DISCLOSURES

• Consultant, New Health Sciences

• Consultant, Terumo BCT
“New” vs. “Old” Blood

+ Koch et al – cardiac surgery, NEJM, 2008
  2X increase mortality (10 vs. 20)

- ARIPI – neonates JAMA, 2012
  no difference (7 vs. 14)

- RECESS – cardiac surgery NEJM, 2015
  no difference (7 vs. 28)

- ABLE – critically ill ICU NEJM, 2015
  no difference (6 vs. 22)

- TOTAL – critically anemic (malaria or sickle cell)
  no difference (8 vs. 32)
Transfused RBCs, especially during the time period acutely following transfusion, are not “normal.”

Multiple factors may impair oxygen delivery

**Storage of RBCs:**
- Impairs RBC deformability
- Decreases 2,3-diphosphoglycerate levels
- Decreases nitric oxide-Hgb (SNO-Hgb)
- Promotes endothelial adherence
- Increases aggregability (pro-thrombotic effects)

![Day 1][1]

![Day 21][2]

![Day 35][3]
Red Blood Cells Stored ≥35 Days are Associated with Adverse Outcomes in High-risk Patients

(*Transfusion, 56:1690, 2016*)

Ruchika Goel*, Daniel J. Johnson†, Andrew V. Scott†, Aaron A. R. Tobian‡
Paul M. Ness‡, Enika Nagababu†, Steven M. Frank†

≥28 days

<table>
<thead>
<tr>
<th>All patients</th>
<th>ICU patients</th>
<th>Elderly patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morbidity</td>
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</tr>
<tr>
<td>1.09 (0.97, 1.15) p=0.2</td>
<td>1.06 (0.94, 1.19) p=0.36</td>
<td>1.01 (0.94, 1.19) p=0.39</td>
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<tr>
<td>Mortality</td>
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<tr>
<td>0.96 (0.81, 1.13) p=0.066</td>
<td>0.98 (0.82, 1.12) p=0.88</td>
<td>0.92 (0.73, 1.17) p=0.49</td>
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<td>1.19 (1.07, 1.32) p=0.002</td>
<td>1.25 (1.08, 1.44) p=0.002</td>
<td>1.22 (1.04, 1.42) p=0.01</td>
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<td>1.18 (1.03, 1.47) p=0.13</td>
<td>1.30 (1.08, 1.54) p=0.009</td>
<td>1.28 (0.99, 1.71) p=0.1</td>
</tr>
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≥28 days **Better** than ≤21 days  →  ≥28 days **Worse** than ≤21 days

≥35 days **Better** than ≤21 days  →  ≥35 days **Worse** than ≤21 days
Is the Age of Blood Controversy Resolved?

• Randomized clinical trials in several adult and pediatric populations show no difference in fresh vs. blood stored for longer periods looking for adverse effects and function issues; results of INFORM study to be presented at AABB are eagerly awaited

• Retrospective studies in patients receiving older blood suggest problems

• Animal studies from NIH of very old blood in very sick animals suggest problems

• Studies by Hod and Spitalnik suggest older blood may worsen outcomes

• Shortened storage periods or better preservative systems may still be prudent options; additional studies may be helpful
OTHER UNANSWERED QUESTIONS (1)

• Do we really need blood storage for 42 days or could the blood transfusion system in the US handle shorter storage limits?
  • Outdating might increase
  • Costs might increase
  • These problems could be mitigated by adoption of newer technology and advanced transport systems used in other industries
OTHER UNANSWERED QUESTIONS (2)

• Will pathogen reduction systems for red cells worsen clinical problems associated with longer blood storage?
OTHER UNANSWERED QUESTIONS (3)

- Can FDA adopt guidelines for industry that would allow enhancements in blood storage solutions to be licensed and implemented that would be cost sensitive?
  - How much of the new knowledge about red cell storage would need to be applied to applications to license modifications of blood storage solutions?
  - If guidelines and requirements become too burdensome, the clinical advantages of better solutions that might help patients may never be realized
The red blood cell storage lesion: the end of the beginning

Simone A. Glynn, Harvey G. Klein, and Paul M. Ness

“Now this is not the end. It is not even the beginning of the end. But it is, perhaps, the end of the beginning.”—Winston S. Churchill, “The Bright Gleam of Victory”

The red blood cell (RBC) storage lesion refers to the series of biochemical, metabolic, and structural changes that occur when RBCs are stored ex vivo. A century has passed since the development by Rous and Turner of the first solution permitting rabbit RBCs.

The consideration that transfusion of longer-stored RBCs could potentially be associated with poorer outcomes was brought to the forefront by several observational studies including a large retrospective study by Koch and colleagues, which reported increased in-hospital mortality and morbidity (in particular sepsis) in patients who had undergone cardiovascular surgery and were transfused with RBC units that had been stored for more than 14 days (compared to patients receiving RBC units).

TRANSFUSION 2016; 56: 1462-1468