FRESH WHOLE BLOOD (FWB) TRANSFUSION

Original Release/Approval		Oct 2006	Note: This CPG requires an annual review.	
Reviewed:	Dec 2008	Approved:	12 Jan 09	
Supersedes:	Fresh Whole Blood (FWB) Transfusion, updated 19 Nov 08			
☐ Minor Changes (***or)***		☐ ***Changes are substantial and require a thorough reading of this CPG***		***(or)***
☒ Significant Changes:		Increased emphasis on 1:1:1 resuscitation for massive transfusion patients; use of FWB in austere settings to treat coagulopathy associated with shock; use of FWB for casualties requiring massive transfusion who do not respond adequately to resuscitation with full component therapy; full component therapy includes pRBCs for anemia, fresh frozen plasma (FFP) to replace clotting factors, platelets for thrombocytopenia and cryoprecipitate (Cryo) for hypofibrinoginemia.		

1. Goal. Provide the rationale and guidelines for FWB transfusion, including but not limited to indications, collection, testing, transfusion, and documentation

2. Background. Whole blood has been used extensively to resuscitate casualties in military conflicts since World War I. Its use in civilian settings is limited due to the wide availability of fractionated components derived from whole blood and provided for specific deficits (e.g., pRBCs for anemia, fresh frozen plasma (FFP) to replace lost/consumed clotting factors, platelets for thrombocytopenia, cryoprecipitate (Cryo) for hypofibrinoginemia.) However, in austere conditions, fractionated blood products are often in limited supply or unavailable. In these settings, FWB may be the only source of blood components available for the management of hemorrhagic shock ***and its associated coagulopathy*** in casualties (*Appendix A*).

Massively transfused casualties (≥ 10 units RBCs in 24 hours) have a high mortality rate (22% at 48 hours and 44% at 30 days) and have the greatest potential to benefit from appropriate transfusion strategies. Large retrospective cohort studies of casualties requiring massive transfusions during Operations IRAQI FREEDOM (OIF) and ENDURING FREEDOM (OEF) demonstrate a significant survival benefit for the massively transfused casualty when RBCs, fresh frozen plasma, and platelets are transfused at a 1:1:1 ratio.

Advantages to FWB: FWB provides FFP:RBC: platelets in a 1:1:1 ratio. Compared to 1 unit of "reconstituted whole blood" from components with 1 unit each of plasma, RBCs, and platelets, FWB is a more concentrated product since it does not contain 3X in volume of anticoagulant and additive solutions. For US casualties presenting in hemorrhagic shock, a transfusion strategy that included FWB with RBCs and plasma-improved survival compared to the use of stored components only (FFP, RBCs, and PLTs). Additionally, FWB is readily available in austere conditions, has no loss of clotting factor and platelet activity associated with cold storage, and has no red blood cell "storage lesion".

Disadvantages to FWB: Fresh whole blood is not FDA-approved and is not intended or indicated for routine use. **Since FWB has both RBCs and plasma, it must be ABO type-specific.** There are risks associated with the use of FWB, including but not limited to increased risk of transmitted blood-borne diseases (e.g., HIV, hepatitis B/C, syphilis), a period of decreased exercise tolerance in donors (who are often members in the casualty's unit), and an

increased risk of clerical errors (e.g., ABO typing) due to the frequently chaotic activity during which FWB is requested. Additionally, field conditions are inherently unsanitary and are presumed to increase the risk of bacterial contamination of the blood. Recent history with >4000 FWB transfusions during OIF/OEF have resulted in one 1 Hepatitis C seroconversion. **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 are unable to be delivered at an acceptable rate to sustain the resuscitation of an actively bleeding patient, when specific stored components are not available (e.g., pRBCs, platelets, Cryo, FFP), or when stored components are not adequately resuscitating a patient with an immediately life-threatening injury.**

3. Recommendations. The use of FWB should be reserved for trauma casualties who are anticipated to require massive transfusion (10 or more units pRBCs in 24 hours), for those with ***clinically significant shock or coagulopathy (e.g. bleeding with associated metabolic acidosis, thrombocytopenia or INR>1.5) when optimal component therapy (e.g., apheresis platelets and FFP) are unavailable or stored component therapy is not adequately resuscitating a patient with immediately life-threatening injuries.***

a. *Facilities where full component therapy is available (e.g. Level III facilities):* Due to infectious concerns the risk:benefit ratio does not justify the routine use of FWB over banked blood products in non life-threatening severe trauma. Conversely, when platelets and FFP inventories are depleted, or in contingencies such as mass casualty (MASCAL) situation where the blood inventory may be exhausted, the use of FWB remains an appropriate life-saving option.

b. Surgical Facilities where component therapy is limited (e.g. no availability of apheresis platelets): Due to risks inherent with the use of FWB it should only be used for patients *with immediate life-threatening injuries.*

c. *Nonsurgical facilities:* FWB ***should not be used*** in a setting without surgical availability.

4. Guidelines. 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 components.

a. In general, the use of FWB should be limited to casualties who are anticipated to require a massive transfusion when the physician determines that optimal component therapy is unavailable or in limited supply, or in patients that are not responding to stored component therapy.

b. The decision to initiate a FWB drive should be made in consultation with the appropriate MTF medical authority (e.g., DCCS, Trauma Director) and Laboratory/Blood Bank OIC.

c. Donor FWB must be an ABO type-specific match to the casualty. If not matched, a fatal hemolytic reaction may occur.

d. The decision to use fresh whole blood 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.

5. Precautions. Donation of fresh whole blood in the field may be dangerous for several reasons:

a. There is no universally compatible FWB type. Transfusions of FWB must be an ABO match. For female casualties of child-bearing potential, there must also be an Rh match. Service members' blood types are not always known with certainty. The blood type on identification tags is occasionally incorrect and must not be relied upon to determine blood type for either donors or recipients.

b. Because it is not subject to the same strict quality controls and infectious disease testing as banked blood, FWB does not meet FDA standards and has an increased risk of blood-borne disease transmission (e.g., HIV, hepatitis B/C, syphilis).

c. In emergency situations, particularly when more than one blood type is being collected, there is an increased risk of a clerical error leading to a life-threatening transfusion reaction.

d. Field conditions are inherently unsanitary and increase the risk of bacterial contamination of the blood.

e. Use of non-standard transfusion equipment may lead to coagulation during the transfusion process.

6. 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. The plan should be reviewed and rehearsed regularly.

a. If practical, establish a pre-screened donor pool using the Blood Donation Questionnaire (DD Form 572 or MS Word version), preferably composed of active duty, active reserve, active National Guard, and other DoD beneficiaries. If practical, testing of the potential donor pool for transfusion-transmitted diseases should be strongly considered. Coalition and Foreign Nationals will not be utilized as donors. Recent laboratory confirmation of blood group/type and non-reactive status for transfusion-transmissible disease tests is ideal, but does not obviate the need for confirmatory testing. The donor file must be maintained and updated frequently.

b. In an emergency, rapidly establish ABO/Rh status of donors and casualties on-site using appropriate reagents/tests in conjunction with previous blood donor history records, if available.

c. Every effort should be made to adhere to the same screening, drawing, labeling, and issuing standards required for US FDA-approved blood products.

d. 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.

e. It is highly recommended, where feasible, to perform on-site testing of potential blood donors using rapid screening immunoassays for infectious diseases (i.e., HIV, HBV, HCV) before FWB is transfused. Regardless whether the local testing is performed pre- or post-transfusion, these tests are not licensed for donor testing and samples must be sent to a reference lab for FDA-approved testing. A mechanism must be in place to ensure that

both the recipient and donor can be notified should the results be positive for infectious disease.

f. A contingency plan should be developed for collecting, storing, and transfusing FWB in MASCAL situations or when it may be deemed 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).

7. Procedure.

a. Where appropriate, set up a "walking blood bank" with pre-screened donors using the Blood Donation Questionnaire. This pool of donors should include active duty, active Reserve, active National Guard, and DoD beneficiaries. The safest donor candidate is one with recent laboratory confirmation of blood group/type and no evidence of transfusion transmissible disease. It is important to update frequently the donor file. Choose prior blood donors in preference to non-donors because they have been tested for transfusion-related infectious diseases in the past.

b. In an emergency, establish ABO/Rh of donors via local testing or previous donor history. **Identification tags for ABO/Rh verification should be utilized as a last resort only.**

c. It is highly recommended, where feasible, that all MTFs perform rapid, on-site viral marker screening tests of potential blood donors using screening immunoassays for infectious diseases (e.g., HIV, HBsAg, HCV) before FWB is transfused. If testing is not possible prior to transfusion, rapid, on-site viral marker testing should be performed as soon as possible on-site and results recorded appropriately. (NSNs for rapid viral marker screening assays are listed in *Appendix B*).

d. Retrospective testing for infectious disease markers will be performed on all donor specimens. This testing will be completed at an FDA-approved, DoD-sanctioned laboratory in accordance with FDA/AABB standards of medical care**. Four EDTA and one red top tube will be collected for retrospective testing.**

e. Identify a blood donor who is ABO-identical with the intended recipient.

f. Clean donor's arm with povidone iodine or appropriate alternate antiseptic agent for at least one minute (or per manufacturer recommendations).

g. Donor blood should be drawn from an arm vein into an in-date, intact commercial blood collection bag. The bag is usually of 600 ml capacity and contains 63 ml of CPD or CPDA-1 anticoagulant. Remove about 450 ml (enough so the bag is almost full). Overfilling the bag may cause clotting, and it is recommended that a scale be used for accuracy if available (measure 450 +/- 50 gm plus weight of blood bag). Draw tubes for typing, cross-matching, and transfusion-transmitted disease testing. **Send donor pilot tubes to a supporting theater Blood Support Detachment for transport via established channels to an FDA-approved DoD reference testing laboratory** (e.g., Lackland AFB, Fort Hood). Label the blood collection bag clearly with ABO/Rh and donor-unique identifying information (i.e., ISBT-128 alphanumeric labels).

h. **After 24 hours, destroy all room-temperature-stored FWB units.** Blood stored for more than 24 hours at room temperature has a significant risk of bacterial growth. If the

whole blood is refrigerated within eight hours of collection, it may be stored for up to five days. Note: Once refrigerated, the blood product will only have RBCs and plasma as platelets quickly become non-viable at $4^{o}C$.

i. When issuing FWB, the surgeon (and anesthesia provider, if appropriate) must be notified regarding the status and history of the unit.

j. Keep a record of donors and recipients transfused to provide appropriate follow-up and testing IAW OASD/HA memo dated 4 Dec 2001. Forward transfusion information to the appropriate Blood Support Detachment/Expeditionary Blood Trans-Shipment Center for follow-up with the CENTCOM Joint Blood Program Office and Joint Theater Trauma Registry. **All FWB collection documentation (DD Form 572), testing and transfusion records are the property of the CENTCOM Joint Blood Program.** Centralized storage of records allows for the long-term retrieval and compliance with blood program regulations.

k. Keep an MTF record of number of units transfused, donor and recipient identification, and clinical outcome.

8. References.

[1] CENTCOM FRAGO 09-1222: Joint Theater Blood Program Update: 4 May 2007

[2] *Emergency War Surgery*, 2004, Third US Revision, Chap 7: Shock and Resuscitation

[3] Theater MTF-specific Standard Operating Procedures (SOPs)

[4] Technical Manual, AABB, Bethesda Maryland, 15th Edition, 2005

[5] Standards for Blood Banks & Transfusion Services, AABB, 25th Ed, February 2008

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APPENDIX A

1. Background: In every conflict since World War I, the military has used whole blood in the resuscitation of combat casualties. In fact, LTG Leonard Heaton once stated that, *"If any single medical program can be credited with the saving of countless lives in World War II and the Korean War, it was the prompt and liberal use of whole blood."* However, following the development of fractionation techniques in the 1950s, the use of whole blood was largely abandoned in civilian trauma centers in favor of blood component therapy. Because the military often practices in austere and remote environments where platelets and FFP are unavailable and even red blood cell supplies are limited, fresh whole blood (FWB) is frequently the only option for transfusion.

As more sophisticated medical assets are pushed closer to the front, military physicians find they have more choices. While FWB is clearly effective, **prospective randomized trials have not been performed comparing its use to component therapy**, which is now more widely available. Similarly, while the risks of banked blood are well known, the risks of untested FWB collected from deployed donors in a field environment are, as yet, uncharacterized. To make an informed decision regarding the use of FWB, physicians must understand the risks and benefits of FWB compared to those of available component therapy.

2. Evidenced-based Review: Prospective FWB donors in-theater are generally young, healthy active duty service members who receive comprehensive preventive health care including vaccination for hepatitis B and regular screening for HIV. Despite these precautions, some transfusion-transmitted infections do not have effective vaccines and are not screened prior to deployment (i.e., HCV, HTLV, syphilis). Furthermore, other transfusion-transmitted infections such as malaria and Leishmaniasis are endemic in many areas where military personnel are deployed. Although presumably low, the prevalence of these infections among prospective donors in theater is unknown.

The FDA has rigorous standards for testing of blood products for transfusion-transmitted infections. While post-transfusion testing is performed on all whole blood donations, pre-transfusion screening of products in the field is limited. Rapid viral tests for HIV-1/2, HBV, and HBC are available at Ibn Sina Hospital (Baghdad) and the 332nd EMDG (Balad). Some Level II facilities have access to rapid HIV-1/2 tests. **CENTCOM guidance on whole blood transfusion highly recommends that such testing be performed prior to transfusion, when practical**. At the present time, these testing kits are available to all facilities where FWB may be collected and transfused.

In approximately 5,300 emergency FWB transfusions in OIF and OEF there has been one identified seroconversion to Hepatitis C. In a retrospective analysis of over 2800 units transfused 3 of these units were positive for hepatitis C, a rate of .11% (Spinella, et al Crit Care Med 2007;35:2576). Whatever the risk of transmitting an infectious disease by transfusing FWB collected in-theater (even if untested), it is clearly much smaller than the risk of death from hemorrhagic shock (<1% compared to 30-50%). However, with increased availability of a variety of banked blood components, military physicians now may have other options besides FWB and pRBCs. While FWB may be the only choice at a Level II facility where platelets and/or FFP are not available, the blood bank capabilities at Level III facilities approach those of

a civilian trauma center. In that setting, the beneficial effects of fresh whole blood compared to component therapy remain controversial.

The actual process of collecting and transfusing FWB in the combat environment presents several logistical problems. While blood donor centers in the US are highly regulated with respect to donor screening procedures, quality control and testing protocols, staff training requirements, and even the physical facility requirements, the collection of whole blood in the field is often performed under less than optimal conditions. Because they are generally not staffed for emergency blood collection, the laboratory often must suspend other activities (e.g., routine labs and blood testing) in order to collect and process the FWB. Finally, because FWB is generally required emergently, the donor site staff may be more prone to technical and clerical errors, particularly when more than one blood type is being collected.

On the other hand, several authors have shown that by reducing the total number of blood products transfused, the use of whole blood actually reduces the chance of clerical errors in the operating room. Importantly, in cases requiring rapid and massive transfusion where ease of administration is important, FWB clearly has an advantage over component therapy.[1] Repine, et al., cite numerous examples of emergency whole blood drives, pointing out that *"once donor populations are defined and characterized in a massive transfusion or mass-casualty situation, the logistical balance tilts toward the utilization of whole blood."* [2] The use of FWB clearly reduces the logistical burden at the bedside, providing for simpler and more rapid transfusion of blood.

It has been suggested that because FWB contains fresher, more functional components which are present in more physiologic concentrations, it should be more effective than banked blood. It is well known that banked red blood cells develop a so-called "storage lesion" (i.e., decreased nitric oxide, decreased pH, decreased 2,3-DPG, decreased ATP) which reduces oxygen-carrying capacity. Other drawbacks of banked blood include hypocalcemia from citrate anticoagulant, hyperkalemia from increases in extracellular potassium during storage, and hypothermia. Some researchers have linked such changes to adverse clinical outcomes.[3] This must be kept in mind while dealing with military trauma casualties with multiple massive injuries and severely compromised physiology. Use of fresher blood (<14 days of storage) and blood warmers should mitigate some of these problems. Currently, USCENTCOM is moving pRBCs into Level III facilities in Iraq and Afghanistan that are <14 days of age for use in the massive transfusion patients.

It has also been suggested there are increased levels of inflammatory mediators in banked blood, which may lead to adverse outcomes.[4] These findings were not confirmed in a 2004 article,[5] but this may be secondary to the use of leukocyte-reduced products. Many of the drawbacks of banked blood cited in older literature have been addressed by measures such as the development of improved additive solutions, the routine use of leukocyte-reduction (particularly at donation), and the advent of apheresis platelets. Despite these improvements recent reports still indicate that leukoreduced RBCs are independently associated with increased mortality in trauma patients and the storage age of RBCs is directly related to this relationship.[7]

To date, there have been no prospective randomized clinical trials comparing FWB to component therapy in the trauma setting. One large retrospective analysis of over 350 patients transfused

blood during OIF showed a significant survival benefit to patients receiving at least one unit of fresh whole blood as a component of their resuscitation. [8]

3. Conclusion. Despite the fact that fresh whole blood is unlikely to become an FDA-approved therapy, given the exigencies of the circumstances within which the military medicine community must operate, this therapy will continue to be a lifesaving addition to the armamentarium of those caring for seriously injured warfighters. It is important for the health care provider to understand the risks associated with this therapy, and to balance these risks with the potential benefit to the patient when choosing this therapy.

4. References

[1] Laine, et al., *Transfusion*, 2003, 43:322-327.

[2] Repine, et al., *J Trauma,* 2006, 60(6S):S59-69

[3] Ho, et al., *Crit Care Med*, 2003, 31(12S):S687-697

[4] Silliman, et al., *J Lab Clin Med*, 1994, 124(5):684-94

[5] Mou SS, et al, *N Engl J Med* 2004, 351(16):1635-1644

[6] Lavee, et al., *J Thorac Cardiovasc Surg*, 1989, 97:204-212

[7] Weinberg, J Trauma 2008, Spinella PC Crit Care Med 2008

[8] Spinella, et al, ATACCC, 2008

APPENDIX B

Expendable Supplies

Item Manufacturer Vendor Order Number

Blood recipient set, indirect Tx Y-type NSN 6515 01 128 1407

Stopcock, IV therapy 3 way, with luer NSN 6515 00 864 8864

Blood Collection Set NSN 6515-01-480-2307

2x2 non-sterile gauze Kendall 3583009022

2x2 sterile gauze Kendall 6510014640826

4% Hibiclens Regent Medical F00234057504

Iodine prep swab Baxter 6510011139208

Chux Kendall 3583001093

Coban 3M 4509015865

Cold Packs Sohgen (European) 6530081350791

Tape 1" 3M 4509015381

Alcohol Prep PDI 4725C69900

Latex Tourniquet Cardinal Health 2002PC6002

Standard tube holder Terumo P-1316R

21-gauge Needles BD 723367210

Ammonia Inhalants James Alexander Co. 6505001060875

4 mL EDTA BD 723367861

7mL Glass Red Top BD 6630011081444

Luer Adapters Kendall 8881225257

Collection Bags Terumo 6515014476871

Tube Sealing Clips Terumo 6515011405268

Covers for temp probe Welch Allyn 67835031101

Reagents and Test Kits

Item Manufacturer Vendor Order Number

BioRapid HBsAG Biokit (Spain) 6550081332246

BioRapid HCV Biokit (Spain) 6550081332247

RPR Control Card BD 6550010498628

RPR Kit BD 6550014932273

OraQuick Advance Rapid HIV ½ Antibody Test Kit

OraSure Technologies 6550015267431

Calibrator Arcent 6630014906201

Control Set Arcent 6550014696200

ACT Tainer Arcent 6550014673603

Tools and Equipment

Item Manufacturer Vendor Order Number

Scissors NA 6515010604280

Hemostatics Bausch & Lomb 6515014593970

Stripper-Sealer-Cutter Terumo 6515011405267

Manual BP Cuff Galls 6515012891967

Rocker/Mixer

Segger/Tube Sealer

Electronic Thermometer Welch Allyn 65150131363242

BD Macro-Vue Rotator BD 9999278051

ProPaq Blood Pressure

Act10 (Hematology analyzer) Coulter 6630014689142

HemaCool Mobile Blood Storage Refrigerator / Freezer

Model: HMC-MIL-1 NSN: 4110-01-506-0895

Helmer Quick Thaw Plasma Thawing System

Model DH8: NSN 6640-01-543-3621

Model DH8 Cover: NSN 6640-01-543-3651

Model DH4: NSN 6640-01-510-3136

Plasma Overwrap bags: NSN 6515-01-511-3624