Advances in the Use of Whole Blood in Combat Trauma Resuscitation

Defense Health Board

Director, Army Blood Program

Deputy Director, Army Blood Program

2 June 2016
Agenda

Whole Blood Pre-hospital

75th Ranger Regiment  ROLO Program

ASBP Manufactured Whole Blood

Future Work
Armed Services Blood Program

Provide quality blood products and support to military healthcare operations worldwide.
Whole Blood on the Battlefield

**Fresh whole blood use by forward surgical teams in Afghanistan is associated with improved survival compared to component therapy without platelets.**

*Transfusion* 2013;53:107S-113S.

Shawn C. Nessen, Brian J. Eastridge, Daniel Cronk, Robert M. Craig, Kyle Remick, Jason Seery, Avani Shah, and Philip O’Leary

**Warm Fresh Whole Blood Is Independently Associated With Improved Survival for Patients With Combat-Related Traumatic Injuries**


Philip C. Spinella, MD, Jeremy G. Perkins, MD, Kurt W. Grathwohl, MD, Alec C. Beckley, MD, and John B. Holcomb, MD

**Comparison of platelet transfusion as fresh whole blood versus apheresis platelets for massively transfused combat trauma patients**


Jeremy G. Perkins, Andrew P. Cappleman, Kurt W. Grathwohl, Francisco J. Rivera, and Kim A. Mead

**Whole Blood: The Future of Traumatic Hemorrhagic Shock Resuscitation**

Alan D. Murdock,† Olle Berséus,† Tor Hervig,§ Geir Strandenes,§ and Turid Helen Lunde§
CPEG Fresh Whole Blood

Joint Theater Trauma System Clinical Practice Guideline

FRESH WHOLE BLOOD (FWB) TRANSFUSION

<table>
<thead>
<tr>
<th>Original Release/Approval</th>
<th>Oct 2006</th>
<th>Note: This CPG requires an annual review.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Supersedes:</td>
<td>Fresh Whole Blood (FWB) Transfusion, updated 17 Jul 2012</td>
<td></td>
</tr>
</tbody>
</table>

☐ Minor Changes (or) ☒ Changes are substantial and require a thorough reading of this CPG (or)
☐ Significant Changes

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

- WB use is based on ABO type specific match, donor & recipient
- Product destroyed after 24 hours
- Collect FWB in emergency situations, no pre-collection/storage
# Blood Utilization

## OEF/OFS and OIF/OND/OIR Patient Transfusions by Blood Product Type

**As of 29 February 2016**

<table>
<thead>
<tr>
<th></th>
<th>Total # of Products Transfused</th>
<th>Total # of Patients Receiving this Product Type</th>
<th>Avg # of Products per Transfused Patient</th>
<th>Low</th>
<th>Mode</th>
<th>Median</th>
<th>High</th>
</tr>
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<tbody>
<tr>
<td>RBC</td>
<td>176,911</td>
<td>36,163</td>
<td>4.9</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>137</td>
</tr>
<tr>
<td>FFP</td>
<td>108,353</td>
<td>18,750</td>
<td>5.8</td>
<td>1</td>
<td>2</td>
<td>4</td>
<td>124</td>
</tr>
<tr>
<td>CRYO</td>
<td>31,315</td>
<td>3,224</td>
<td>9.7</td>
<td>1</td>
<td>10</td>
<td>10</td>
<td>120</td>
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<tr>
<td>A-PLT</td>
<td>11,430</td>
<td>5,166</td>
<td>2.2</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>42</td>
</tr>
<tr>
<td>WB</td>
<td>10,242</td>
<td>1,733</td>
<td>5.9</td>
<td>1</td>
<td>2</td>
<td>4</td>
<td>61</td>
</tr>
<tr>
<td>DRBC*</td>
<td>946</td>
<td>456</td>
<td>2.1</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>16</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Total # of Products Transfused to All Patients</th>
<th>Total # of Patients Receiving at Least One Unit of Any Product Type</th>
<th>Avg # of Products per Transfused Patient</th>
<th>Low</th>
<th>Mode</th>
<th>Median</th>
<th>High</th>
</tr>
</thead>
<tbody>
<tr>
<td>339,197</td>
<td>39,891</td>
<td>8.5</td>
<td>1</td>
<td>1</td>
<td>4</td>
<td>401</td>
</tr>
</tbody>
</table>

* Began using DRBCs in 2008 based on JTTS CPG.
Blood on the Battlefield

• Whole Blood Transfusion 2001-2016 focused at R2/R3

• 90% of combat deaths occur before reaching R2

• 25% of combat deaths preventable

• 90% of preventable deaths – due to Hemorrhage


TCCC Guidelines Change 14-01

28 June 2014
TCCC Fluid Resuscitation

- TCCC Guidelines for Medical Personnel – 3 June 2015
  
  7. Fluid resuscitation
    
    a. The resuscitation fluids of choice for casualties in hemorrhagic shock, listed from most to least preferred, are: whole blood*; plasma, RBCs and platelets in 1:1:1 ratio*; plasma and RBCs in 1:1 ratio; plasma or RBCs alone; Hextend; and crystalloid (Lactated Ringers or Plasma-Lyte A)

- Some progress on use of plasma far forward, but ASBP unable to provide platelets in pre-hospital setting

- TCCC Guidance has focused attention on WB use pre-R2/R3
Low Titer Group O Whole Blood

- Proposed low-titer Group O WB for emergency situations when type-specific WB unavailable
- Donor pool screened prior to deployment
- WB maintains normal TEG/hemostatic parameters out to almost 21 days but platelet function begins to drop after 14 days

ABO Incompatibilities

• Major ABO Incompatibility
  – Transfusion of donor RBCs to a patient with incompatible ABO antibodies
  – Acute Hemolytic Transfusion Reactions – severe, can be fatal
  – Typically caused by larger, complement activating IgM class ABO antibodies
  – May be caused by smaller IgG class ABO antibodies if present in high concentration
  – No risk if transfusing type specific WB or type O WB

• Minor ABO Incompatibility
  – Transfusion of donor ABO antibodies which are incompatible with patient RBCs
  – Clinically apparent reactions are rare and typically mild
  – No data on risk from WB, but apheresis platelet studies available
  – 2 reactions observed in 3816 transfusions with non-group O patients receiving group O platelets (0.05%)*
    – Using titrated donors, risk estimated as 1:120,000 for out of group transfusions**
  – 25 case reports of hemolytic transfusion reactions, 1975-2009, with transfusion of group O platelets to non-group O recipients***
    • 2 fatalities involving cancer patients

* Fauzie D, Transfusion 2004; 44(Suppl):36A
*** Bersus O, Transfusion 2013; 53:114S-123S
ABO Antibody Titer Testing

• Titer Testing
  – May be performed to limit risk of minor ABO incompatibility
  – Titer result traditionally reported as the highest donor plasma dilution which results in visible agglutination – ie...Anti-A 1:128 or Anti-B 1:64
  – Uses Reagent A & B red cells
  – Saline used as diluent, tubes centrifuged and observed for visible agglutination
  – Anti-Human Globulin (AHG) may be added to test for IgG
  – Wide variation between countries on need to test for both IgM and IgG and acceptable titer values
  – Variation in testing methodology – tube vs. gel card testing
• Spring 2015, Ranger Regiment requested support for ROLO (Ranger O Low Titer) program

• **Goal:** Identify low-titer Group O WB donors prior to Deployment of personnel from CONUS

• Program initiated at Ft. Benning, GA with 3rd Battalion, 12 May 2015

• Screening coordinated with Sullivan Memorial Blood Center, Ft. Benning, GA
75th Ranger Regiment

Whole Blood and Titers

ASBP-572

- Same screening form used for routine blood donors
- No vitals conducted at time of pre-screen
- Donor signs consent
• Collection of Group O Donors must be coordinated with the ABP, designated BDC and Department of Pathology.
• Volunteer (potential) donors complete an ASBP-572 and interview process with BDC staff.
• Rangers are briefed that program is voluntary
• Tubes for Transfusion Transmitted Disease (TTD) testing collected/labeled:
  • HBsAg
  • Anti-HBc
  • HBV Nucleic Acid Test (NAT)
  • Anti-HCV + HCV NAT
  • Anti-HIV-1/2 + HIV-1 NAT
  • Anti-HTLV I/II
  • Syphilis (RPR)
  • ABO/Rh, Antibody Screen
  • West Nile Virus NAT
  • T. cruzi
TTD and Titer Results

- Tube for titer testing collected/labeled:
  - Must be coordinated with local MTF, Department of Pathology.
  - Titers ≥ 1:256 are considered “High Titer”.
  - Titers < 1:256 are considered “Low Titer”.

- Titer testing is ordered and resulted in CHCS.

- **Titer results** + **ABO/Rh** + **TTD & Antibody Screen Results** + **ASBP-572’s** = Donors and results placed into TMDS for visibility by Regimental Medical Officers and Readiness Coordinators

- Deferrals placed into ASBP Blood Establishment Computer System

- All positive testing results are reported to Regimental Surgeon, PA and Medical Readiness Coordinator for proper counseling and follow-up testing if required.

- **Planning and coordination required!**
ROLO Expansion

TMDSPortal

Blood

Update donation - update tests

The following donor:

Nationality: United States of America
Branch: U.S. Army
Gender: M
ABO/Rh: O POS
Military Unit: 1-75 RR RASPI

...donated the following blood products

DIN: W01210750023  Donation Date: 25 Jan 2016  Donation Location: 75th Ranger Regiment (BN5001)

Donated Product(s):

<table>
<thead>
<tr>
<th>PRODUCT DESCRIPTION</th>
<th>ABO/RH</th>
<th>EXP DATE</th>
<th>DISPOSITION</th>
<th>LOCATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>PRESCREEN - PRESCREEN</td>
<td>O POS</td>
<td>25 Jan 2017</td>
<td>AVAILABLE</td>
<td>75th Ranger Regiment (BN5001)</td>
</tr>
</tbody>
</table>

Enter rapid testing results here:

ABO/Rh: Select ABO/Rh – □ HIV: [ ] □ HCV: [ ] □ HBsAg: [ ]
RPR: [ ] □ Other Test Types: [ ]
Date Tested: [ ] Sample sent to: [ ] on:

Enter TTD testing results here:

ABO/Rh: [ ] O Positive □ ABS: [ ] Negative □ STG: [ ] Negative □ HBsAg: [ ] Negative □ HBcAb: [ ] Negative □
HCV: [ ] Negative □ HIV 1/2: [ ] Negative □ HTLV 1/2: [ ] Negative □ WNV: [ ] Negative □ NAT: [ ] Negative □ Chagas: [ ]
Comments: [ ] [ ] [ ]

Date Shipped CONUS: [ ] Date Tested: [ ] Donor Notified? [ ]
DO-Y22 Complete?: [ ] Yes [ ]

UNCLASSIFIED//FOR OFFICIAL USE ONLY
ABP Policy and SOP

ABSOP for Special Operations Donor Screening

Overview

Facility Identification and Address

<<Insert Facility Name & Address>>

Purpose

To standardize the collection, testing, and screening of Special Operations Command (SOCOM) whole blood donors prior to deployment.

MEMORANDUM FOR ALL ARMY BLOOD DONOR CENTERS

SUBJECT: Procedures for the Screening of Special Operations (SO) Whole Blood Donors Prior to Deployment

Army Blood Program Policy Letter 2016-03-01
4 March 2016
ROLO Pre-Screen Results

- 11 personnel with positive viral markers or antibody screens
- One individual confirmed positive for HCV
- Retest at 1 year interval
- 79 Re-titers
  - 10 Low to High
  - 6 High to Low

62% Low Titer

- High Titer
- Low Titer
ROLO Whole Blood Options

- Two options for providing ROLO Whole blood
  
  **Option 1:** Use of Low Titer Group O donor for Emergency FWB collection
  
  **Option 2:** Collection of Group O Low Titer WB Pre-Mission
  
  Pre-screen data is critical for either option
  
  Ranger Regiment medical staff have TMDS accounts to access donor information
  - TTD Results
  - Titer Results
ROLO use in CENTCOM

• Ranger Regiment Surgeon coordinated with CENTCOM Blood Program for pre-mission collection of low titer Group O WB

• WB collected by Blood Support Detachment located at Bagram Airfield

• Rangers collected prior to high-risk missions

• Typically collected 2-4 units at a time 1 day prior to mission

• BSD collecting whole blood in CPDA-1 anticoagulant – 35 day expiration

• BSD followed JTS CPG procedure for donor collection to include:
  – DD572
  – Rapid Testing (HIV/HCV/HBV/RPR/Malaria)
  – Retrospective samples for send-out testing
### Low Titer O Whole Blood

**Blood Product Name:** Low Titer O Whole Blood

**Approved By:** JBPO

**Date Approved:** 29 February 2016

**Effective Date:** 29 February 2016

**Other Names:**
- ROLO WB

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#### Classification/Indications

Low titer O whole blood is to be used in resuscitation of bleeding patients in the pre-hospital setting.

This product is collected from donors who have been pre-screened with FDA approved infectious disease testing and have been tested to determine an anti-A/B titer level of ≤1:256.

Low titer O is considered universal and may be administered for to all blood types.

#### Contraindications

Do Not:
- Use for non-bleeding patients
- Use solely for volume expansion

#### Supplied

- Volume is 450 mLs.
- Hct 33%.
- Whole Blood can be stored for 35 days 1 to 6°C.
- Low Titer O Whole Blood will be drawn upon request and in quantities to support near term mission requirements.
ROLO use in CENTCOM

First ROLO pre-mission collection performed on 9 March 2016
### ROLO Pre-Mission WB Collections in CENTCOM

<table>
<thead>
<tr>
<th>Category</th>
<th>Quantity</th>
</tr>
</thead>
<tbody>
<tr>
<td># ROLO WB Units Collected</td>
<td>19</td>
</tr>
<tr>
<td># ROLO WB expired/destroyed</td>
<td>11</td>
</tr>
<tr>
<td># ROLO WB Transfused</td>
<td>1</td>
</tr>
<tr>
<td># ROLO WB in Inventory</td>
<td>7</td>
</tr>
</tbody>
</table>

Data as of 12 Mar 2016
Whole Blood Manufactured in CONUS

- CONOPS for Ranger use of WB was requiring more blood than ROLO donors could support

- Most ASBP donor centers are FDA licensed for Whole Blood Manufacture

- Army Blood Program established Whole Blood Production at Armed Services Blood Bank Center – Pacific Northwest, Joint Base Lewis McCord, WA

- Facility collects in Citrate Phosphate Dextrose (CPD) anticoagulant – 21 day expiration
ASBP Manufactured Whole Blood

- Product is FDA licensed and receives required testing prior to distribution
- Titer testing is sent out under a contracted testing service
- Titer Methodology: Tube, 1:150 saline dilution, immediate spin at RT
- Testing for IgM Anti-A and Anti-B
- Acceptable titer <1:150, each unit tested
- **21 Day Shelf Life for WB, RBC unit has 42 Day Shelf Life**
CONUS Whole Blood Shipments

<table>
<thead>
<tr>
<th>Licensed Low Titer O Whole Blood</th>
</tr>
</thead>
<tbody>
<tr>
<td># WB Units Collected</td>
</tr>
<tr>
<td># WB Units titer ≥ 1:150</td>
</tr>
<tr>
<td># WB Shipped</td>
</tr>
<tr>
<td># WB Transfused</td>
</tr>
</tbody>
</table>

23 March 2016 – date of first Whole Blood collection for production of low titer Group O Whole Blood

Currently ship 10 units every two weeks

7 days lost on shelf life by the time units arrive to AFG
CONUS Whole Blood Shipments

- Armed Services Blood Program Office memo 11 Apr 2016
- Requesting each Service Blood Program to be capable of producing low titer Group O WB NLT 1 Oct 2016
- Most donor centers are licensed for Whole Blood production, but no longer produce it
- Requires SOP and labeling updates
- Requires identification of a titer testing service

DEPARTMENT OF DEFENSE
ARMED SERVICES BLOOD PROGRAM OFFICE
DEFENSE HEALTH HEADQUARTERS
7700 ARLINGTON BLVD.
FALLS CHURCH, VA 22042

MEMORANDUM FOR: Army Blood Program
Navy Blood Program
Air Force Blood Program

SUBJECT: Low Titer Group O Whole Blood for Contingency Support

1. Low titer Group O Whole Blood (WB) is a blood product which has been tested and found to have anti-A/anti-B antibody titers of <1:256. This product may be given to a recipient of any ABO type during damage control resuscitation based on the Tactical Combat Casualty Care (TCCC) guidelines dated 2 June 2014. Low titer Group O WB may be supplied to far forward special operations medical teams or to Role of Care 2/3 facilities which lack apheresis platelets.

2. ASBPO requests each Service Blood Program to be capable of producing FDA licensed low titer Group O Whole Blood NLT 1 Oct 2016 at one or more of their blood donor centers to support our blood program. Each donated unit of whole blood must be tested and found to have anti-A and anti-B titers of <1:256 as per current guidelines. While ASBPO is not requesting the Service Blood Programs maintain a whole blood inventory for routine mission support, the Services have the discretion to utilize this product to augment local facility massive transfusion protocols when deemed appropriate by the medical director and service transfusion medical consultant.

3. ASBPO point of contact for this action is [Redacted].
## Titer Testing

### Titer Testing Comparison

<table>
<thead>
<tr>
<th></th>
<th>Licensed WB</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ROLLO Pre-Screen</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Tube Method</strong></td>
<td>Tube Method</td>
</tr>
<tr>
<td><strong>Manual Serial Dilutions</strong></td>
<td>Automated Serial Dilutions</td>
</tr>
<tr>
<td><strong>RT Incubation 15 Min</strong></td>
<td>No RT Incubation</td>
</tr>
<tr>
<td><strong>Spin and Read for Agg</strong></td>
<td>Spin and Read for Agg</td>
</tr>
<tr>
<td><strong>Reported as highest dilution w/ aggultination</strong></td>
<td>Only 1:150 dilution tested</td>
</tr>
<tr>
<td><strong>IgM only</strong></td>
<td>IgM only</td>
</tr>
<tr>
<td><strong>&lt;1:256 Acceptable</strong></td>
<td>&lt;1:150 Acceptable</td>
</tr>
</tbody>
</table>
Titer Testing

- Almost all blood used in WWII was low titer O WB
- <1:256 cutoff titer used after severe reaction in 1944, units labeled low or high titer
- Korean War - Almost 400,000 units of group O WB used, no reactions attributed to low titer O WB
- Vietnam War – 230,323 WB units (all ABO groups) transfused Sep 1967 to Feb 1969
  - 1 case of AHTR caused by Group O WB unit labeled as high titer, used by mistake
- No acceptable titer standard from regulatory agencies (FDA, CAP, AABB, etc)
- ROLO program starting to initiate 1 year retesting
- Current process reduces risk of morbidity and mortality
- Benefit of transfusing WB closer to POI where blood component therapy is unavailable outweighs risk of minor ABO incompatibility
Navy & Air Force Initiatives

• Navy Blood Program completed pre-screen for USS Boxer 13-14 Jan 2016
  – NMC San Diego donor center conducted blood drive with USS Boxer
  – Crew had medical history, ABO/Rh, TTD, and titer testing performed by donating whole blood
  – Testing results provided to USS Boxer Senior Medical Officer
  – IgM titer testing; <1:256 acceptable

• Air Force Blood Program coordinating with AF Special Operations to determine support requirements
Way Ahead

Current & Future Efforts

• Continued retesting of Ranger Regiment personnel to determine if titers change significantly
• Pre-screening program expanding to other USASOC Units
• ASBP formed Working Group to consider joint standardization of pre-screening program
• Cold stored apheresis platelets; IPT formed

Questions

• Should Whole Blood be available at R2/R3 care or only in pre-hospital setting?
• Expansion of WB Donor Pre-Screening to conventional forces?
• Availability of licensed WB to conventional forces?
• Balancing traditional collection mission with whole blood pre-screen support
• Increased WB use balanced against increased blood product destructions
• DoD funded studies on titer testing and critical values?
QUESTIONS