causes platelet activation, which leads to increased clearance and reduced survival *in-vivo* compared to RT stored platelets.[12] This pre-activated state may offer an advantage in bleeding trauma patients who need rapid platelet action. However, the shorter *in-vivo* half-life may be a disadvantage when giving prophylactic transfusions to thrombocytopenic hematology patients.[13] CSP units are similar in content to WB and apheresis units. The FDA recommends that CSP units are maintained at 1-6 C. Variances have been granted to allow storage at 1-6 C for up to 14 days without agitation.[14] CSP should be maintained between 1-10 C during transport.

Conclusion: As medical technology has advanced so have the number and types of platelets to address a variety of patient needs. Due to the methods of collection, some of these products are frequently in short supply. Additional options to address inventory concerns include consideration of decreasing the standard platelet dose from 3.0 x 10^{11} to 2.5 x 10^{11} as is done globally.[11]

TABLE

References:

1. Slichter, SJ, Harker, LA. Preparation and storage of platelet concentrates. II. Storage variables influencing platelet viability and function. Br J Haematol 1976; 24: 403-19.
2. FDA Guidance for Industry. Bacterial Risk Control Strategies for Blood Collection Establishments and Transfusion Services to Enhance Safety and Availability of Platelets for Transfusion. September 2019, Updated December 2020. [Available at: https://www.fda.gov/media/123448/download (Accessed November 6, 2021)]
3. Acker, J, Razatos, A. Whole blood and apheresis collection of blood components intended for transfusion. Technical Manual. 20th ed. Bethesda, MD: AABB Press, 2020.
4. Gammon R, ed. Standards for blood banks and transfusion services. 32nd ed. Bethesda, MD: AABB 2020.
5. Huddle NM, Cook RJ, Blajchman MA, *et al.* Assessing the effectiveness of whole blood-derived platelets stored as a pool: a randomized block non-inferiority trial. Transfusion 2005;45:896-903.
6. Jones, JM, Sapiano, MRP, Mowla, S, *et al*. Has the trend of declining blood transfusions in the United States ended? Findings of the 2019 National Blood Collection and Utilization Survey. Transfusion. 2021; 61: S1– S10. https://doi.org/10.1111/trf.16449
7. Cid J, Lozano M. Risk of Rh(D) alloimmunization after transfusion of platelets from D+ donors to D- recipients (letter). Transfusion 2005;45:453-454.
8. O'Brien, KL, Haspel, RL, Uhl, L. Anti-D alloimmunization after D-incompatible platelet transfusions: a 14-year single institution retrospective review. Transfusion 2014;54:650-654.
9. Van der Meer, PF, de Korte, D. Cid, J, eds. Blood component preparation: From benchtop to bedside. Bethesda, MD: AABB Press, 2011:55-81.
10. Cohn CS, Delaney M, Johnson ST, Katz LM, eds: Technical Manual. 20th ed. AABB Press; 2020:148.
11. Gammon RR, Devine D, Katz LM, *et al*. Buffy coat platelets coming to America: Are we ready? Transfusion 2021;61:627-633.
12. Murphy S, Gardner FH: Effect of storage temperature on maintenance of platelet viability--deleterious effect of refrigerated storage. N Engl J Med 1969; 280: 1094-8
13. Holcomb, JB, del Junco, DJ, Fox, EE, *et al*., The prospective, observational, multicenter, major trauma transfusion (PROMMTT) study: comparative effectiveness of a time-varying treatment with competing risks. JAMA Surg 2013; 148: 127-36
14. U.S. Food and Drug Administration. Exceptions and Alternative Procedures Approved Under 21 CFR 640.120. [Available at: https://www.fda.gov/vaccines-blood-biologics/regulation-blood-supply/exceptions-and-alternative-procedures-approved-under-21-cfr-640120 (Accessed November 6, 2021)]

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