Lessons Learned in the War on Terror

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Disclosures

• I have no conflicts
• The opinions expressed herein are my opinions and do not represent the opinions of the US government, the Department of Defense or the United States Army

“The only victor in war is medicine”
The Mayo Brothers - WWII
Conflict in Afghanistan

- Longest ongoing conflict in US history – 13 yrs
  - Officially over 12/28/2014
- Most advanced medical system ever deployed
- Invaluable lessons learned must not be lost
- Advances made during a period of max resources

Advances

- Joint Theater Trauma System
- Personal protective equipment, vehicles
- Tourniquets: Extremity, Junctional, Abdominal
- Hemostatic dressings
- Blood products
  - Whole blood
  - Frozen red blood cells
  - Lyophilized plasma
- Transcontinental ECMO
- Transportation in and out of theater
Unique Challenges

- Expansive area
- 4 continents
- 3 services, 23 nations
  - Communication
  - Command structures
  - Variations in the practice of medicine
- Hostile and austere environments
- No existing infrastructure
- Record keeping
- Intercontinental transport
### Best Results in History

<table>
<thead>
<tr>
<th></th>
<th>WW II</th>
<th>Vietnam</th>
<th>OIF/OEF</th>
</tr>
</thead>
<tbody>
<tr>
<td>% KIA</td>
<td>25</td>
<td>18</td>
<td>16</td>
</tr>
<tr>
<td>% DOW</td>
<td>4</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td>CFR (%)</td>
<td>19</td>
<td>16</td>
<td>10</td>
</tr>
</tbody>
</table>

### JTTS Vision

That every soldier, sailor, airman and marine injured on the battlefield or in the theater of operations has the optimal chance for survival and maximal potential for functional recovery.
DoDTR

- Largest Combat Injury database in existence
- Comprehensive initial Database
  - Demographic
  - Anatomic
  - Injury severity scoring
  - Outcomes
- Tri-service injury data derived from level IIb, III, IV and V medical charts
- Includes 130,000 total/33,000 US Casualties

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**OEF Monthly Admissions**

Monthly Level III Admissions – 1 Year

Feb 10 – Jan 11 (Jan = 478)

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**Number of Role 3 DoDTR Admissions: OEF 15 Month Patient Workload**
**JTTS Director**

- Coordinate trauma care OEF/OIF
- Recommend resource allocation
- Ensure integrity of DoDTR
- Update and initiate CPGs
- Lead weekly video-teleconference
- OOS Missions/Monthly Medevac report
- Serve as theater trauma consultant
  - Travel to the treatment facilities
  - Consult on novel technologies and strategies

**Video Teleconference**

- Performed weekly
- Presentations
  - Pre-hospital
  - Level II/Level III
  - LRMC
  - CONUS
- Immediate feedback to caregivers
- Allows monitoring/enforcement of CPGs
Clinical Practice Guidelines

- 44 CPG’s to date
- Broad spectrum of medical problems
- Guideline vs. Standard of Care
- Most recent: “Prehospital Trauma Care in the Tactical Setting”

Why CPGs?

- Provides guidance to rotating treatment teams in an environment of constant change
- Some degree of consistency
- Implement “Lessons Learned”
- Part of the PI Process
**CENTCOM JTTS CPG Process**

- Based on best available data, evidence-based
- SME consensus
- Monitored by in-theater team
- Updated annually or as need arises
  - Topic for CPG introduced by any SME
  - Directors produce working draft with SME input
  - Circulated to prior JTTS Directors, Service Trauma consultants
  - JTS Director final clinical approval authority
- Placed on public website: www.usaisr.amedd.army.mil/clinical_practice_guidelines.html

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**Military ATLS**

*Especially Mass Casualties*

- Circulation
- Airway
- Breathing
Immediate versus Delayed Fluid Resuscitation for Hypotensive Patients with Penetrating Torso Injuries


ABSTRACT

Background

Fluid resuscitation may be detrimental when given before bleeding is controlled in patients with trauma. The purpose of this study was to determine the effects of delaying fluid resuscitation until the time of operative intervention in hypotensive patients with penetrating injuries to the torso.

Methods

We conducted a prospective trial comparing immediate and delayed fluid resuscitation in 598 adults with penetrating torso injuries who presented with a prehospital systolic blood pressure of 90 mm Hg. The study setting was a city with a single centralized system of prehospital emergency care and a single receiving facility for patients with major trauma. Patients assigned to the immediate-resuscitation group received intravenous cannulation and standard fluid resuscitation before they reached the hospital and in the trauma center, and those assigned to the delayed-resuscitation group received intravenous cannulation but no fluid resuscitation until they reached the operating room.

Results

Among the 289 patients who received delayed fluid resuscitation, 203 (70 percent) survived and were discharged from the hospital, as compared with 193 of the 309 patients (62 percent) who received immediate fluid resuscitation (P = 0.04). The mean estimated intraoperative blood loss was similar in the two groups. Among the 238 patients in the delayed-resuscitation group who survived to the postoperative period, 55 (23 percent) had one or more complications (adult respiratory distress syndrome, sepsis syndrome, acute renal failure, coagulopathy, wound infection, and pneumonia), as compared with 69 of the 227 patients (30 percent) in the immediate-resuscitation group (P = 0.08). The duration of hospitalization was shorter in the delayed-resuscitation group.

Conclusions

For hypotensive patients with penetrating torso injuries, delay of aggressive fluid resuscitation until operative intervention improves the outcome.

CoTCCC Guidelines

- Minimize fluid
- Evaluate LOC
- Palpate for weak or absent pulse
- Hextend for resuscitation

Double Blind Trial
Randomization

*Reassess SBP or radial pulse and repeat algorithm after each bag is infused.

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### Incremental RBCs and Crystalloid

<table>
<thead>
<tr>
<th></th>
<th>Standard Renalization (n=95) Mean (SD)</th>
<th>Controlled Renalization (n=99) Mean (SD)</th>
<th>Difference [Standard-Controlled] (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prehospital</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cytosaphid</td>
<td>0.36 (0.33)</td>
<td>0.73 (0.19)</td>
<td>0.37 (0.18, 0.35)</td>
</tr>
<tr>
<td>6 to 24 hr from ED arrival</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cytosaphid</td>
<td>1.73 (1.37)</td>
<td>0.99 (1.34)</td>
<td>0.74 (0.33, 1.15)</td>
</tr>
<tr>
<td>Red blood cells</td>
<td>0.27 (0.42)</td>
<td>0.73 (0.13)</td>
<td>-0.46 (-0.63, -0.29)</td>
</tr>
<tr>
<td>All blood products*</td>
<td>0.40 (0.64)</td>
<td>1.05 (0.62)</td>
<td>-0.65 (-1.21, -0.09)</td>
</tr>
<tr>
<td>Total fluids</td>
<td>2.18 (2.58)</td>
<td>2.07 (1.58)</td>
<td>0.11 (0.07, 0.15)</td>
</tr>
<tr>
<td>6 to 24 hr from ED arrival</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cytosaphid</td>
<td>3.56 (2.21)</td>
<td>3.88 (0.99)</td>
<td>-0.32 (-1.22, 0.57)</td>
</tr>
<tr>
<td>Red blood cells</td>
<td>0.38 (0.38)</td>
<td>1.17 (0.93)</td>
<td>-0.80 (-1.32, -0.28)</td>
</tr>
<tr>
<td>All blood products*</td>
<td>0.84 (2.24)</td>
<td>1.61 (0.53)</td>
<td>-0.77 (-1.81, 0.27)</td>
</tr>
<tr>
<td>Total fluids</td>
<td>4.45 (4.04)</td>
<td>5.61 (0.75)</td>
<td>-1.18 (-2.26, -0.10)</td>
</tr>
</tbody>
</table>

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### 24 Hour Mortality

<table>
<thead>
<tr>
<th></th>
<th>Controlled (%)</th>
<th>Standard (%)</th>
<th>Adjusted odds ratio</th>
<th>95% CI (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Patients</td>
<td>96** 5 (5.2)</td>
<td>95 14 (14.7)</td>
<td>0.39 (0.12, 1.26)</td>
<td></td>
</tr>
<tr>
<td>Blunt</td>
<td>63 2 (3.2)</td>
<td>62 11 (17.7)</td>
<td>0.17 (0.03, 0.92)</td>
<td></td>
</tr>
<tr>
<td>Penetrating</td>
<td>32 3 (9.4)</td>
<td>33 3 (9.1)</td>
<td>1.93 (0.19, 19.17)</td>
<td></td>
</tr>
</tbody>
</table>

*Adjusted for age, mechanism and ISS
**One patient with GI bleed and no trauma
In case someone wonders why blunt and penetrating don't add up for CR group, it is because there was a patient with a GI bleed who was enrolled (no trauma).

emeier, 8/11/2014
**Evacuation Scheme**

[Image of map]

**Evolving Solutions**

- Increased skill of providers
  - Paramedics
  - ICU nurses
- Ability to transport blood products and other resources
- Fixed wing for greater distances
Damage Control Resuscitation

- Primary Goals
  - Hemorrhage control
  - Avoid lethal triad: Minimize crystalloid
- Risk factors for MT
  - SBP < 110
  - HR > 105
  - HCT < 32
  - pH < 7.25
- Transfusion Goal – 1:1:1

85% chance of MT

- Last in first out
- FWB only if components not available or patient not responding
- Platelets obtained in theater
- Additional fibrinogen required
- rFVIIa option if coagulopathy persists
- TXA for patients requiring MT
**LIFO: Rationale**

- Older RBCs associated with storage lesion
- Retrospective analysis:
  - older cells = more complications
  - more blood= more complications
- Goal: reduce dose of potentially deleterious agent in patients at greatest risk
- Use “fresher RBC” in patients at risk for MT
- Low tempo = up to 65% wastage

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**Mortality by Plasma : RBC Ratio**

$n = 252$ MT’s (2003-2004)

- Low RBC: 1:8
- Medium RBC: 1:2.5
- High RBC: 1:1.4

Mortality

- 65%
- 34%
- 19%

P < 0.05

Fresh Whole Blood

- Not FDA Approved
- CPG & SOP recommend
  - Donors pre-screened and typed in theater
  - Rapid screening at donation
  - Only when components not available or pt not responding
- What is the risk/benefit?

Component Therapy vs Whole Blood

<table>
<thead>
<tr>
<th>Component</th>
<th>Fresh Whole Blood</th>
</tr>
</thead>
<tbody>
<tr>
<td>PRBC</td>
<td>Hct 55% 50 mL</td>
</tr>
<tr>
<td>Platelets</td>
<td>5.5 x 10^10</td>
</tr>
<tr>
<td>FFP</td>
<td>80% 275 mL</td>
</tr>
</tbody>
</table>

1U PRBC + 6U PLT + 1U FFP + 10 pk Cryo
- Hct 29%
- PLT 87K
- Coag activity 85%
- 750 mg fibrinogen

Whole Blood vs Components

<table>
<thead>
<tr>
<th>TABLE 2: Blood products used by fresh whole blood (FWB)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No FWB (n = 354)</td>
</tr>
<tr>
<td>-----------------</td>
</tr>
<tr>
<td>FWB (U)</td>
</tr>
<tr>
<td>Total RBCs (U)</td>
</tr>
<tr>
<td>Total plasma (U)</td>
</tr>
<tr>
<td>Total blood products (U)</td>
</tr>
<tr>
<td>Factor VIII given</td>
</tr>
<tr>
<td>Massive transfusion</td>
</tr>
</tbody>
</table>

Continuous variables reported as mean ± SD; median (LowerQ, UpperQ).
Categorical variables reported as n (%).
RBCs = red blood cells; SD = standard deviation.

Nessen et al. Transfusion 2013;53:107S-113S.
**Propensity Analysis**

**TABLE 7. Stratified propensity score analysis predicting the effect of the use of FWB on death**

<table>
<thead>
<tr>
<th></th>
<th>Odds ratio</th>
<th>95% CI</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>FWB use</td>
<td>0.11</td>
<td>0.02, 0.78</td>
<td>0.03</td>
</tr>
<tr>
<td>Injury Severity Score</td>
<td>1.06</td>
<td>1.01, 1.11</td>
<td>0.01</td>
</tr>
<tr>
<td>Glasgow Coma Score</td>
<td>0.71</td>
<td>0.63, 0.79</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

CI = confidence interval; FWB = fresh whole blood.

Nessen et al. *Transfusion* 2013;53:1075-113S.

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**Type O FWB**

- 51% received type – specific FWB
  - Mortality = 6.1%
- 49% received uncrossmatched type O FWB
  - Mortality = 6.7%
- No transfusion reactions noted
**Why Not FWB?**

<table>
<thead>
<tr>
<th>Component</th>
<th>Storage</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>PRBCs</td>
<td>4C</td>
<td>42 Days</td>
</tr>
<tr>
<td>Platelets</td>
<td>22C (Agitator)</td>
<td>5 Days</td>
</tr>
<tr>
<td>Cryo</td>
<td>-20C</td>
<td>1 Year</td>
</tr>
<tr>
<td>FFP</td>
<td>-20C</td>
<td>1 Year</td>
</tr>
</tbody>
</table>

**Incidence of Confirmed Positive Samples**

<table>
<thead>
<tr>
<th></th>
<th>Deployed Donors Rapid Screened</th>
<th>Deployed Donors Not Screened</th>
<th>Nondeployed Donors*</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV (%)</td>
<td>0/466 (0)</td>
<td>0/2971 (0)</td>
<td>0/34,129 (0)</td>
</tr>
<tr>
<td>HCV (%)</td>
<td>0/407 (0)</td>
<td>3/2427 (0.12)</td>
<td>24/41,297 (0.06)</td>
</tr>
<tr>
<td>HBsAg (%)</td>
<td>0/410 (0)</td>
<td>0/2427 (0)</td>
<td>25/41,297 (0.06)</td>
</tr>
<tr>
<td>HTLV (%)</td>
<td>NA</td>
<td>2/2231 (0.07)</td>
<td>25/41,297 (0.06)</td>
</tr>
</tbody>
</table>

*Military and civilian donors from Fort Hood, TX

Cryopreservation

- Chelsea Naval Hospital – 1000 units, 1956
- MGH - 14,000 units transfused, ’60s and ’70s
- Vietnam War - Thousands of units transfused
- NYBC - Rare phenotypes, thalassemia, etc.
- ARC - Rare donor registry
- 9/11 - 287,000 extra units collected
  - 50,000 units wasted
  - 9500 units frozen

Cryopreservation

- Blood frozen at -80C 2 – 6 days after donation
- Glycerol to protect cells
- 10 year storage life
- Frozen and deglycerolized with ACP – 215
- Closed system
- > 80% RBC retention
- Approximately 90 minutes
- Storage 14 days after thawing

Study Sites
**Demographics, LOS**

<table>
<thead>
<tr>
<th></th>
<th>Old LPRBCs (n = 86)</th>
<th>Young LPRBCs (n = 82)</th>
<th>CPRBCs (n = 86)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>48 (28,67)</td>
<td>52 (29,62)</td>
<td>49 (31,63)</td>
</tr>
<tr>
<td>Male/Female</td>
<td>46/40</td>
<td>50/32</td>
<td>57/29</td>
</tr>
<tr>
<td>ISS</td>
<td>19 (11,26)</td>
<td>19 (10,32)</td>
<td>19 (14,29)</td>
</tr>
<tr>
<td>Hospital Days</td>
<td>13 (9,22)</td>
<td>13 (8,20)</td>
<td>18 (10,26)</td>
</tr>
<tr>
<td>ICU Days</td>
<td>5 (2,11)</td>
<td>6 (2,11)</td>
<td>7 (3,14)</td>
</tr>
<tr>
<td>Vent Days</td>
<td>0 (0,4)</td>
<td>0 (0,5)</td>
<td>1 (0,9)</td>
</tr>
</tbody>
</table>

**p = NS**

**HCT Change**

**Tissue Oxygenation (StO₂)**

**p = NS**
**Outcomes**

<table>
<thead>
<tr>
<th></th>
<th>Old LPRBCs (n = 85)</th>
<th>Young LPRBCs (n = 82)</th>
<th>CPRBCs (n = 86)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute Renal Failure</td>
<td>8%</td>
<td>9%</td>
<td>12%</td>
</tr>
<tr>
<td>ARDS</td>
<td>2%</td>
<td>6%</td>
<td>5%</td>
</tr>
<tr>
<td>VAP</td>
<td>11%</td>
<td>13%</td>
<td>16%</td>
</tr>
<tr>
<td>Sepsis</td>
<td>7%</td>
<td>6%</td>
<td>9%</td>
</tr>
<tr>
<td>Other Infections</td>
<td>26%</td>
<td>30%</td>
<td>28%</td>
</tr>
<tr>
<td>DVT</td>
<td>15%</td>
<td>17%</td>
<td>15%</td>
</tr>
<tr>
<td>Pulmonary Embolus</td>
<td>7%</td>
<td>4%</td>
<td>6%</td>
</tr>
<tr>
<td>Death</td>
<td>3%</td>
<td>4%</td>
<td>4%</td>
</tr>
</tbody>
</table>

*p = NS

**Blood Products**

<table>
<thead>
<tr>
<th></th>
<th>Old LPRBCs</th>
<th>Young LPRBCs</th>
<th>CPRBCs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Storage duration (days)</td>
<td>32 (23,36)</td>
<td>7 (5, 11)*</td>
<td>1 (1, 3)**</td>
</tr>
<tr>
<td>Units Transfused</td>
<td>2 (1,3)</td>
<td>2 (1,3)</td>
<td>2 (1,4)</td>
</tr>
<tr>
<td>a2-Macroglobulin (mg/dL)</td>
<td>130 (78, 251)</td>
<td>140 (85, 222)</td>
<td>0.9 (0.9, 1.5)**</td>
</tr>
<tr>
<td>Haptoglobin (mg/dL)</td>
<td>75 (38, 130)</td>
<td>73 (37, 130)</td>
<td>2.8 (0.8, 3.6)**</td>
</tr>
<tr>
<td>Serum Amyloid P (ng/ml)</td>
<td>5.5 (3.6, 8.7)</td>
<td>5.6 (3.8, 10.3)</td>
<td>0.1 (0.0, 0.1)**</td>
</tr>
<tr>
<td>C-Reactive Protein (pg/ml)</td>
<td>49 (18, 162)</td>
<td>100 (30, 408)*</td>
<td>14 (8, 20)*</td>
</tr>
<tr>
<td>Hemoglobin (ng/ml)</td>
<td>3508 (2073, 4093)</td>
<td>2427 (897, 3558)*</td>
<td>3356 (2178, 4171)*</td>
</tr>
<tr>
<td>2, 3 DPG (g/L)</td>
<td>0.1 (0.0, 0.2)</td>
<td>0.2 (0.8, 0.37)*</td>
<td>0.3 (0.1, 0.4)*</td>
</tr>
</tbody>
</table>

*p < 0.05 vs old, *p < 0.05 vs young

**Conclusions**

- CPRBCs have a superior biochemical profile
- CPRBCs, old LPRBCs and young LPRBCs
  - Equivalent effects on StO₂
  - Equivalent clinical effects
  - Effects on inflammation similar
  - Biochemical effects and effects on coagulation similar
**Implications**

- CPRBCs can be stored in massive quantities
- Flexible blood supply used interchangeably
- Austere conditions
- Rural locations
- Ideal for disaster scenarios

**Lyophilized Plasma**

- Retention of factor activity
- Stable across broad temps
- Rapidly solubilized
- Available anywhere
- Austere conditions to Level 1 trauma centers

**Residual Activity**

![Graph showing residual activity of different factors.

Blood loss after liver injury


Kabul Data

TABLE 1. Transfusion Data Before Administration of FDP

<table>
<thead>
<tr>
<th>Blood Products, Fluids, and Agents Given</th>
<th>Before the Use of FDP</th>
<th>After the Use of FDP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Percent of Patients</td>
<td>32</td>
<td>9</td>
</tr>
<tr>
<td>Red Blood cells (units)</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Whole blood (units)</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Cryoplatin (L)</td>
<td>1</td>
<td>.2-.5</td>
</tr>
<tr>
<td>Colloid (ml)</td>
<td>530</td>
<td>800-3,000</td>
</tr>
<tr>
<td>dVIII (mg)</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Fibrinogen (g)</td>
<td>1.5</td>
<td>1.3</td>
</tr>
</tbody>
</table>

OEF CUMULATIVE ROLLING MONTHLY AVERAGES: Nov 2003 – Sep 2013

WWII – Vietnam – OEF – Operation NEXT ONE

Thanks to Dr. Kirby Gross COL, MC, USA