HBOCs: The PolyHeme Study
Did it work?

Donald A. Locasto, MD
Assistant Professor, Dept. of Emergency Medicine
University of Cincinnati
Disclaimer – no conflicts
What is the problem?
What is the problem?

• *CDC*: Trauma as the leading cause of death among Americans under age 45.
What is the current prehospital fix for trauma?

Saline and speed
What is the REAL fix?

Blood, a trauma center and a Surgeon
Is there an alternative prehospital treatment?
PolyHeme®

- cross-linked polymer of human Hb in which two or more tetramers are covalently linked.
What is hemoglobin?

Hemoglobin tetramer
New Resuscitation Paradigm

Normal

Plasma

Red Cells

Blood Loss

Volume Deficit

Plasma

Red Cells

Resuscitation

PolyHeme

HBOC + Plasma

Red Cells
- 32 Level 1 Trauma Centers
- 150 Physician Investigators
- 3500 EMT - Paramedics
- 300 EMS vehicles

USA Multicenter PolyHeme Resuscitation Trial

Study Objective

To determine survival of patients in hemorrhagic shock treated with:

PolyHeme or Standard of Care

[Map of the USA showing cities involved in the study]
Study Design: Prehospital

Severely injured trauma patients were assigned to one of two groups by chance.

Test (PolyHeme®) (Case)
Receive IV PolyHeme

Standard of Care (Control)
Receive IV Salt Water
# Enrollment

## PolyHeme Resuscitation Trial

<table>
<thead>
<tr>
<th>Study Entry (Prehospital)</th>
<th>POLYHEME ($n = 350$)</th>
<th>CONTROL ($n = 364$)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age ($\pm$SEM) – years</strong></td>
<td>36 $\pm$ 0.8</td>
<td>38 $\pm$ 0.9</td>
</tr>
<tr>
<td>Male</td>
<td>78 %</td>
<td>79 %</td>
</tr>
<tr>
<td>Penetrating</td>
<td>53 %</td>
<td>52 %</td>
</tr>
<tr>
<td>SBP ($\pm$SEM) – mmHg</td>
<td>78 $\pm$ 0.7</td>
<td>78 $\pm$ 0.6</td>
</tr>
<tr>
<td>ISS ($\pm$SEM)</td>
<td>20 $\pm$ 0.8</td>
<td>19 $\pm$ 0.7</td>
</tr>
<tr>
<td>Transport time – min</td>
<td>26</td>
<td>26</td>
</tr>
</tbody>
</table>
Results: Study Overall

714 patients
82 patients died

349 Received PolyHeme®
46 Deaths (13%)

365 Received Control
36 Deaths (10%)
Protocol Violations

• 124 Patients.
  – 71 in the PolyHeme Group
  – 53 in the Control group
• Some shouldn’t have been enrolled
  – No blood pressure in field
  – Head injury or abnormal brain function
  – Undergoing CPR
• Did not receive the assigned treatment
Results: Protocol Followed Correctly

590 patients
60 patients died

279 Received PolyHeme®
31 Deaths (11%)

311 Received Control
29 Deaths (9%)
### Efficacy: Day 30 Mortality

<table>
<thead>
<tr>
<th>Study Group</th>
<th>As Randomized (n = 714)</th>
<th>As Treated (n = 714)</th>
<th>Per Protocol (n = 590)</th>
</tr>
</thead>
<tbody>
<tr>
<td>POLYHEME</td>
<td>13% (47 / 350)</td>
<td>13% (46 / 349)</td>
<td>11% (31 / 279)</td>
</tr>
<tr>
<td>CONTROL</td>
<td>10% (35 / 364)</td>
<td>10% (36 / 365)</td>
<td>9% (29 / 311)</td>
</tr>
</tbody>
</table>

*p = NS for all treatment comparisons*
Non Inequality: Day 30 Mortality

As Randomized (n = 714)

As Treated (n = 714)

Per Protocol (n = 590)

7% Boundary

UCI = 7.65%

UCI = 7.06%

UCI = 6.21%

Polyheme Lower

No Difference Between Groups

Polyheme Higher

Observed Mortality difference and upper and lower CI
# Secondary Endpoint

## PolyHeme Resuscitation Trial: Safety Analysis

<table>
<thead>
<tr>
<th>Adverse Event (Reported by the PI)</th>
<th>POLYHHEME (n = 349)</th>
<th>CONTROL (n = 365)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adverse Events (AEs)</td>
<td>324</td>
<td>322</td>
<td>0.04</td>
</tr>
<tr>
<td></td>
<td>= 93%</td>
<td>= 88%</td>
<td></td>
</tr>
<tr>
<td>Serious Adverse Event (SAEs)</td>
<td>141</td>
<td>126</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>= 40%</td>
<td>= 35%</td>
<td></td>
</tr>
</tbody>
</table>
Study Implications: Benefit-to-Risk

- PolyHeme intended for use in bleeding patients without early access to blood
  
  *** Not in place of blood ***

- Benefit-to-risk considerations
  - Patients at risk of dying
  - High mortality without blood
  - No available alternative carries oxygen
PolyHeme can provide a survival benefit to bleeding patients without access to blood
Where?
Next Step

Submission to the FDA for product approval.

Future Issue: Permissive Hypotension
Questions?

PolyHeme Investigators

Ernest E. Moore, MD
Dennis W. Ashley, MD
Tony W. Baskin, MD
Andrew C. Bernard, MD
Andy J. Boggust, MD
Robert A. Cherry, MD
James Cipolla, MD
Mark D. Cipolle, MD, PhD
Lawrence N. Dicbel, MD
Therese M. Duane, MD
Julie A. Dunn, MD
Timothy C. Fabian, MD
Samir M. Fakhry, MD
Gerard J. Fulda, MD
Richard L. Gamelli, MD
Gerardo A. Gomez, MD
David B. Hoyt, MD
Harrison M. Lazarus, MD
Donald A. Locasto, MD
Mark A. Malangoni, MD
Mary C. McCarthy, MD
Michael Moncure, MD
Frederick A. Moore, MD
Stephen E. Morris, MD
Lawrence H. Roberts, MD
George H. Rodman Jr., MD
Carl Rosati, MD
Michael J. Sise, MD
Ronald M. Stewart, MD
Steven N. Vaslef, MD, PhD
Leonard J. Weireter Jr., MD
Denver Health Medical Center
Medical Center of Central Georgia
Brooke Army Medical Center
University of Kentucky Medical Center
The Mayo Clinic
Penn State – Milton S. Hershey Medical Center
St. Luke's Hospital & Health Network
Lchigh Valley Hospital
Sinai Grace Hospital & Detroit Receiving Hospital
Virginia Commonwealth University Medical Center
Johnston City Medical Center Hospital
University of Tennessee – Elvis Presley Trauma Center
INOVA Fairfax Hospital
Christiana Care Health Services
Loyola University Medical Center
Wishard Memorial Hospital
University of California – San Diego Medical Center
LDS Hospital
University of Cincinnati – The University Hospital
Metro Health Medical Center
Miami Valley Hospital
University of Kansas – Medical Center Research Institute
University of Texas – Houston Memorial Herman Hospital
University of Utah – University Hospital
Jon Michael Moore Trauma Center
Methodist Hospital of Indiana
Albany Medical Center
Scripps Mercy Hospital
The University of Texas Health Science Center San Antonio
Duke University Medical Center
Sentara Norfolk General Hospital