Get ready: whole blood is back and it's good for patients

The ongoing war has convinced a new generation of clinicians that whole blood (WB) benefits bleeding patients.[1–4] As with many changes in civilian trauma care, the use of WB has transitioned from a wartime practice to the civilian world, becoming routine at many centers.[5] At last count, 19 leading trauma centers are using this approved product as their first line transfusion, with some starting prehospital (both ground and air ambulance) and continuing into the Emergency Department (ED) and Operating Room. Seheult and colleagues have been leaders in this civilian effort, along with a multinational group of collaborators.[6–13]

The Pittsburgh group instituted low titer group O WB (LTOWB) transfusion protocols in 2014 and has systematically documented their approach and outcomes in multiple studies over the last 4 years.[6–10] In this issue of **TRANSFUSION**, Seheult and colleagues report a retrospective, observational study of their recent experience, performed in a rigorous fashion, with appropriate analysis and without overstating their results.[6] They show that civilian trauma patients receiving WB plus components did as well or better than patients matched by propensity score who received components and no WB. There were trends toward lower mortality and faster lactate normalization in the LTOWB group, as well as early and higher (closer to 1:1) transfusion ratios in the LTOWB group. Previously, this same group has shown that the fears of hemolysis are unfounded, similar to the results from the military studies, albeit with larger number of transfused WB units.[9] These results will encourage other donor centers, blood banks, and clinicians caring for bleeding patients to collaboratively establish WB programs. Furthermore, these and additional unpublished data will set the stage for randomized studies of WB.

The WB story is a fascinating example of evolution of clinical care. WB was the standard transfusion product for 50 years and obviously was a balanced approach to transfusion. In the early 1970s it essentially disappeared from clinical use, replaced with unbalanced component therapy, in which plasma to red blood cell (RBC) ratios often reached 1:10, with platelets given even less often. This drastic change occurred without supporting outcome data in bleeding patients. Interestingly, it was during this era that acute respiratory distress syndrome, multiple organ failure, abdominal compartment syndrome, and profound coagulopathy became common. We started caring for patients in the mid 1980s and it was routine to see patients with overt clinical coagulopathy. Over the last decade clinicians around the world have reversed this iatrogenic resuscitation error and are now transfusing bleeding patients in a balanced fashion, with amounts of plasma, platelets, cryoprecipitate, and RBCs that attempt to replicate WB. At the same time, the deleterious effects of even small amounts of crystalloid have become widely recognized, and plasma is used as the primary resuscitation fluid. Cannon and colleagues have promulgated clinical guidelines supporting early balanced resuscitation in patients predicted to receive a massive transfusion.[14] Early blood product transfusion, within minutes of injury, yields better outcomes and patients now rarely suffer from a clinically apparent coagulopathy.[15,16] Results with this early and balanced method are superior to the previous approach. However, blood banks and bedside clinicians all report difficulty with coordinating the preparation, thawing, checking, delivering, and transfusing all these products at the same time and in the correct order. Frankly it's just hard to do. WB is easier and exposes the recipient to far fewer donors potentially making it safer from a number of angles, including human error.

But WB is scary, it is "new," represents change, upsets the routine between donor center and blood bank, will alter current inventory levels, is shrouded in myth, and frankly is just inconvenient. But all indications suggest it's a superior product. It is one component that delivers plasma, platelets, fibrinogen, and RBCs in the correct ratio, in one bag, at one time, with a shelf life that can extend to 35 days.[12] Placing RBCs and thawed/liquid plasma on ambulances and in the ED has been associated with improved survival; however, with different expiration dates this has proved cumbersome to manage. Platelets have even shorter expiration dates (4 days) and different storage requirements than plasma and RBCs, while cryoprecipitate requires thawing before it can be transfused. WB eliminates these issues, providing one component, minimally "processed," stored in its native milieu that delivers all these critical elements in one bag, greatly simplifying the storage, delivery transfusion, and administrative issues surrounding transfusion of the bleeding patient. WB is easily carried prehospital, for the first time in two generations providing for patients the highest quality of all elements in blood critical to hemorrhage control within minutes of injury. Transfusing patients with WB while they are bleeding, irrespective of the patient's location, is now possible and is the definition of patient-centered care.[17,18] The logistical advantage of WB versus attempting to recreate WB with component therapy is clear. The nursing personnel that "check the blood" at the bedside are some of the strongest proponents of WB, as they must contend daily with the paperwork and order of transfusion chaos that exists at the bedside while attempting to "recreate" WB from components (Fig. 1). WB simplifies these issues by decreasing the

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Fig. 1. The normal chaos of component massive transfusion, trying to reconstitute WB out of components versus just transfusing WB. [Color figure can be viewed at wileyonlinelibrary.com]

paperwork and eliminating the ratio/order question. It is well known that administrative errors are the most common transfusion misadventure and WB will likely decrease those errors.

There is great concern about alloimunization with WB.[19–21] Is this an area that is also tradition versus data based? The bedside clinicians are not cavalier about this issue; however, we are trying to weigh a risk-to-benefit equation of alloimunization in patients that at best have a 25% mortality within the next 105 minutes. For example, only a small minority of female patients of childbearing age are transfused. The risk of alloimunization by transfusing O+ LTWB to a Rh– woman of child bearing age is commonly reported at 22% (3%–30%) and an even smaller risk for her future child.[19–21] If she is in hemorrhagic shock and requires a laparotomy, her mortality is more than 40%. If immediate transfusion of WB can lower that mortality, is it in her best interest to do so? How do we balance the risk of alloimunization with the larger potential benefit of having O+ LTWB available prehospital and in the ED for all genders of hemorrhagic shock patients, versus trying to manage only an O– LTWB supply?

WB is not the answer for all patients, and in fact, it will be used in a very small number of patients. As bleeding slows and transfusion becomes guided by laboratory values, component therapy will be utilized. It is interesting to consider if using WB early will result in earlier hemostasis and decrease the overall number of blood products transfused.

While WB was the standard product transfused in civilian hospitals until the mid 1970s, and is still an approved product, most blood centers have lost the expertise to produce LTOWB. There are issues with the computer systems, cost, impact on other products, supply of O– versus O+ LTWB, what is the right titer, what is the right titer method, leukoreduced or not, platelet-sparing filter or not, 21-day or 35-day storage, and what to do with expiring WB? While challenging, we are convinced that these issues are answerable. Nineteen centers have already started and more are on the way. A similar challenge comes with training bedside clinicians in the use of WB. Two generations of civilian clinicians have not been trained (except those who served in the military) on when and how to use WB; the textbooks, training courses, and registries will need to be updated.

There are approximately 5000 hospitals in the United States. While RBCs are widely available, many (most?) cannot meet the standard of infusing RBCs, plasma, platelets and cryoprecipitate *immediately* upon arrival of a patient in hemorrhagic shock. There are approximately 35,000 ambulances in the United States. Today few carry any blood products, although recent data support improved outcomes with prehospital transfusion.[22,23] In these situations, every minute really does count. Even if those products are available in the blood bank, it often takes 30–40 minutes to prepare and deliver them to the bedside, during which a substantial percentage of bleeding patients will die.[16,24–26] The standard can be met by providing all hospitals with WB. How many ambulances will carry WB? Some are today, more will tomorrow. Many will say this vision is impossible and entirely unrealistic. What would they say if their loved one was transported or admitted to one of the many hospitals that can't provide that standard? More than 150,000 patients die after injury every year in the United States and bleeding is the leading cause of potentially preventable cause of death. When viewed as a public health crisis, WB is an intervention than can be used to help address those potentially preventable deaths at every level of care. The time is now to make WB widely available.

CONFLICT OF INTEREST

The authors have disclosed no conflicts of interest.

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