Whole Blood Transfusion

COL Andrew P. Cap, MC USA; LTC Andrew Beckett, MC CAF; MAJ Avi Benov, MC IDF; LTC Matthew Borgman, MC USA; LTC Jacob Chen, MC IDF; LTC Jason B. Corley, MSC USA; COL (ret) Heidi Doughty, MC UK; MAJ Andrew Fisher, SP USA; COL Elon Glassberg, MC IDF; COL (ret) Richard Gonzales, MSC USA; COL Shawn F. Kane, MC USA; LTC (ret) Wilbur W. Malloy, MSC USA; COL Shawn Nessen, MC USA; COL Jeremy G. Perkins, MC USA; MAJ Nicolas Prat, MC France; LTC Jose Quesada, MSC USA; COL Michael Reade, MC ADF; MG Anne Sailliol, MC France; PROF Philip C. Spinella, US; CAPT Zsolt Stockinger, MC USN; CDR Geir Strandenes, MC Norway; COL Audra Taylor, MSC USA; PROF Mark Yazer, MD US; PROF Barbara Bryant, MD; COL Jennifer Gurney, MC USA

ABSTRACT Whole blood is the preferred product for resuscitation of severe traumatic hemorrhage. It contains all the elements of blood that are necessary for oxygen delivery and hemostasis, in nearly physiologic ratios and concentrations. Group O whole blood that contains low titers of anti-A and anti-B antibodies (low titer group O whole blood) can be safely transfused as a universal blood product to patients of unknown blood group, facilitating rapid treatment of exsanguinating patients. Whole blood can be stored under refrigeration for up to 35 days, during which it retains acceptable hemostatic function, though supplementation with specific blood components, coagulation factors or other adjuncts may be necessary in some patients. Fresh whole blood can be collected from pre-screened donors in a walking blood bank to provide effective resuscitation when fully tested stored whole blood or blood components are unavailable and the need for transfusion is urgent. Available clinical data suggest that whole blood is at least equivalent if not superior to component therapy in the resuscitation of life-threatening hemorrhage. Low titer group O whole blood can be considered the standard of care in resuscitation of major hemorrhage.

INTRODUCTION

This Clinical Practice Guideline (CPG) provides the rationale and guidelines for both stored (SWB) and fresh whole blood (FWB) transfusion, including but not limited to product definitions, indications, collection, storage, testing, transfusion, and donor health.

DEFINITIONS

WB in the anticoagulantscitrate phosphate dextrose (CPD), citrate phosphate double dextrose (CP2D) or citrate phosphate dextrose adenine (CPDA-1) is an FDA-approved product when it is collected, stored and tested for transfusion-transmitted disease (TTD) by a licensed blood donor center. It can be stored for 21 days at 1–6°C in CPD and CP2D, or for 35 days at 1–6°C in CPDA-1 and is designated SWB in this CPG.¹ Currently, CPD and CPDA-1 SWB are provided by the Armed Services Blood Program (ASBP). The shelf life of SWB is determined by the capacity of the anticoagulant solution to sustain red blood cell (RBC) integrity. SWB retains in vitro hemostatic parameters to an acceptable level during the maximum approved storage duration^{2,3} (i.e. up to 35 days in CPDA-1); however, after the first 2 weeks of storage,

Published by Oxford University Press on behalf of Association of Military Surgeons of the United States 2018. This work is written by (a) US Government employee(s) and is in the public domain in the US.

the hemostatic function of WB may vary and supplementation with fresher whole blood units or blood components, especially platelets (PLTs), may be necessary to promote hemostasis.

FWB refers to WB collected on an emergency basis from a "walking blood bank" (WBB). FWB can either be stored at room temperature and used within 24 hours of collection⁴ (current practice is to destroy it if not used, though available data suggest that it could be used for up to 72 hours following collection and storage at room temperature) or it can be refrigerated within 8 hours of collection, after which point it becomes SWB. FWB is considered to have full hemostatic function. FWB is collected from pre-screened donors when possible, but does not undergo complete TTD testing prior to transfusion; this fact makes it not approvable by the FDA in the civilian setting. Because FWB presents a higher risk of disease transmission, it is reserved for situations in which tested blood products are unavailable and the need for transfusion is urgent.

The most important safety consideration in transfusing WB is that donor RBCs be compatible with the recipient's preformed anti-A and/or anti-B antibodies to avoid acute hemolytic transfusion reactions (a.k.a., major mismatch). WB from group O donors contains RBCs that are compatible with all recipients, but the plasma in group O WB contains anti-A and anti-B antibodies that could cause hemolysis in a non-group O recipient (a.k.a., minor mismatch). There are two approaches to mitigating this risk: (1) transfuse only group-specific WB (i.e. A to A, B to B, AB to AB and O to O) or (2) anti-A and

Joint Trauma System, 3698 Chambers Pass, Joint Base San Antonio, Fort Sam Houston, TX 78234.

doi: 10.1093/milmed/usy120

anti-B antibody titers can be measured in group O WB and only units containing a low titer of antibody (e.g., titer <256 saline dilution, immediate spin method) are designated "low titer O WB" (LTOWB) and these are used as "universal WB."^{5,6} LTOWB has been used extensively to resuscitate combat casualties and was the standard of care in WWII, and the conflicts in Korea and Vietnam.⁷ Note that LTOWB may be either SWB or may be collected from pre-screened O donors in a WBB protocol and thus be considered FWB (e.g., the Ranger O Low titer or ROLO protocol).^{8,9}

In practice, the only SWB supplied by the ASBP to deployed units will be LTOWB due to the relatively higher risk of donor-recipient blood group mismatch and resulting hemolysis if group-specific WB is transfused, compared to the much lower risk of hemolysis with LTOWB⁷ because of the group O RBCs.¹⁰ ASBP collects WB from male and neverpregnant female donors, or from female donors testing negative for anti-human leukocyte antigens antibodies (this mitigates risk of transfusion-associated acute lung injury, transfusionrelated acute injury, and is an AABB/FDA requirement). WB is collected from both Rh-positive and negative donors. Every effort should be made to transfuse Rh-negative WB or RBCs to female recipients of reproductive potential (<50 years of age) and of unknown blood group to avoid alloimmunization to the D antigen in Rh-negative patients, and thus reduce the risk of hemolytic disease of the fetus/newborn (HDFN) in future pregnancies. Collecting LTOWB from WBB prescreened donors is also preferred to group-specific transfusion when circumstances require the use of FWB (i.e. FWB should be LTOWB whenever possible). In short, most WB transfused during future contingency operations will be LTOWB, and most of this is likely to be SWB. Use of LTOWB is recognized under AABB Standard 5.15.1 (31st Edition, AABB Standards, in effect beginning 01 April 2018).¹¹

All WB products (SWB, FWB, and LTOWB) are indicated for the resuscitation of patients experiencing massive blood loss. WB, and in particular LTOWB, is the preferred resuscitation product for the pre-hospital treatment of patients in hemorrhagic shock¹² and in general for bleeding patients requiring emergency blood release. WB should be reserved for these emergency circumstances and should not be routinely used to treat isolated blood component deficiencies (e.g., anemia in a non-bleeding, hospitalized patient). This CPG will distinguish between stored whole blood (SWB) and FWB, and discuss uses and limitations of both products.

BACKGROUND

The first documented animal-to-animal (dog) blood transfusion was performed at Oxford in 1665 by Richard Lower, followed by the first animal-to-human blood transfusion in 1667 by Jean-Baptiste Denis. The first human-to-human blood transfusion was performed by the British obstetrician James Blundell in 1818. In the early 1900s, the ABO blood grouping system was classified by Landsteiner and, based on this landmark finding, the first pre-transfusion crossmatch was done by Ottenberg in 1907. An early method of Rh typing was invented by Landsteiner and Wiener in the year 1940.¹³ In military settings, whole blood has been used extensively to resuscitate casualties in military conflicts since 1917, during World War I.¹⁴ Whole blood is the starting point for most blood donations and continues to be used extensively worldwide where component production is not available, and to a lesser extent for priming cardiopulmonary bypass pumps in children undergoing cardiac surgery.¹⁵

Blood safety and sustainability are global issues. Using blood components supports the sustainability of blood services where demand can outstrip supply. Component use also permits optimal storage conditions for each of the components of blood, minimizes hemolytic reactions and supports precision treatment. Examples include the use of RBCs for anemia, fresh frozen plasma (FFP) to replace lost or consumed clotting factors, PLTs for thrombocytopenia and platelet abnormalities, and cryoprecipitate for hypofibrinoginemia. Whole blood contains all of these elements in a smaller volume of anticoagulant and preservative thereby providing a more concentrated product for treating bleeding patients who need all elements of blood replaced. The widespread use of component therapy is driven by blood product availability. For the reasons outlined above, blood banks have preferred to stock components over WB.

The clinical data comparing WB to components have recently been reviewed.¹⁶ Currently, available clinical data indicate that use of WB to treat hemorrhage results in outcomes that are at least as favorable as those that can be expected with component therapy that includes RBCs, plasma and PLTs.

Severely injured combat casualties requiring transfusion have a significant mortality rate (range 10-20%) and have the greatest potential to benefit from early and appropriate transfusion strategies.¹⁷ A large retrospective cohort study of casualties requiring transfusions during Operations Iraqi Freedom (OIF) and Enduring Freedom (OEF) suggests a significant survival benefit for transfused casualties when RBCs, FFP, and PLTs are initially transfused at a 1:1:1 ratio.¹⁸ A recent randomized trial in civilian trauma patients demonstrated that a 1:1:1 transfusion ratio resulted in improved early hemostasis, and reduced death from hemorrhage in the first 24 hours, though no statistically significant improvement in overall 24 hours or 30 days survival.¹⁹ Two retrospective analyses in combat casualties comparing FWB to component therapy (including PLTs) have also been published. One study showed a potential survival benefit to the use of FWB during resuscitation of severe combat injuries, and the other showed FWB to be equivalent to component therapy.²⁰ These studies underscore the importance of providing all elements of whole blood (RBCs, plasma and PLTs) to severely bleeding patients and suggest that use of either WB or components in a 1:1:1 ratio for resuscitation of bleeding patients is acceptable especially early in the resuscitation

when the coagulopathy of trauma is often present;²¹ product choices can be guided by practical considerations. One retrospective registry study has evaluated outcomes for civilian patients who received SWB vs. components and found that component use was associated with increased risk of mortality compared to use of SWB.²² Another recent study has found that stored LTOWB does not cause hemolysis when used in resuscitation of non-group O civilian trauma patients²³ when 1–2 units were transfused; these results have been extended to recipients of even greater quantities of WB, namely 3–4 units.

ADVANTAGES OF WB OVER COMPONENTS

SWB and FWB provide FFP:RBC:PLTs in a nearly physiologic ratio and return to the bleeding patient what has been lost. It should be noted that the 1:1:1 ratio of blood components (PLTs:plasma:RBC) recommended for damage control resuscitation does not faithfully reconstitute WB. The 1:1:1 ratio yields a dilute blood mixture²⁴ with a hematocrit of 29%, a platelet count of approximately 90,000/µL, and coagulation factors diluted to approximately 62% of WB concentrations due to the presence of anticoagulants and red cell additive solution. By contrast, WB units, which do not contain extended storage RBC additive solutions, offer a hematocrit of 35-38%, a platelet count of 150,000-200,000/, and coagulation factors at approximately 85% of pre-donation levels. In addition, WB delivers all needed elements of blood in only one product, which only requires refrigeration for storage (i.e. the same conditions that already exist for RBC storage and transport). In contrast, component therapy requires multiple products and storage modalities (refrigeration, freezing and generally room temperature storage with agitation for PLTs - though PLTs can also be refrigerated), greatly increasing workload and complexity for clinical teams.

SWB collected in licensed blood centers offers the same level of TTD safety as component therapy collected in licensed centers. It should be noted that due to the extremely short shelf life of standard room temperature-stored PLTs (5 days), all platelet products transfused in the deployed setting are collected in theater and do not undergo TTD testing prior to transfusion, making them a non-approved FDA product. Recent studies show that apheresis platelet products can be stored under refrigeration for longer than 5 days. Indeed, available evidence suggests that considerable hemostatic function is retained for at least 21 days during cold storage²⁵ and that refrigerated PLTs are superior to room temperature-stored PLTs for acute hemostasis.^{26,27,28} A randomized trial of refrigerated vs. room temperature-stored apheresis PLTs in cardiac surgery patients demonstrated reduced blood loss in patients receiving refrigerated PLTs.²⁹ Currently, cold storage of apheresis PLTs is limited to 10 days in theater by CENTCOM policy so even these platelet products must be collected on-site and do not undergo TTD testing prior to transfusion (non-approved FDA product). Therefore, SWB collected in licensed centers and fully

tested presents a lower TTD risk than component therapy using in-theater collected PLTs or FWB.

For U.S. casualties presenting in hemorrhagic shock, a transfusion strategy that included FWB with RBCs and plasma was associated with an improved survival compared to the use of stored components only (FFP, RBCs, and PLTs).³⁰ Compared with SWB or component therapy, FWB is more readily available in austere conditions and requires only the presence of donors and simple collection equipment, though safe collection and transfusion of FWB requires appropriate pre-deployment training^{31,32} and careful donor evaluation. FWB has no loss of the labile clotting factors or platelet activity that is often associated with storage, has close to physiological hematocrit and is not impacted by the RBC "storage lesion." The term RBC storage lesion describes the changes in the RBCs during ex vivo storage and includes things like loss of membrane plasticity, diphosphoglycerate, adenosine triphosphate, nitric oxide, and other factors leading to potentially reduced delivery of oxygen to tissues and contribution to a variety of pathophysiologic processes.³³ It should be noted that several recent randomized trials assessing the effects of RBC storage age have not found a clinically detectable deleterious effect of the red cell storage lesion in the populations evaluated. A secondary analysis of the ABLE trial indicates that in large volume transfusion (>7 units of RBCs), RBCs of increased storage age were associated with increased mortality, but this result could also be due to confounding by indication, i.e. the patients had a higher rate of mortality because of more extensive bleeding not due to receipt of older RBCs. The effect of red cell storage, whether in component therapy or SWB has not been rigorously evaluated in certain vulnerable populations, requiring high volume transfusions, such as trauma patients³⁴ where confounding by indication would also be present and its effect difficult to tease out from the possible effect of the age of the transfused RBCs.

Overall, both SWB and FWB offer at least comparable performance and safety compared with components, as well as very compelling logistical advantages that are particularly important in pre-hospital resuscitation and indeed, in most deployment settings, but also in severely bleeding patients requiring emergency blood release during hospital-based resuscitations. The use of SWB presents a major advantage compared to balanced, platelet-containing component therapy bundles due its increased storage duration and resulting availability of platelet-containing resuscitation. With storage of SWB for up to 35 days in CPDA-1, the effective platelet storage duration is increased 7-fold compared with standard room temperature apheresis platelet unit storage (the current standard),³⁵ although further study is required to determine the hemostatic efficacy of cold stored PLTs at 35 days. This permits maintenance of an inventory of a platelet-containing product (SWB) in austere environments where apheresis PLTs are unavailable. Also, it should be recognized that platelet units are often in short supply even in major medical centers, so use of SWB will alleviate platelet shortages

across the spectrum of healthcare delivery platforms. In view of this and since the vast majority of preventable hemorrhage deaths occur pre-hospital, the logistical benefit of SWB is compelling and makes SWB preferable to blood components for both in- and pre-hospital resuscitation. Based on the above efficacy, safety, and logistical considerations, the JTS Committee on Tactical Combat Casualty Care and international trauma organizations such as THOR have recommended WB as the preferred resuscitation product for patients with traumatic hemorrhagic shock.^{7,12,36}

CONSIDERATIONS IN CHOOSING SWB OR FWB

There are risks associated with the use of FWB, including but not limited to increased risk of transfusion-transmitted infections (e.g., HIV, hepatitis B/C, syphilis), and an increased risk of clerical errors leading to major mismatch when ABOidentical WB is provided, due to the potentially chaotic and urgent conditions during which FWB is used. Additionally, field conditions are inherently unsanitary and might increase the risk of bacterial contamination of the FWB. Recent history with approximately 10,000 FWB transfusions to U.S. personnel during OIF/OEF have resulted in one Hepatitis C (HCV), one Human T-Lymphocyte Virus (HTLV) seroconversion, and one fatal case of transfusion-associated graft-versus host disease that was potentially due to a FWB transfusion.³⁷ FWB is not FDA-approved and is not intended or indicated for routine use. It is NOT appropriate, as a matter of convenience, to use FWB as an alternative to more stringently controlled blood products for patients who do not have severe, immediately life-threatening injuries. FWB is to be used only when other blood products cannot be delivered at an acceptable rate to sustain the resuscitation of an actively bleeding patient, when specific stored products are not available (e.g., SWB, RBCs, FFP, PLTs, cryoprecipitate), or when stored components are not adequately resuscitating a patient with an immediately lifethreatening injury. It should be noted that studies of FWB donors have not documented significant decrements in military-relevant task performance following donation. Thus, concerns that FWB collections will adversely affect mission outcomes have not been substantiated and should not preclude WBB activation when conditions for FWB use are met.³⁸

In patients receiving emergency released type O RBCs or A/AB plasma or LTOWB (SWB or FWB), every effort should be made to obtain a pre-transfusion blood sample in order to establish the recipient's native blood group. If blood samples are obtained after transfusion with LTOWB or O RBCs, it may be impossible to definitively establish a patient's blood group with the equipment available in the deployed setting. As a result, patients of unknown blood group receiving LTOWB will continue to receive LTOWB or group O RBC units for their acute transfusion requirements for up to a month following admission. This can deplete inventories of LTOWB and group O RBCs as well as the A or AB plasma inventories.

WB RECOMMENDATIONS

- SWB, which will in U.S. military practice be LTOWB, is the preferred product for resuscitation of severe bleeding (both pre-hospital and in-hospital). SWB simplifies the logistics of the transfusion and may facilitate more rapid resuscitation of casualties, and may enhance a facility's capacity to manage mass casualty (MASCAL) challenges.
- The indication for SWB is life-threatening hemorrhage. The assessment that a hemorrhage is life-threatening is mainly established clinically, and should be driven by an assessment of the patient's vital signs, hemodynamics, physical exam, mechanism of injury and laboratory measures of shock and hemostasis if available. The use of FWB should be reserved for when SWB or full component therapy is unavailable.
- Blood component therapy (1:1:1) is an acceptable option for treating life-threatening hemorrhage when SWB is not available. The potential reduced efficacy, safety, and logistical aspects of blood component therapy should be taken into consideration when choosing between resuscitation strategies (Table I).

GUIDELINES FOR WALKING BLOOD BANK PROGRAM FOR FWB

Full procedural details including documentation for WBB is available on the JTS website.

Efficacy	 The cold stored PLTs provide improved hemostasis compared with room temperature PLTs Whole blood is a more concentrated product that contains a smaller quantity of anticoagulant and additive solution than an equal amount of conventional components
Safety	 Reduced risk of hemolysis from the low titer minor incompatible plasma compared to the risk from untitered minor incompatible plasma or PLTs Reduced risk of bacterial contamination compared to room temperature-stored PLTs Long-standing safety record with over 1 million units transfused in combat and civilian settings
Logistic	 Increased access to PLTs for both pre-hospital and early in-hospital resuscitations Simplifies the logistics of the resuscitation and accelerates the provision of all blood components needed to treat hemorrhagic shock

TABLE I. Benefits of Low Titer Group O Whole Blood for Hemorrhagic Shock

Source: Yazer MH, Cap AP, Spinella PC. Raising the Standards on Whole Blood. J Trauma Acute Care Surg. 2017 Dec 28

The decision to use FWB is a medical decision that must be made by a physician who has full knowledge of both the clinical situation and the availability of compatible blood products. A WBB Program should be established based on a risk assessment and the potential for massively bleeding casualties. The calculation of risk should include a medical intelligence assessment which includes infection prevalence and the need for preventative force protection measures. Coordination with the Joint Blood Program Officer (JBPO) is required to establish a WBB Program. In general, the use of FWB should be limited to casualties who are anticipated to require a transfusion when the physician determines that SWB or optimal component therapy is unavailable or in limited supply, or in patients that are not responding to SWB or component therapy. The decision to initiate a FWB drive should be made in consultation with the appropriate MTF medical authority (e.g., DCCS, Trauma Director, Trauma Surgeon) and Laboratory/Blood Bank OIC. At Role 2 facilities, the lead surgeons and/or facility OIC should be consulted on the decision to initiate the drive.

Pre-screened donors registered into the WBB Program are preferably composed of active duty, active reserve, active National Guard, and other DoD beneficiaries. The preferred donors for FWB are fully pre-screened, low titer O donors. The question of whether previously low titer donors need to have their anti-A and -B verified as low titer again before their subsequent donated WB units are issued as LTOWB is controversial but is likely to become the standard of care in the civilian setting.^{39,40} Next, consider fully pre-screened donors of other blood groups for group-specific transfusions (e.g., A to A). Donors who have not been pre-screened for TTDs should be considered only when no other donors are available; careful history-taking can improve donor risk stratification.⁴¹ Note that in chaotic circumstances such as tactical care under fire or MASCAL scenarios, or if blood grouping equipment is not available in adequate quantities, use of group O FWB of unknown anti-A and anti-B titer may be safer than attempting to match blood groups between donors and recipients, since the risk of hemolysis from major mismatch is greater than the risk of transfusing a very high titer group O unit (very high titers units being relatively uncommon) to a non-group O recipient. Indeed, this strategy was successfully employed by a Forward Surgical Team in Afghanistan.42

U.S. donors should be screened to U.S. FDA standards. Coalition Forces should be screened to relevant mandated international or national standards (e.g., according to European Blood Directive standards for NATO partners). Coalition Forces will not be utilized routinely as donors, due to national variances in screening for blood borne diseases and differences in disease prevalence. However, blood may be collected from pre-screened coalition partner forces if the screening program has been reviewed by the JBPO and deemed acceptable by the Combatant Command Surgeon and the ASBP. Screening results from Coalition Forces must be available to the JBPO; therefore coordination with the JBPO is required. Planned coalition activity should address the interoperability of donor panels. Non-Coalition Force foreign nationals should be used as a last resort.

The decision to use FWB that has not been completely screened for infectious agents is a medical decision that must be made after thorough consideration of risks and benefits. Decision-making should be adequately documented in the casualty record.

The blood type on identification tags is occasionally incorrect (last correlated data demonstrated about a 4% error rate)^{43,44,45} and must not be relied upon routinely to determine blood type for either donors or recipients. Identification tags for ABO/Rh verification should be utilized as a last resort only.

Use of non-standard blood donation material and equipment may lead to coagulation activation and/or clotting during the collection process potentially affecting the safety, purity, or potency of the blood product or causing an adverse transfusion reaction; therefore, only authorized equipment should be utilized.

Prior to issuing FWB for transfusion, the ABO and Rh type of the unit should be verified. ASBP-approved rapid infectious disease tests (e.g., HIV, HCV, and HBV) should also be performed to the greatest extent possible before transfusion. If unable to perform prior to transfusion, rapid infectious disease testing should still be performed on donor samples post transfusion.

Theater Medical Data Stores (TMDS), Blood Portal, shall be utilized to record FWB donations and infectious disease testing results. Frequency of FWB donation must be tracked. In general, WB units should not be collected from donors more frequently than every 8 weeks (56 days). This interval between donations is important to allow the donor to recover RBC mass and iron stores and should not be shortened except under the most extreme circumstances. Donors who give blood frequently may develop iron deficiency even in the absence of anemia. Iron deficiency can cause fatigue, difficulty concentrating, pica, restless leg syndrome (RLS), and eventually anemia if untreated. Iron deficiency can be diagnosed by measuring serum ferritin levels (deficiency defined as ferritin <30 mcg/L in males and <20 mcg/L in females). In deployed settings, it may be impossible to measure ferritin levels but donors at particular risk of iron deficiency include: young donors (to early 20's), premenopausal females, frequent donors (males $\geq 3 \times$ /year, females $\geq 2 \times$ /year), and donors near hemoglobin cutoff for donation (males 13.0 g/dL, females 12.5 g/dL). Consideration should be given to screening ferritin prior to deployment in high-risk donors, particularly low titer O donors who may be called upon to donate more frequently. Consideration should be given to empiric iron supplementation in high-risk donors or donors with symptoms of iron deficiency (available as ferrous sulfate 325 mg (65 mg elemental iron), ferrous gluconate 325 mg (38 mg elemental iron), or multivitamins with iron (18–19 mg

elemental iron);^{46,47} one tablet per day for 60–120 days may be adequate to replete iron stores). Patients with documented iron deficiency (low ferritin levels as above) should be offered iron supplementation and monitored for response.

WBB PLANNING

Since the need for FWB cannot be predicted, a robust contingency operational plan should be developed by the MTF staff to include the Laboratory/Blood Bank and surgical and anesthesia providers in coordination with the Joint Blood Program Officer. Due to the limited number of laboratory personnel and requirement for those same personnel to complete other laboratory testing requirements, the plan must include other personnel to assist in the donor screening and collection processes. The plan should be reviewed and rehearsed regularly. Equipment and consumables should be inspected with due attention paid to storage conditions and expiry dates.

The key elements for planning and readiness to administer FWB are knowledge and rehearsal of blood donor prescreening and emergency whole blood collection.

- A contingency plan should be developed for collecting, storing, and transfusing FWB in MASCAL situations or when it may be deemed that the current blood inventory will be exhausted prior to re-supply (e.g., when multiple type-O trauma casualties are exhausting the type-O RBC inventory).
- The physical donation site should be organized in such a way as to maintain the integrity of the screening and donation process, and to minimize the possibility of clerical errors. This is especially important in emergency situations involving more than one casualty.
- Every effort should be made to adhere to the same screening, drawing, labeling, and issuing standards required for U.S. FDA-approved blood products.
- Pre-screened donors in the WBB Program determined to be suitable should be utilized, to the greatest extent possible, before using personnel who: (1) have been prescreened or donated in the past but do not have current (within 90 days) screening and infectious disease testing;
 (2) have no pre-screen or donation history. All donors must be rescreened at the time of donation.
- Use LTOWB donors if available. Otherwise, upon determining the ABO/Rh status of the casualty, activate the WBB Program, re-calling pre-screened donors with the same ABO/Rh using the TMDS > Manage Donor > View Donor List, if available, or other communication networks. All donors should have blood group and titers (for LTOWB donors) verified in TMDS at the time of donation and blood group should be re-tested (e.g., by Eldon card). Titers for LTOWB donors should be no more than

12 months prior to donation. The ABO and RhD group should be the same on the dogtag and records. Before any FWB is transfused, rapid infectious disease testing (i.e. HIV, HBV, HCV) of donor specimens shall be performed, to the greatest extent possible.

- Retrospective samples must be sent to a licensed laboratory for FDA-approved TTD testing, regardless of whether the rapid infectious disease testing is performed pre- or post-transfusion, as these tests are not licensed for donor testing.
- Upon the notification of confirmed positive infectious disease results, a medical provider or preventive medicine personnel will be notified to ensure that the donor is notified and counseled. Donors and unit commanders must understand the importance of donor tracing.
- If a patient receives a confirmed positive infectious disease unit, the JBPO will notify the Armed Services Blood Program immediately to initiate patient notification and an evaluation of both the donor and patient.
- In accordance with HA Policy 10-002, Policy on the Use of Non-U.S. Food and Drug Administration, recipients of FWB shall receive follow-up advice and infectious disease testing as soon as possible, and at 3-, 6-, and 12-months post-transfusion.
- Only one unit of FWB should be collected per donor. In situations where there are a limited number of donors and a dire need for blood, no more than two units may be taken from a donor. When selecting a donor from which to collect two units, those with larger body masses are probably less at risk of developing iron deficiency than those with smaller body masses. Performance decrements may occur after two-unit collections and volume resuscitation of the donor may be necessary. Collection of more than one unit per donor should only be considered under extreme circumstances and these should be thoroughly documented.

WB PEDIATRIC CONSIDERATIONS

- WB has been administered to pediatric patients in recent conflicts. WB has not been rigorously studied in pediatric trauma resuscitation, but both FWB and SWB have been shown to reduce blood loss, and improve platelet function in pediatric cardiac surgery compared to blood components.
- There is no physiologic reason not to use WB in children with life-threatening hemorrhage. It should be titrated to clinical response similar to the resuscitation of an adult patient.

REFERENCES

- Circular of Information for the use of human blood and blood components. October 2017. Available at https://www.fda.gov/downloads/ BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/ Guidances/Blood/UCM364587.pdf
- Pidcoke HF, McFaul SJ, Ramasubramanian AK, et al: Primary hemostatic capacity of whole blood: a comprehensive analysis of pathogen

reduction and refrigeration effects over time. Transfusion 2013; 53 (Suppl 1): 137S-49S.

- Siletz A, Burruss S, Gruber T, et al: Cryer HM. Leukocyte filtration lesion impairs functional coagulation in banked whole blood. J Trauma Acute Care Surg 2017; 83(3): 420–6.
- 4. Hughes JD, Macdonald VW, Hess JR: Warm storage of whole blood for 72 hours. Transfusion 2007; 47(11): 2050–6.
- Belin TR, Yazer MH, Meledeo MA, et al: An evaluation of methods for producing low-titer group O whole blood to support military trauma resuscitation. J Trauma Acute Care Surg 2017; 82(6S Suppl 1): S79–86.
- Yazer MH, Seheult J, Kleinman S, et al: Who's afraid of incompatible plasma? A balanced approach to the safe transfusion of blood products containing ABO-incompatible plasma. Transfusion 2018; 58(2): 532–8.
- Strandenes G, Berséus O, Cap AP, et al: Low titer group O whole blood in emergency situations. Shock 2014; 41(Suppl 1): 70–5.
- Fisher AD, Miles EA, Cap AP, Strandenes G, Kane SF: Tactical damage control resuscitation. Mil Med 2015; 180(8): 869–75. doi:10.7205/ MILMED-D-14-00721.
- Bahr M, Yazer MH, Triulzi DJ, Collins RA: Whole blood for the acutely hemorrhaging patient: a novel idea or rediscovery? Transfus Med 2016; 26: 406–14.
- Yazer MH, Waters JH, Spinella PC: Use of uncrossmatched erythrocytes in emergency bleeding situations. Anesthesiology 2018; 128(3): 650–6.
- Yazer MH, Cap AP, Spinella PC: Raising the standards on whole blood. J Trauma Acute Care Surg 2017. doi:10.1097/ta.000000000001778.
- Butler FK, Holcomb JB, Schreiber MA, et al: Fluid resuscitation for hemorrhagic shock in tactical combat casualty care: TCCC guidelines change 14-01–2 June 2014. J Spec Oper Med 2014; 14(3): 13–38.
- Arya RC, Wander GS, Gupta P: Blood component therapy: which, when and how much. J Anaesthesiol Clin Pharmacol 2011; 27(2): 278–84.
- 14. Stansbury LG, Hess JR: The 100th anniversary of the first blood bank. Transfusion 2017; 57(11): 2562–3.
- Mou SS, Giroir BP, Molitor-Kirsch EA, et al: Fresh whole blood versus reconstituted blood for pump priming in heart surgery in infants. N Engl J Med 2004; 351(16): 1635–44.
- 16. Spinella PC, Cap AP: Whole blood: back to the future. Curr Opin Hematol 2016; 23(6): 536–42.
- Shackelford SA, Del Junco DJ, Powell-Dunford N, et al: Association of prehospital blood product transfusion during medical evacuation of combat casualties in Afghanistan with acute and 30-day survival. JAMA 2017; 318: 1581.
- Pidcoke HF, Aden JK, Mora AG, et al: Ten-year analysis of transfusion in Operation Iraqi Freedom and Operation Enduring Freedom: increased plasma and platelet use correlates with improved survival. J Trauma Acute Care Surg 2012; 73(6 Suppl 5): S445–52.
- Holcomb JB, Tilley BC, Baraniuk S, et al: Transfusion of plasma, platelets, and red blood cells in a 1:1:1 vs a 1:1:2 ratio and mortality in patients with severe trauma: the PROPPR randomized clinical trial. PROPPR Study Group. JAMA 2015; 313(5): 471–82.
- Spinella PC, Perkins JG, Grathwohl JG, et al: Warm fresh whole blood is independently associated with improved survival for patients with combat-related traumatic injuries. J Trauma 2009; 66: S69–76.
- 21. Harris T, Davenport R, Mak M, Brohi K: The evolving science of trauma resuscitation. Emerg Med Clin North Am 2018; 36(1): 85–106.
- 22. Jones AR, Frazier SK: Increased mortality in adult patients with trauma transfused with blood components compared with whole blood. J Trauma Nurs 2014; 21(1): 22–9.
- Seheult JN, Triulzi DJ, Alarcon LH, Sperry JL, Murdock A, Yazer MH: Measurement of haemolysis markers following transfusion of uncrossmatched, low-titre, group O+ whole blood in civilian trauma patients: initial experience at a level 1 trauma centre. Transfus Med 2017; 27(1): 30–5.

- Hess JR: Resuscitation of trauma-induced coagulopathy. Hematology Am Soc Hematol Educ Program 2013; 2013: 664–7.
- 25. Getz TM, Montgomery RK, Bynum JA, et al: Storage of platelets at 4°C in platelet additive solutions prevents aggregate formation and preserves platelet functional responses. Transfusion 2016; 56(6): 1320–8.
- 26. Cap AP, Spinella PC: Just chill-it's worth it! Transfusion 2017; 57(12): 2817–20.
- 27. Pidcoke HF, Spinella PC, Ramasubramanian AK, et al: Refrigerated platelets for the treatment of acute bleeding: a review of the literature and reexamination of current standards. Shock 2014; 41(Suppl 1): 51–3.
- Cap AP: Platelet storage: a license to chill! Transfusion 2016; 56(1): 13–6.
- 29. Apelseth TO, Kristoffersen EK, Kvalheim VL, et al, Transfusion with Cold Stored Platelets in Patients Undergoing Complex Cardiothoracic Surgery with Cardiopulmonary Bypass Circulation: Effect on Bleeding and Thromboembolic Risk. Available at https://aabb.confex.com/aabb/ 2017/meetingapp.cgi/Paper/2121; accessed March 5, 2018.
- Spinella PC, Perkins JG, Grathwohl KW, et al: Warm fresh whole blood is independently associated with improved survival for patients with combat-related traumatic injuries. J Trauma 2009; 66(4 Suppl): S69–76.
- 31. Strandenes G, De Pasquale M, Cap AP, et al: Emergency whole-blood use in the field: a simplified protocol for collection and transfusion. Shock 2014; 41(Suppl 1): 76–83.
- Doughty H, Thompson P, Cap AP, et al: A proposed field emergency donor panel questionnaire and triage tool. Transfusion 2016; 56(Suppl 2): S119–27.
- Hess JR: Measures of stored red blood cell quality. Vox Sang 2014; 107(1): 1–9.
- Belpulsi D, Spitalnik SL, Hod EA: The controversy over the age of blood: what do the clinical trials really teach us? Blood Transfus 2017; 15(2): 112–5.
- Siletz A, Burruss S, Gruber T, et al: Leukocyte filtration lesion impairs functional coagulation in banked whole blood. J Trauma Acute Care Surg 2017; 83(3): 420–6.
- Spinella PC, Pidcoke HF, Strandenes G, et al: Whole blood for hemostatic resuscitation of major bleeding. Transfusion 2016; 56(Suppl 2): S190–202.
- 37. Gilstad C, Roschewski M, Wells J, et al: Fatal transfusion-associated graft-versus-host disease with concomitant immune hemolysis in a group A combat trauma patient resuscitated with group O fresh whole blood. Transfusion 2012; 52(5): 930–5.
- 38. Strandenes G, Skogrand H, Spinella PC, et al: Donor performance of combat readiness skills of special forces soldiers are maintained immediately after whole blood donation: a study to support the development of a prehospital fresh whole blood transfusion program. Transfusion 2013; 53(3): 526–30.
- 39. Assing K, Rasmussen MH, Yazer MH, Sprogøe U: Minimal variation in anti-A and -B titers among healthy volunteers over time: implications for the use of out -of- group blood components. J Trauma Acute Care Surg 2017; 82(6S Suppl 1): S87–90.
- Yazer MH, Cap AP, Spinella PC, et al: How do I Implement a whole blood program for massively bleeding patients. Transfusion 2018. doi:10.1111/trf.14474.
- Doughty H, Thompson P, Cap AP, et al: A proposed field emergency donor panel questionnaire and triage tool. Transfusion 2016; 56(Suppl 2): S119–27.
- 42. Nessen SC, Eastridge BJ, Cronk D, et al: Fresh whole blood use by forward surgical teams in Afghanistan is associated with improved survival compared to component therapy without platelets. Transfusion 2013; 53 (Suppl 1): 107S–13S.
- Rentas FJ, Clark PA: Blood type discrepancies on military identification cards and tags: a readiness concern in the U.S. Army. Mil Med 1999; 164(11): 785–7.

- 44. Frohman EM: Blood typing errors on U.S. army identification cards and tags. Mil Med 1989; 154(5): 273–4.
- Gaydos JC, Polk AJ, Cowan DN, et al: Blood typing errors on U.S. Army identification (ID) cards and tags. Mil Med 1990; 155(4): A19.
- 46. Mast AE, Bialkowski W, Bryant BJ, et al: A randomized, blinded, placebo-controlled trial of education and iron supplementation for

mitigation of iron deficiency in regular blood donors. Transfusion 2016; 56: 1588–97.

47. Bialkowski W, Kiss JE, Wright DJ, et al: Estimates of total body iron indicate 19 mg and 38 mg oral iron are equivalent for the mitigation of iron deficiency in a longitudinal study. Am J Hematol 2017; 92: 851–7.