Fresh Whole Blood (FWB)

Definition:

- *Fresh blood that has been drawn recently but NOT separated into its components.*
- *Contains red blood cells, plasma, clotting cascade factors, and platelets.*

Indications:

- *Coagulopathy in the austere setting when component therapy is not available.*
- *Need for oxygen carrying capacity when PRBCs are not available*

1. Background

Either whole blood or PRBCs can be used to resuscitate the trauma patient. To maximize blood product availability for transfusions to treat defined deficits, most blood banks currently provide only blood components (e.g., PRBCs, FFP, and platelets). PRBCs are ordinarily considered the component of choice to restore hemoglobin.

Current experiences in OIF and OEF with the use of fresh whole blood confirm that it is highly effective in resuscitating critically injured casualties in the austere environment. This is not a new practice as FWB has been used in all combat zones by US military physicians since WWI. In fact, blood utilization in OIF is consistent with previous conflicts as 89% of OIF casualties receiving FWB were massively transfused (≥ 10 units). Massively transfused patients in a civilian trauma center with equivalent total blood exposure develop dilutional coagulopathy and have a 30% mortality. FWB represents an intuitively effective means to confront this coagulopathy during ongoing resuscitation efforts.

FWB is neither intended nor indicated for routine use. It is NOT appropriate, as a matter of convenience, as an alternative to more stringently controlled blood products. It 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 or when specific components are not available (pRBC's, platelets, cryoprecipitate, FFP)

2. Recommendations: The use of FWB should be reserved for trauma victims who are anticipated to require massive transfusion (10 or more units pRBC's or 20 units of components in 24 hours) or for patients with clinically significant coagulopathy (bleeding with thrombocytopenia (PLT < 50 or INR>1.5) when optimal component therapy (particularly apheresis platelets and cryoprecipitate) is unavailable.

a. Level III facilities (where full component therapy including apheresis platelets is available): the risk:benefit ratio may not justify the routine use of FWB over banked blood products, even in severe trauma. However, when platelet and FFP inventories are depleted, or in contingencies such as MASCAL situations when the blood inventory may be exhausted, the use of FWB remains a life-saving option.

b. Level III and Level II + or Level II Surgical facilities (where apheresis platelets are **not** available): FWB *may* improve survival compared to RBCs and FFP alone in severely injured patients. It is a clinical judgment of the physician whether the benefits of using FWB outweigh the risks, given the other components available. In this setting, FWB may best be viewed as an alternative source of platelets.

c. Level II and below: the use of FWB remains a life-saving tool in the management of severe trauma, providing proper training and planning has occurred, and proper equipment is available. (Refer to #6 below.)

3. Guidelines:

a. The decision to use fresh whole blood is a medical decision that must be made by a physician who has full knowledge of the clinical situation, as well as the availability of compatible blood components.
b. In general, the use of fresh whole blood should be limited to poly-trauma patients who have three or more severe wounds when the physician determines that optimal component therapy -- including FFP, apheresis platelets, and cryoprecipitate -- is unavailable or inadequate.
c. The decision to initiate a fresh whole blood drive should be made in consultation with the Medical Director or OIC of the Blood Bank to both determine the availability of compatible blood components, as well as to coordinate the fresh whole blood drive.
d. **FWB must be patient group/type-specific (ABO identical) to the patient, otherwise a fatal hemolytic reaction may result.**
e. Because of the inherent risks of fresh whole blood, the ordering physician should sign an Emergency Release Consent Form acknowledging that the FWB does not meet FDA standards, particularly when viral testing has not been performed and/or regular banked blood products are available. The decision to use the non-standard blood is a medical decision that must be made with a full knowledge of the facts of the case and should be adequately documented in the patient medical record.

4. Precautions: Drawing fresh whole blood in the field may be dangerous for several reasons:

a. **There is no universally compatible fresh whole blood type.** Transfusions of fresh whole blood should be patient group/type (ABO Rh) identical. Service members' blood types are not always known with certainty. The blood type on

"dog tags" is occasionally inaccurate 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, fresh whole blood does not meet FDA standards.
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.

5. Planning:

a. Since the need for fresh whole blood cannot be predicted, a robust contingency plan must be developed by the Medical Director or OIC of the Blood Bank, in conjunction with the surgical and anesthesia providers. That plan should be reviewed and rehearsed regularly.
b. If practical, establish a pre-screened donor pool, preferably composed of active duty, active reserve, active National Guard, or other DoD beneficiaries. 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. Keep the donor file current.
c. In an emergency, establish blood groups/types of donors by rapid testing or previous donor history records, if available.
d. Every effort should be made to adhere to the same screening, drawing, labeling and issuing standards required for routine donations.
e. 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.
f. It is highly recommended, where feasible, to perform on-site testing of potential blood donors using rapid screening immunoassays for infectious diseases -- specifically HIV, HBV and HCV -- before fresh whole blood 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.
g. A contingency plan should be developed for collecting, storing, and transfusing FWB in MASCAL situations. Similarly, when it is deemed that the current blood inventory will be exhausted prior to re-supply, consideration should be given to initiating a FWB drive, even when banked components are still available. This is especially pertinent when multiple type-O trauma patients are exhausting the O RBC inventory, a minimal level of which should be maintained for emergencies.

6. Appropriate equipment:

- 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

7. Procedure

a. When planning or when arriving at a remote location try to set up a "walking blood bank" with pre-screened donors, preferably active duty, active reserve, active national guard, or DoD beneficiaries. This may avoid having to rely on "dog tags" as a basis for transfusion. Recent laboratory confirmation of blood group/type and non-reactive transfusion transmissible disease tests represent the best screening candidate. Keep the donor file current.
b. Try, even in an emergency, to get regularly issued blood products.
c. In an emergency, establish blood groups/types of donors via local testing or previous donor history. It is highly recommended, where feasible, that all MTFs perform on-site testing of potential blood donors using rapid screening immunoassays for infectious diseases, specifically HIV, HBsAg and HCV, before fresh whole blood is transfused. (NSNs are listed in *Appendix B*.) In addition, all MTFs will have retrospective (after-the-fact) testing for infectious disease markers performed on all donors in accordance withestablished DOD standards of medical care. Choose prior blood donors in preference to non-donors because they have been tested for infectious diseases in the past. Rely on "dog tags" only as a last resort.
d. **Choose a group-specific donor**.
e. Clean the donor's arm with povidone iodine for at least one minute or per kit recommendations.
f. Draw the blood from an arm vein into an in-date, intact commercial blood bag. The bag is usually of 600 ml capacity and contains 63 ml of CPD or CPDA-1 anticoagulant. Draw about 450 ml, "a pint," so that the bag is almost full (overfilling may cause clotting and recommend scale be used for accuracy, when available, to measure 450 +/- 50 ml). Draw tubes for typing, cross-matching, and transfusion transmitted disease testing. Send donor pilot tubes to a supporting theater lab for transport via established channels to an approved reference testing laboratory (i.e., Ft Hood, LRMC or 59 MDW). Even retrospective (after-the-fact) testing is useful to provide reassurance of safety or explanations of untoward events. Label the bag clearly with blood type and donor identifying information; e.g., last four of social security number plus date or unique blood bag segment number plus date.
g. After 24 hours, destroy all warm-stored (room temperature) fresh whole blood units. If the blood is kept at room temperature, keep it no longer than 24 hours. Blood stored warm for more than 24 hours has a significant risk of bacterial growth and in addition, some clotting factors and platelet function will be lost.
h. When "issuing" the blood to an operating team, ensure that the anesthetist/anesthesiologist and surgeon understand that this is an emergency – drawn unit and tell them the history of the unit.

i. Keep a record of donors and patients transfused so they can be tested upon return to stateside; forward transfusion information to the appropriate BSU/EBTC for follow-up with the Joint Blood Program Office (JBPO).
j. Keep a record of number of units transfused, who the donors were, and outcome.

k. <u>Remember, the decision to use the non-standard blood is a medical decision that must be made with a full knowledge of the facts of the case and should be adequately documented in the patient medical record.</u>

References:

CENTCOM Theater Blood Distribution and Information Guide
Service-specific Standard Operating Procedures (SOPs)
Emergency War Surgery, Third United States Revision
AABB Technical Manual, 14th Edition. America Association of Blood Banks. Bethesda, Maryland. 2002

Appendix A

1. Background: In every conflict since WWI, the military has used whole blood in 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 lived 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 1950's, the use of whole blood was largely abandoned in civilian trauma centers in favor of blood component therapy. But, 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 that they have more choices. While FWB is clearly effective, it is unknown whether it is *more* effective than 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; namely, hepatitis C virus (HCV), human T-cell leukemia virus (HTLV), and 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. And while standard donor screening is performed, potential donors may feel pressured to compromise the screening process, either by their command or out of a desire to help their fellow soldiers. In any case, deployed soldiers would not be allowed to donate blood in the United States under FDA regulations.

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 is limited. Rapid viral tests for HIV 1/2, HBV, and HBC are available at Ibn Sina Hospital in Baghdad and at the 332 EMDG; and some level II facilities have access to rapid HIV1/2 tests. CENTCOM guidance on whole blood transfusion highly recommends that such testing be performed *prior* to transfusion, when practical. At the present time these kits are available to all facilities where FWB may be collected and transfused. They just have to be ordered. As a result, of approximately

5,300 emergency transfusions, there have been at least 2 documented cases of HCV and 11 documented cases of HBV contamination in FWB use in OEF/OIF. (ASBP)

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%). But, with the increased availability of other banked blood components, military physicians now may have other options besides just FWB and RBCs. 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 CSHs approach those of a stateside trauma center. In that setting, the consensus opinion among civilian blood bankers appears to be that the "*routine use of pathogen-untested blood products merely to obtain some potential relatively small functional benefit from fresh blood* [is not justified]". (California Blood Bankers Society Forum)

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 (eg., routine labs and blood testing) in order to collect and process the FWB. Finally, because FWB is generally required emergently, the donor center 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. It also reduces exposures and, by extension, infectious disease transmission risk. Importantly, in cases requiring rapid and massive transfusion where ease of administration is important, FWB clearly has a clear advantage over component therapy. (Laine, et al., Transfusion, 2003, 43:322-327) 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*." (Repine, et al., J Trauma, 2006, 60(6S):S59-69) The use of FWB clearly reduces the logistical burden at the patient bedside, providing for simpler and more rapid infusion of blood.

It is well known that banked red blood cells develop a so-called "storage lesion" (decreased pH, decreased 2,3-DPG, and decreased ATP) which reduces oxygen-carrying capacity. Other drawbacks of banked blood include hypocalcemia from citrate anticoagulant, hyperkalemia from hemolysis, hypothermia, and RBC aggregation. Some researchers have linked these changes to adverse clinical outcomes (Ho, et al., Crit Care Med, 2003, 31(12S):S687-697).) This needs to be kept in mind when dealing with military trauma patients 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.

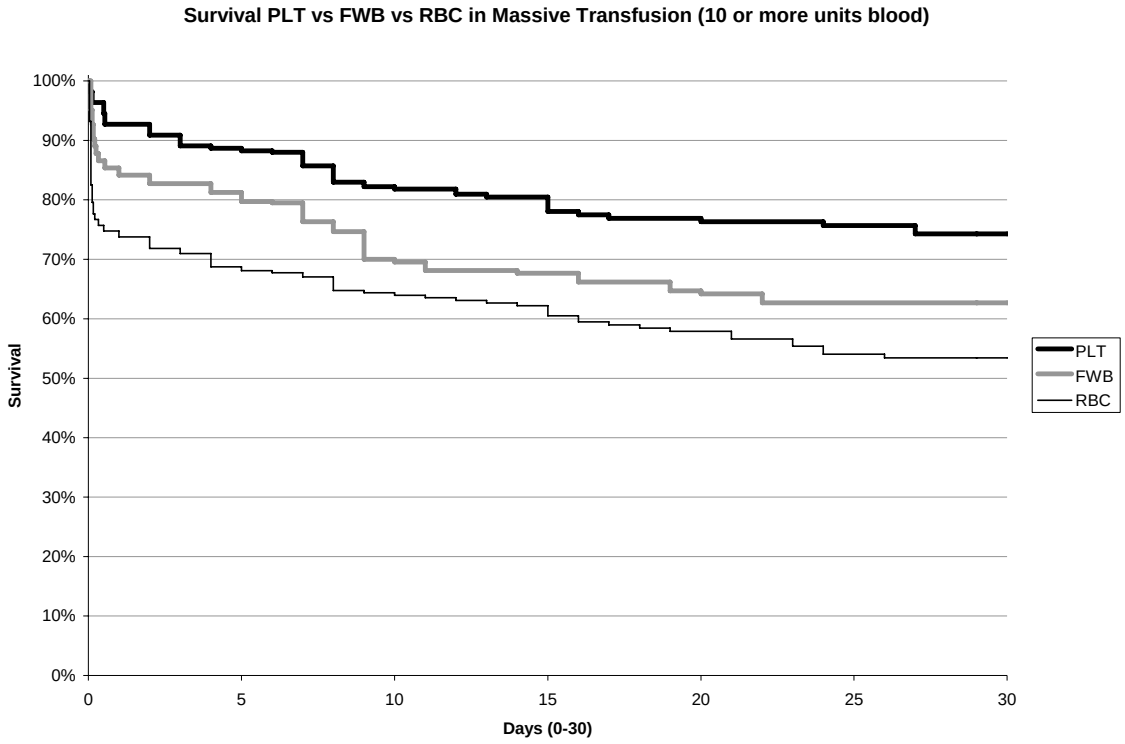
It has also been suggested that there are increased levels of inflammatory mediators in banked blood which may lead to adverse outcomes (Silliman, et al., J Lab Clin Med, 1994, 124(5):684-94) These findings were not confirmed in Mou's more recent NEJM article, however, perhaps because of the use of leukocyte-reduced products. Indeed, many of the drawbacks of banked blood cited in the 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.

While the physiology and risks of blood component therapy have been extensively studied, the use of FWB has not. 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. This theoretical advantage has never been proven clinically, however. "*The notion has long been accepted that the use of fresh whole blood…guarantees the provision of all cellular and noncellular blood components. Moreover, it seems intuitive that a manipulated or reconstituted product should be less desirable than a natural, unmanipulated product. Such beliefs have been supported over time by potentially biased anecdotal clinical observations and various theoretical explanations, which have remained untested.*" (Mou, et al., N. Engl. J. Med., 2004, 351(16):1635)

The immunomodulatory effects of FWB also remain unknown. Fresh whole blood contains fully activated donor leukocytes and may even induce a transient graft-versus-host response. In their NEJM article, Mou, et al., speculated that the less favorable outcomes in the group receiving FWB may be related to the "*inflammatory mediators*" not evaluated in their study but which "*cannot be dismissed*".

When reading the literature in this area, it is important to note the distinctions between *fresh* whole blood and whole blood which may be only 24-36 hours old, but which has been refrigerated. Platelet activity and, to a lesser extent, coagulation factor activity are diminished by chilling and storing whole blood even for short periods of time. Similarly, there are significant physiologic and clinical differences between the pooled platelets used in older studies and apheresis platelets which are commonly used today (and are available in-theater). Apheresis platelets are more active, contain fewer white cells, and expose recipients to only a single donor's blood.

To date, there have been no prospective randomized clinical trials comparing FWB to component therapy in the trauma setting. Retrospective data from the Combat Support Hospital in Baghdad during OIF in 252 massively transfused patients, however, has shown that resuscitation with FWB shows a trend toward improved survival over RBCs, FFP,and cryo alone, but this difference was not statistically significant (see Figure 1). Only apheresis platelets used as part of the resuscitation were shown to be associated with improved survival ($p<0.05$). (Perkins, et al., manuscript in preparation)



Erber, et al., conducted a retrospective study of massive blood loss in trauma and demonstrated a reduction in total blood usage by using FWB compared to routine component therapy. Interestingly, a reduction was only seen in the patients that survived. (Erber, et al., Med J Aust., 1996, 165(1):11-3) Reeves-Viet, et al., showed a similar reduction in total blood usage in thoracoabdominal aorta reconstruction between patients receiving whole blood and those who received packed red cells. (Reeves-Viet, et al., Nurse Anesth., 1991 2(4):184-7) Clearly, FWB is effective in resuscitation following massive blood loss; and according to these studies, it may reduce total blood product usage (and all the attendant risks).

FWB has also been compared to banked blood in a number of other clinical settings, among them: pediatric and adult cardiac surgery, transplant surgery, and others. In their prospective, randomized, double-blind study in NEJM, Mou, et al, demonstrated that the use of FWB for cardiopulmonary-bypass circuit priming in neonates and infants does *not* confer a significant clinical advantage over reconstituted blood with respect to survival or length of ICU stay. (Mou, et al., N. Engl. J. Med., 2004, 351(16): 1635) On the contrary, the use of FWB was associated with a prolonged stay in the intensive care unit, increased perioperative fluid overload, and an increased duration of mechanical ventilation.

Manno, et al., performed a similar study which yielded mixed results. While there was a benefit to the FWB group aged <2 years, he found no significant difference in 24-hour blood loss among children > 2 years following open-heart surgery with CPB who received either FWB or reconstituted blood. (Manno, et al., Blood, 1991, 77: 930)

Looking at the adult population, Mohr, et al., compared the effectiveness of FWB with that of platelet transfusions in patients having CBP surgery and reported no statistical difference in postoperative blood loss after a transfusion of 1 unit of FWB compared with transfusion of 10 units of platelets. (Mohr, et al., J Cardiovasc Surg., 1988, 96:530)

These more recent observations are also supported by Counts, et al., who pointed out that bleeding following massive transfusion is primarily due to dilutional thrombocytopenia rather than coagulation factor deficiencies. (Counts, et al Ann Surg, 1979, 190:91-99) In fact, this finding has been consistently confirmed. In a study of blood use in orthotopic liver transplantation, Laine, et al., showed here was no statistically significant difference in coagulation profiles between groups receiving FWB versus RBC and FFP. (Laine, et al., Transfusion, 2003, 43(3):322-7). Similarly, in his Blood paper Manno, et al., concluded that the difference in blood usage in his study between FWB and reconstituted blood was not explained by postoperative coagulation tests.

Interestingly, both Mohr and Manno went even further and concluded that any hemostatic benefit from FWB is attributable to platelets. This finding was also suggested by Lavee, et al., who used electron microscopy to compare platelet aggregates from patients who received FWB with those receiving pooled platelets. (Lavee, et al., J Thorac Cardiovasc Surg, 1989, 97:204-212) These results suggest that FWB can perhaps best be viewed as an alternative source of platelets when none are available.

Appendix B

Expendable Supplies

Item Manufacturer Vendor order number

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 KitOraSure 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/Mixter
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