LifeServe BLOOD CENTER
Your Blood. Your Hospital. Your Neighbors.
Blood Bulletin
America's Blood Centers
It's About Life.

The Return of Whole Blood — A Blast from the Past

By: Samantha Ngamsuntikul, MD, Associate Medical Director at South Texas Blood & Tissue Center; a subsidiary of BioBridge Global; Jed Gorlin, MD, MBA, Vice President of Medical and Quality Affairs at Memorial Blood Centers and Nebraska Community Blood Bank, Divisions of Innovative Blood Resources, a division of New York Blood Center; Thomas Watkins, DO, PhD, Chief Medical Officer at MEDIC Regional Blood Center; Nancy Van Buren, MD, Medical Director at Innovative Blood Resources, a division of New York Blood Center; Mark H. Yazer, MD, Professor of Pathology at University of Pittsburgh. The authors disclose no conflicts

Key Points

- Low-titer group O whole blood (LTOWB) is most commonly collected from qualified O positive donors with "low titers" of anti-A and anti-B antibodies.
- LTOWB platelet function may be preserved for at least 14 days of storage.
- Transfusion of LTOWB can occur in both the prehospital and hospital setting.
- The risk of fetal demise from hemolytic disease of the fetus and newborn due to anti-D alloimmunization in Rh(D)-negative females is low following transfusion of LTOWB.

Background: The use of low-titer group O whole blood (LTOWB) for trauma resuscitation and/or massive transfusion has recently resurged following its long and successful use in the military. LTOWB provides balanced hemostatic resuscitation of red blood cells, platelets, and plasma that can be transfused in the prehospital or in-hospital settings.

Donor considerations:

- LTOWB is commonly transfused to trauma patients before their blood type is known and is therefore often out of group. Units with anti-A and/or anti-B titers <256 are commonly used in the United States (U.S.) today[1].There is a lack of standardization around the titer cutoff and standardized assays.
- Type O male donors or type O female donors who have never been pregnant or who test negative for anti-HLA antibodies may qualify to donate whole blood if they have not recently taken anti-platelet function medications.
- Due to supply constraints, most centers provide Rh(D)-positive LTOWB as opposed to Rh(D)-negative LTOWB.

Component: Components can vary depending on[2] whether the unit is leukoreduced, and if so, whether the leukoreduction filter depletes the platelet content or whether it is platelet sparing. Finally,[3] the type of preservative/anticoagulant solution will determine the unit's maximum length of storage.

- *In vitro* platelet function beyond 14 days of storage is reduced compared to fresher units although the clinical significance of these changes is still being investigated.
- LTOWB is subjected to required relevant transfusion-transmitted infection screening and may or may not be leukoreduced with a platelet-sparing filter.
- **Leukoreduction** – The only platelet-sparing filter for whole blood is part of a collection set that contains citrate-phosphate-dextrose (CPD) as its preservative anticoagulant, so the maximum storage length is 21 days.[2]

Transfusion:

- **Prehospital** – LTOWB is used in the prehospital setting (air or ground ambulances) to provide hemostatic resuscitation as early as possible after injury[3]. In the prehospital setting, LTOWB is transfused to patients meeting a specific set of criteria that can include heart rate, shock index and signs of hemorrhage. Both adults and pediatric patients can receive LTOWB.
- **Hospital setting** – Trauma patients are the major recipients of LTOWB, but use is also occurring in post-partum hemorrhage, gastrointestinal bleeding, and in patients with other etiologies of massive bleeding[4].

Special considerations:

- **Rh(D)-alloimmunization** – Since many blood centers only supply Rh(D)-positive LTOWB, one must consider the risks of Rh(D) sensitization of Rh(D)-negative females of childbearing potential. The risk of receiving an Rh(D)-positive unit must be weighed against whether an exposed Rh(D)-negative female will survive the trauma, whether she will make the anti-D antibody, and whether she might become pregnant in the future with a Rh(D)-positive fetus, and the ensuing risk of adverse events from hemolytic disease of the fetus and newborn (HDFN). The D-alloimmunization rate in trauma is still an area of investigation. Two recent and similarly designed observational studies revealed rates of 7.8 percent and 42.7 percent[5]. While most trauma patients are not females of childbearing potential, should alloimmunization occur, modern management of HDFN, where available, has resulted in near disappearance of severe fetal hydrops, and a very low rate of fetal demise[6].

- **Pediatric**s – In the pediatric population, the risk of Rh(D)-alloimmunization after exposure to Rh(D)-positive LTOWB is predicted to vary with age, ranging from essentially 0 percent for neonates to approximately 6.5 percent for patients between 18-20 years of age[7]. Although few studies have been published on the use of LTOWB in pediatrics, a small propensity-matched study demonstrated that children receiving LTOWB demonstrated faster resolution of the base deficit and reduced quantities of blood products compared to children who received component therapy[8].

Conclusion: Multiple studies demonstrate non-inferiority of whole blood in comparison to component therapy and the convenience of carrying a single product in the space-constrained air ambulance setting cannot be denied. A recent meta-analysis found it comparable in the trauma setting[9]. Whether it yields superior outcomes, in contrast, awaits several large prospective multicenter trials that are still several years from completion. In the meantime, LTOWB provides balanced resuscitation in a single unit, which may be important in the early stages of the resuscitation before the results of coagulation testing are available. A multidisciplinary approach is required for implementation of a LTOWB program given the logistics and practical considerations for the transfusion of this product[10].

References:

1. Jackson, B., Murphy, C. and Fontaine, M.J. Current state of whole blood transfusion for civilian trauma resuscitation. *Transfusion*. 2020: 60: S45-S52.
2. Stubbs, J.R., Zielinski, M.D., and Jenkins, D. The state of the science of Whole Blood: lessons learned at Mayo Clinic. *Transfusion*. 2016; Apr 56(Suppl2) S173-S181.
3. Zhu, C.S., Pokorny, D.M., Eastride, B.J., *et al*. Give the trauma patient what they bleed, when and where they need it: establishing a comprehensive regional system of resuscitation based on patient need utilizing cold-stored, low-titer O+ whole blood. *Transfusion*. 2019; 56:1429-1438.
4. Braverman, M.A., Smith A., Pokorny D.M., *et al*. Prehospital whole blood reduces early mortality in patients with hemorrhagic shock. *Transfusion*. 2021; 61:S15-S21.
5. Yazer M.H., Triulzi, D.J., Sperry, J.L., Corcos, A., Seheult, J.N. Rate of RhD-alloimmunization after the transfusion of RhD-positive red blood cell containing products among injured patients of childbearing age: single center experience and narrative literature review. *Hematology* 2021; 26:321-327.
6. Zweirs, C., Oepkes, D., Lopriore, E., *et al*. The near disappearance of fetal hydrops in relation to current state-of-the-art management of red cell alloimmunization. *Prenat Diagn*. 2018; 38:943-950.
7. Yazer, M.H., Spinella, P.D., Seheult, J.N., *et al*. Risk of future haemolytic disease of the fetus and newborn following the transfusion of Rh(D)-positive blood products to Rh(D)-negative children. *Vox Sang*. 2021 Jun 23. Doi:10.1111/vox.13169.
8. Leeper, C.M., Yazer, M.H., Triulzi, D.J., *et al*. Whole blood is superior to component transfusion for injured children: A propensity matched analysis. *Ann Surg*. 2020; 272(4):590-594.
9. Crowe E., DeSantis, S.M., Bonnette, A., *et al*. Whole blood transfusion versus component therapy in trauma resuscitation: a systematic review and meta- analysis. *J Am Coll Emerg Physicians* 2020; Doi: 10.1002/emp2.12089.
10. Yazer, M.H., Cap, A.P., Spinella, P.C., *et al*. How do I implement a shole blood program for massively bleeding patients? *Transfusion*. 2018; 58:622-628.

Blood Bulletin is issued periodically by America's Blood Centers. Publication Editor: Mack Benton. The opinions expressed herein are opinions only and should not be construed as recommendations or standards of ABC, ABC SMT Committee, or its board of directors. Publication Office: 1717 K St. NW, Suite 900, Washington, DC 20006. Tel: (202) 393-5725; Fax: (202) 393-1282; E-mail: memberservices@americasblood.org.