Arkansas Trauma System Evidence-Based Guidelines for Whole Blood Transfusion

Section Editor: Charles D. Mabry MD FACS

Introduction-

Whole Blood (WB) transfusion of injured military personnel was begun in WWI in France and was the accepted method of giving blood during the intervening years to WWII and then onto the Vietnam War. While the military initially used warm, recently donated WB, from "walking blood bank" non-injured servicemen, methods were developed to safely store WB in refrigerated conditions, and cold WB use became the norm in most combat hospitals. By the peak of the Vietnam War, the military had used over 1 million units of cold-stored WB. [1] Civilian use of WB closely followed military use and WB was considered to be the standard of care in America.

The development of the ability to separate blood components into packed red-blood cells (PRBC), fresh-frozen plasma (FFP), and platelets changed the patterns of blood transfusion in America in the 1970s. Component therapy became the norm and whole blood became harder and harder to find for transfusion. PRBCs and normal saline / Ringer's lactate became the standard of care for stabilization and transfusion of trauma patients in the 1970s and continued until research in coagulopathy associated with trauma in the 1990s placed more emphasis on prevention of hypothermia, correction of acidosis, and use of FFP and platelets, in addition to PRBCs.

The wars in Afghanistan and Iraq brought about several important changes in how we approach the trauma patient: 1) damage control resuscitation and damage control surgery [2] ; 2) balanced component therapy (using a ratio of 1:1:1 for PRBCs, FFP, and platelets) [3] ; and 3) organized transfusion, via the Massive Transfusion Protocol (MTP). [4] [See Appendix sections at end of article for more detail]

A revival of the use of WB by the military was also going on during these Middle East wars, with return of the "walking blood bank" especially in austere combat environments and was found to show promise and utility over standard component therapy. [5] [6]

Current Experience and Use of Whole Blood

The experience and lessons learned from those conflicts have been translated into actual practice patterns for American trauma centers, including the use of whole blood in some locations. [7] We now have over a decade of experience with the use of WB transfusion for trauma patients and as a general rule, WB shows several advantages over component therapy for the initial stabilization and treatment of the badly injured trauma patient. [8]

What are the terms used for WB? We will refer to cold-stored whole blood as WB, as opposed to the military use of fresh, warm whole blood, since the latter is not approved for use in America and is only used in the military arena. Additionally, following on the experience of the military, WB now harvested and used in America is Type O and “hemolysin low titer” or more commonly referred to as Type O “low titer” WB. That is, the O type blood is tested for low levels of hemolysin antibodies to A and B antibodies, and when below certain levels, is then used for WB, and blood with higher titers, is then processed in the usual methods and used as component therapy.

What are the Contents of Whole Blood Compared to Component Therapy? - A unit of WB contains more RBCs, along with plasma and platelets, with less total anticoagulant than a 1:1:1 ratio of PRBCs, FFP, and stored platelets. WB has a hematocrit approaching normal patient’s blood, and the benefit of 150 ml of plasma that provides for volume expansion and non-labile clotting factors. It is now felt that WB, when available and used early in the course of trauma treatment, offers better quality and effect of blood components transfused than equal volumes of 1:1:1 component therapy. [9] Component therapy (1:1:1 ratio) has the addition of anticoagulants in each component, plus additives, that yields a hematocrit of only 29%, platelet counts of 90,000 /microliter, and coagulation factors with 62% effectiveness of WB. [1] [10]

How should we use WB along with Component Therapy? There are no fixed standards for this at present, however, given the small supply of WB there are several practice patterns that appear in the current literature:

- Use WB at the earliest possible time in the trauma resuscitation process. This lessens the coagulopathy of trauma, reduces the amount of IV fluids needed, and tends to stabilize the patient sooner.
- Continue with Component Therapy after the first 1-4 WB units are given.
- Remember to supplement MTP therapy with IV Calcium due to the large amounts of Calcium binding additives contained in MTP products.

What about the platelets in WB versus Component Therapy? The platelets in WB remain active for up to 14 days after harvesting. One recent study looked at the effectiveness of WB platelets versus component therapy. [11] The authors found that in patients undergoing heart surgery that one unit of WB increased platelet counts equal to a standard six platelet unit transfusion and the mean platelet volume increased comparable to a 10-unit platelet transfusion. The American Association of Blood Banks (AABB) standards require platelets to be stored at room-temperature, but over time the platelets become dysfunctional due to “platelet storage lesion” and under the AABB standards, platelets cannot be stored for more than 5 days, along with undergoing bacterial testing due to the lack of refrigeration. On the other hand, by keeping the platelets in the WB, and keeping the WB refrigerated, recent research has shown that the platelets maintain their function for at least 21 days and are more active than room-temperature stored platelets. [12]

How safe is it to transfuse WB versus Component Therapy? In general, there are little, if any differences, in the safety of using low titer Type O WB now available in America, compared to PRBCs or traditional component therapy. There are multiple comparisons, both in the military as well as in civilian trauma systems showing equal safety, and better efficacy of WB than component therapy.[13] [14]

How long can WB be stored? WB can be stored for up to 21 days at 1–6°C in the anticoagulants citrate phosphate dextrose, or for 35 days at 1–6°C in citrate phosphate dextrose adenine. Many centers will repurpose the WB into PRBCs before the expiration date (15-20 days), so as to not waste the PRBC component of WB.

How effective is WB compared to Component Therapy? Numerous articles are now available comparing WB to component therapy, in various settings, study designs, etc. The largest experience in using WB is in the Texas trauma systems, both in Houston as well as in San Antonio areas. San Antonio has used WB in a helicopter delivery model since 2018. [1] [15]

- **Mortality-** In general, there does not appear to be a consistent mortality benefit to the use of WB compared to component therapy, but there are several considerations that must be taken into account. Many of the patients enrolled into these comparative studies are severely injured and some don't survive past the ED or trauma bay to receive further transfusions that may show a difference. Also, there is a limited supply of WB, and thus for badly bleeding trauma patients, they are typically switched to component therapy after the first 2-4 units of WB, co-mingling WB and component groups in many studies after the first few units of transfusion of WB. However, two recent studies, one being a retrospective study of ACS TQIP data, [16] and one from an institutional study, [13] have shown both 24 and hospital-stay decreases in death in the group receiving. One other study showed improved trauma bay and 24 hour survival using WB. [17] The 10-year experience of the military in the Middle East wars did show a convincing improved survival for those treated with WB. [5]
- **Total use of blood products-** In general, use of WB early in the trauma resuscitative stage results in less total blood products being used and less complications associated with trauma. [13], [18] , [19] [20] Several authors have noted that the exception to this is major head trauma where multiple anticoagulants and other trauma tissue byproducts may cause increase bleeding compared with trauma patients without head trauma.
- **Current Studies on the use of WB-** While there is a good amount of evidence supporting the use of WB for initial therapy in trauma resuscitation, it is difficult to organize and properly scale randomized trials in the world of trauma, therefore, there still remains many unanswered questions. There are three ongoing trials for early trauma resuscitation with WB for severely bleeding patients, the PPOWER trial, the STORHM trial, and the SWAT trial. We will update this evidence-based protocol as these studies come to publication.

Appendix- Resuscitation in Trauma

Damage control resuscitation [21] [22] combines permissive hypotension, restriction of IV crystalloid solutions with quick transport to the operating room to achieve control of hemorrhage. Avoiding hypothermia and acidosis are also key components of Damage Control Resuscitation to avoid worsening hypocoagulation. [1, 5, 23]

Principles of Damage-Control Resuscitation

Avoid or correct hypothermia
Apply direct pressure or a tourniquet proximal to sites of hemorrhage in the extremities; pack junctional wounds with hemostatic dressings
Delay fluid administration until the time of definitive hemostasis in selected patients (those with penetrating trauma to the torso and short prehospital transport times)
Minimize crystalloid infusions (<3 liters in the first 6 hr)
Use a massive-transfusion protocol to ensure that sufficient blood products are rapidly available
Avoid delays in definitive surgical, endoscopic, or angiographic hemostasis
Minimize imbalances in plasma, platelet, and red-cell transfusions in order to optimize hemostasis
Obtain functional laboratory measures of coagulation (e.g., by means of thromboelastography or rotational thromboelastometry) to guide the transition from empirical transfusions to targeted therapy-
Selectively administer pharmacologic adjuncts to reverse any anticoagulant medications and to address persistent coagulopathy medications.

From Cannon, Jeremy W. "Hemorrhagic shock." New England Journal of Medicine 378, no. 4 (2018): 370-379. And--

Cannon, Jeremy W., Mansoor A. Khan, Ali S. Raja, Mitchell J. Cohen, John J. Como, Bryan A. Cotton, Joseph J. Dubose et al. "Damage control resuscitation in patients with severe traumatic hemorrhage: a practice management guideline from the Eastern Association for the Surgery of Trauma." Journal of Trauma and Acute Care Surgery 82, no. 3 (2017): 605-617

Evaluation of the patient for hemorrhagic shock:

Always assure the ABC's of trauma: airway, breathing, and circulation with a rapid, but careful primary assessment.[24]

Questions to ask:

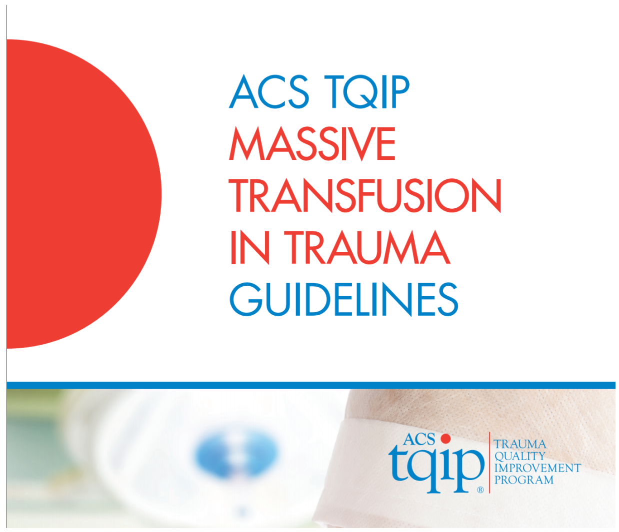
1. **What is the blood pressure and pulse? What is the Shock Index? Is the patient in shock &/or not perfusing adequately?**
2. **If the patient is in shock: does the patient have a patent and adequate airway?**
3. **If there is a good airway, is the patient breathing and ventilating adequately?**
4. **Are there any many signs of obvious external bleeding? Are there penetrating wounds that could be causing shock? Have we applied tourniquets and direct pressure to control bleeding?**
5. **Assess and reassess for the presence of shock with the Shock Index**: The best indicator of hemorrhagic shock is the **shock index = pulse / systolic blood pressure**. [25] Patients not in shock should have a shock index of < 1. As the patient begins to bleed, the pulse rate will increase as one compensatory mechanism. When shock compensation fails, the systolic pressure will fall. Thus, as the patient worsens, the shock index will go from 0.6 to > 1.0, indicating that the patient is getting into trouble that must be quickly treated.

Shock Index Examples		
Pulse	Systolic Blood Pressure	Shock Index
80	120	0.67
100	120	0.83
120	100	1.20
130	100	1.30
140	80	1.75

6. **EMS: Reporting the vital signs, including the shock index, enroute on a regular basis will help the receiving Trauma Center appropriately respond and prepare for the patient's arrival**.
7. **Trauma Center: Use of the shock index in the ED will help quickly identify those patients needing massive transfusion and surgical intervention, and also detect patients who were initially stable but now are going into shock.** [26 27]

Massive Transfusion Protocol (MTP) is the planning and preparation of a trauma center to administer blood products in a 1:1:1 ratio of PRBC, fresh frozen or liquid plasma, and platelets to replace blood lost to hemorrhage.

The ACS has recently published the TQIP Massive Transfusion in Trauma Guidelines [28] and the reader is directed to that excellent resource for trauma center based MTP protocols and guidelines.



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