Rapid Testing of Transfusion Transmitted Infectious Disease

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Remote Damage Control Resuscitation Conference
Disclaimer

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Outline

• Background
  – OEF/OIF/OND Experience
  – Doctrine

• Support of FWB collections

• Risk mitigation of emergency blood collections
  – Policy supporting FWB efforts

• Regulatory Issues

• Development of Rapid testing capability
  – ABO Rh test
  – Rapid POC test
  – NAT testing
Timeline

2001  1st use of FWB in combat
2004  Use of locally available rapid tests (Biokit)
2007  Evaluation of rapid test kits
2006  Conversion to use of rapid FDA approved HIV1/2 test (Orasure)
2008  Clinical Practice Guideline on use of rapid test kits for emergency WB collections
2010  RFP for Rapid Nucleic Acid Tests (HIV1/2, HBV, HCV) awarded for early development
2010  RFP for Rapid Diagnostics (HBc and HCV)
2011  FDA approval of HCV rapid test (Orasure)
2012  Approval for Advanced Development of rapid Transfusion Transmitted Disease Diagnostic (RT2D2) program
2015  Fielding of multiplexed rapid diagnostic for HIV1/2, anti-HBc, HBsAg, and HCV

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US Experience

- **Number of Emergency Whole Blood collections:** >10,500
  - **Number of Emergency Whole Blood transfusions:** 8941 (ASBPO data as of 30 Sept 11, SAFMLS 2012)

- **Incidence rate:**
  - **US Population**
    - HBV – 1:200K-1:500K
    - HCV – 1:1.39M
    - HIV – 1: 2.0 M
  - **Military OEF/OIF/ONDOEF/OIF/OND:**
    - HCV 2.1/1000
    - HBV 4/1000
    - HIV 0/1000 (Transfusion, 2011)
Blood Products Transfused

The graph shows the RBC to FFP transfusion ratio from 2001 to 2011. The ratio peaked in 2006 at 15.1 and has since decreased, with values for 2011 at 1.5. The table below provides the actual counts for each year:

<table>
<thead>
<tr>
<th>Year</th>
<th>RBC Transfused</th>
<th>FFP Transfused</th>
<th>Whole Blood Transfused</th>
<th>RBC:FFP Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>2001</td>
<td>48</td>
<td>7</td>
<td>0</td>
<td>6.8</td>
</tr>
<tr>
<td>2002</td>
<td>1163</td>
<td>77</td>
<td>12</td>
<td>15.1</td>
</tr>
<tr>
<td>2003</td>
<td>5469</td>
<td>879</td>
<td>308</td>
<td>6.2</td>
</tr>
<tr>
<td>2004</td>
<td>12748</td>
<td>3635</td>
<td>1086</td>
<td>3.6</td>
</tr>
<tr>
<td>2005</td>
<td>23005</td>
<td>10262</td>
<td>852</td>
<td>2.2</td>
</tr>
<tr>
<td>2006</td>
<td>25787</td>
<td>16102</td>
<td>2166</td>
<td>1.6</td>
</tr>
<tr>
<td>2007</td>
<td>26573</td>
<td>17205</td>
<td>1948</td>
<td>1.5</td>
</tr>
<tr>
<td>2008</td>
<td>17447</td>
<td>11458</td>
<td>333</td>
<td>1.5</td>
</tr>
<tr>
<td>2009</td>
<td>11741</td>
<td>8242</td>
<td>513</td>
<td>1.4</td>
</tr>
<tr>
<td>2010</td>
<td>15626</td>
<td>13156</td>
<td>1041</td>
<td>1.2</td>
</tr>
<tr>
<td>2011</td>
<td>15656</td>
<td>10591</td>
<td>793</td>
<td>1.5</td>
</tr>
</tbody>
</table>
### Blood Transfusions by Product and Nationality of Recipient

**OEF/OND Combined**

As of 30 September 2011

<table>
<thead>
<tr>
<th>Transfused Patients</th>
<th>Total</th>
<th>U.S. Only</th>
<th>Non-U.S.</th>
<th>Percent U.S. Only</th>
<th>Percent Non-U.S.</th>
</tr>
</thead>
<tbody>
<tr>
<td>WB</td>
<td>8,941</td>
<td>4,696*</td>
<td>4,245</td>
<td>52.5%</td>
<td>47.5%</td>
</tr>
<tr>
<td>RBCs</td>
<td>153,011**</td>
<td>44,063</td>
<td>108,948</td>
<td>28.8%</td>
<td>71.2%</td>
</tr>
<tr>
<td>Platelets</td>
<td>8,980</td>
<td>3,687</td>
<td>5,293</td>
<td>41.1%</td>
<td>58.9%</td>
</tr>
<tr>
<td>FFP</td>
<td>90,824</td>
<td>29,041</td>
<td>61,783</td>
<td>32.0%</td>
<td>68.0%</td>
</tr>
<tr>
<td>CRYO</td>
<td>24,409</td>
<td>9,700</td>
<td>14,709</td>
<td>39.7%</td>
<td>60.3%</td>
</tr>
</tbody>
</table>

*Only 10% of total U.S. Wounded In Action (WIA) required whole blood transfusions. WIA = 46,542 (OEF/OND combined as of 10/3/11)*

(Source: DoD PERSONNEL & PROCUREMENT STATISTICS)

**10 DRBC’s reported for OEF mission in September 2011, but not included.**

**As of September 1, 2010 OIF mission has been transitioned to OND.**
Doctrine

- Joint Publications 4-02.10, Chapter IV Blood Management.
- Army Technical Manual 4-02.70 Standards for Blood Banks and Transfusion Services
- Army Technical Manual 8-227-12, Armed Services Blood Program, Joint Blood Program Handbook:
  - Transfusion Indications
    - Fresh whole blood: Fresh whole blood (FWB) is neither intended nor indicated for routine use.
    - The decision to use FWB that has not been screened using rapid field tests and/or completed FDA-approved donor testing for infectious agents is a medical decision that must be made after thorough consideration of risks and benefits.
  - Emergency Blood Collections
**ROLE 3 Blood Products:**
- All Blood Products
- RBCs Group O, A, B
- FFP Group AB, A, B, O
- Platelets in theater (Pedigree donor)
- FWB (untested)

**ROLE 2 Blood Products:**
- Limited Blood Products
- Group O RBC
- AB Plasma
- FWB (Untested)

**ROLE 1 Blood Products:**
- NONE
Theater Viral Marker Retrospective and Pre-Screen Testing

Period Ending 29 February 2012

<table>
<thead>
<tr>
<th>Viral Marker</th>
<th># Confirmed Positive</th>
<th>% Positive</th>
<th>Positivity Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV</td>
<td>2</td>
<td>0.0043%</td>
<td>1:23,428</td>
</tr>
<tr>
<td>HCV</td>
<td>23</td>
<td>0.049%</td>
<td>1 : 2,037</td>
</tr>
<tr>
<td>HBV</td>
<td>19</td>
<td>0.036%</td>
<td>1 : 2,805</td>
</tr>
<tr>
<td>HTLV</td>
<td>25*</td>
<td>0.053%</td>
<td>1 : 1,874</td>
</tr>
</tbody>
</table>

46,855 Samples Tested

One documented TTI (HCV) in 2005. Another (HTLV-1) in 2011. Both whole blood donations. * No FDA-approved confirmation test for HTLV.
Policy

- Updated HA policy Letter on use of non-FDA approved Blood Products
- ASBPO guidelines
- Joint Publications
- Clinical Practice Guidelines

- DoD Health Affairs Policy 01-020, 4 Dec 2001
- Army Policy on use of Non-FDA Licensed Blood and Blood Products, 12 March 2003
- DoD Health Affairs Policy, 10-002, 19 March 12
Theater Blood Transfusion Protocols

- Hypotensive patient (SBP < 110)
  And
  Physical exam evidence of hemorrhage as cause of hypotension
  Transfusion is likely

- Profound hypotension (SBP < 50)
  OR
  Obvious hemoperitoneum with hypotension
  OR
  Obvious pelvic fracture and hypotension
  OR
  Massive hemoptysis and hypotension
  OR
  Traumatic or near traumatic amputation

  No
  Yes

- Patient is likely to require < 4 units PRBCs
  Transfuse 2 units PRBCs
  Base deficit closing, adequate urine output, clinical coagulopathy resolving?

  Yes
  No

- Patient is likely to require > 4 units PRBC
  Prepare for massive transfusion
  Thaw 4 units FFP and transfuse
  Predicted need for > 10 units PRBCs transfusion?

  No
  Yes

  Transfuse PRBC
  Continue to transfuse PRBC or FFP to reach AWB to FFP at 1:1 level
  Shock corrected?

  Yes
  No

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Blood Collection Equipment

- Blood Collection Sets
- Rapid Testing kits
Market Surveys

- 2004: Locally available rapid tests
- 2007: Walter Reed Army Institute of Research Retro-virology lab analysis of rapid tests commercially available worldwide
- 2010: Program Announcements for Rapid NAT platforms
- 2011: Requests for Proposals for Rapid POC diagnostic platforms
Evaluation of Existing platforms

- 2007 WRAIR market analysis worldwide for HCV and HBsAg and HIV rapid tests reviewed
- Recommendation:
  - HIV: Orasure HIV1/2 test (FDA approved diagnostic)
  - HCV: Orasure HCV test (FDA approved diagnostic)
  - HBV: CTK Bioteck Onsite HBsAg (Non-FDA approved diagnostic)
Development of Rapid Testing Capability

- **Rapid POC diagnostics**
  - Processing Time: <30 minutes (5 minutes)
  - Whole blood sample
  - Sensitivity: >98%
  - Specificity: >99%
  - Multiplexed

- **Rapid Nucleic Acid Test diagnostics**
  - Processing time: <30 minutes (?)
  - Whole Blood sample
  - Sensitivity: <100 copies/ml
  - Multiplexed

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Testing Capability from Blood Center to the Battlefield

(Product Development)
Regulatory Issues

• Donor Screening Tests versus Clinical Diagnostics
• Intended uses are different
• Sensitivity and Specificity are different
• Clinical trials are different for each for approval
• Regulated from different departments of FDA
Current Labeling of HIV1/2 and HCV Rapid Assays in Use

• OraQuick HIV rapid Test:
  – "The OraQuick ADVANCE Rapid HIV-1/2 Antibody Test is not approved for use to screen blood or tissue donors."

• OraQuick HCV Rapid test:
  – "Not for use in screening whole blood, plasma, or tissue donors. Performance characteristics have not been established for testing a pediatric population less than 15 years of age or for pregnant women."
Intended Use Statement for RT2D2

• “XXX Test may also be used in emergency situations for the purpose of screening blood donors on the day of donation to assist in determining eligibility to donate blood, provided that other risk mitigation measures are employed.”

• The results of the rapid test will be used to determine eligibility for individuals to donate blood to be collected, labeled, and used, “For Emergency Use Only” as specified in the Armed Service Blood Program (ASBP) Health Affairs (HA) Policy 10-002.

• Following establishment of eligibility to donate blood, use of the rapid test will not negate the requirement to complete the required tests as per 21.C.F.R.610.40.

• The rapid test will serve as a risk mitigation measure, providing an additional check prior to collection of blood to be released and labeled “For Emergency Use Only”.

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Policy Issues

• Developed for intended use.
• 10 USC 1107. Off label use.
• HA Policy letter 10-002, Mar 10
• RT2D2 development effort approved April 12 to move forward.
US Department of Defense Health Affairs
Policy Letter

• 2001, 01-020: Provided guidance for use of Non-FDA approved blood products for US forces
• 2010, 10-002: Updated 2001 policy to include risk mitigation guidance for emergency use of FWB when no FDA approved blood products are available or FWB is clinically indicated.
  – Tracking of recipients
  – Must seek testing from US donor centers
  – Use of ASBP approved rapid tests (FDA licensed if possible)
  – Work to develop FDA approved rapid tests
Rapid Transfusion
Transmitted Disease Diagnostics

• MedMira awarded contract for development effort for FDA approval of a multiplexed rapid Point of Care (POC) test for HIV1/2, HBV, HCV.
Rapid Transfusion Transmitted Disease Diagnostics

- Micronics and Meso Scale Diagnostics awarded grants for early development effort for rapid multiplexed (HIV1/2, HBC, HCV) Nucleic Acid Test platform for Transfusion Transmitted Diseases.
- Down selection scheduled early FY 15 for movement to Advanced Development.
Rapid ABO Rh Capability

- Micronics developed ABO Rh card thru US Gov funding received FDA approval 510K approval for “Education and Information purposes”.
- Use in the field for identification of blood type of donors.
- Not the test of record. Still required to perform serological testing in hospitals.
- Used where no laboratory testing is available

- Cross-match card in early development.
Questions