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-115S.

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

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. Beekley, 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. Capra, Kurt W. Grathwohl, Francisco J. Regli, and John B. Holcomb

**WHOLE BLOOD: THE FUTURE OF TRAUMATIC HEMORRHAGIC SHOCK RESUSCITATION**

Alan D. Murdock, ‡ Olle Berséus, ‡ Tor Hervig, § Geir Strandenes, § and Turid Helen Lunde§
# CPG 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>
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<tbody>
<tr>
<td>Supersedes: Fresh Whole Blood (FWB) Transfusion, updated 17 Jul 2012</td>
<td></td>
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</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

<table>
<thead>
<tr>
<th>Blood Product</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>
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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>
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<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>
</tr>
<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><strong>10,242</strong></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>

### Total Transfusions to All Patients

<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><strong>339,197</strong></td>
<td><strong>39,891</strong></td>
<td><strong>8.5</strong></td>
<td><strong>1</strong></td>
<td><strong>1</strong></td>
<td><strong>4</strong></td>
<td><strong>401</strong></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 crystalloids (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 $\geq 1:256$ 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!
ABP Policy and SOP

ABSOP for Special Operations Donor Screening

Overview

Facility Identification and 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
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
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 ADMINISTRATION GUIDELINES**

<table>
<thead>
<tr>
<th>Blood Product Name:</th>
<th>Approved By:</th>
<th>Page 1 of 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low Titer O Whole Blood</td>
<td>JBPO</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Date Approved:</th>
<th>Effective Date:</th>
</tr>
</thead>
<tbody>
<tr>
<td>29 February 2016</td>
<td>29 February 2016</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Classification/Indications</th>
</tr>
</thead>
</table>

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 prescreened 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

- 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>Description</th>
<th>Count</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
• 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
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
## Titer Testing

### Titer Testing Comparison

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