



The Return of Whole Blood – A Blast from the Past

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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.) today¹. 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 on² 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 injury³. 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 bleeding⁴.

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 percent⁵. 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 demise⁶.

- **Pediatrics** – 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 age⁷. 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 therapy⁸.

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 setting⁹. 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 product¹⁰.

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