Age of Blood Evaluation (ABLE) Trial in the Resuscitation of Critically Ill Patients
Clinical consequences of prolonged red blood cell storage

• Maximum length of storage (FDA, AABB):
  – Hemolysis < 1% (0.8% in Europe)
  – ≥ 75% of red cells still alive in circulation of healthy volunteers 24 hours post-transfusion.
    • Criteria advocated in the 40s (Mollison & Young. Quart J Exp Physiol 1942;31:359-92).

• NOT based upon...
  – Laboratory or clinical efficacy evaluations.
  – Potential adverse effects of time from storage process.

• Do not know if older blood has same effect as fresh blood.
### RBC storage lesion

#### Biomechanical changes
- Membrane Phospholipid Loss
- Membrane Phospholipid Re-distribution
- Protein oxidation
- Lipid Peroxidation

#### Biochemical changes
- 2,3 DPG Depletion
- ATP Depletion
- Calcium
- Metabolic Modulation
- Loss of Nitric Oxide
What is Feasible?

What is Ethical?

What choices did we have?

**Option 1:**
- Fresh RBC units vs. Old RBC units

**Option 2:**
- Fresh RBC units vs. Standard RBC units

**Option 3:**
- Standard RBC units vs. Old RBC units
Overall objective

- To determine if transfusing ‘fresh’ RBCs (stored for less than 8 days) as compared to standard issue red cells improves 90 day mortality and morbidity
Basic design

Fresh blood
(< 8 days)

2510 critically patients

Usual transfusion strategy (up to 42 days)

Pre-storage leukoreduction

90 day mortality
Eligibility criteria

Inclusion criteria:
- Adult ICU patients
- Require at least 1 unit of RBCs
- Expected need for mechanical ventilation > 48 hrs

Exclusion criteria:
- Age less than 16 years of age.
- Previous enrolment in this study.
- Brain death or suspected brain death.
- Require uncrossmatched blood
- Difficulties with cross-match

Expected mortality 25-30%
Feasible to supply fresh RBCs
Recruitment done: May 14, 2014

- 27% France, UK, Netherland and Belgium
- 72% of recruitment from Canada
PRELIMINARY RESULTS
Baseline characteristics – all patients

<table>
<thead>
<tr>
<th>Baseline data</th>
<th>Number of patients</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>APACHE $\geq 20$</td>
<td>1677</td>
<td>69.6</td>
</tr>
<tr>
<td>Severe cardiac disease with symptoms at rest</td>
<td>191</td>
<td>7.9</td>
</tr>
<tr>
<td>Type of patients:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Medical</td>
<td>1712</td>
<td>83.9</td>
</tr>
<tr>
<td>• Surgical (non trauma)</td>
<td>327</td>
<td>16.0</td>
</tr>
<tr>
<td>• Trauma*</td>
<td>372</td>
<td>15.4</td>
</tr>
</tbody>
</table>

* Includes 156 patients with traumatic brain injury
<table>
<thead>
<tr>
<th>Adherence (Standard issue) - delivery of older units available</th>
<th>100%</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Proportion of RBC units stored &lt; 7 days</td>
<td>2.8%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Adherence (Fresh)</th>
<th>90.49%</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Proportion of RBC units stored ≤ 7 days</td>
<td></td>
</tr>
</tbody>
</table>
Length of storage of RBC units

Last update: January 24, 2013
### Did we perform an intervention?

<table>
<thead>
<tr>
<th></th>
<th>Fresh group</th>
<th>Standard group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average age of blood (days)</td>
<td>6.11 ± 4.85</td>
<td>21.97 ± 8.48</td>
</tr>
</tbody>
</table>

- Difference in the length of storage: **15.86 days**
- Targeted difference in grant: **> 10 days**
## Outcomes – All patients

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Number of patients</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>90-day mortality</td>
<td>870</td>
<td>36.0</td>
</tr>
<tr>
<td>ICU mortality</td>
<td>609</td>
<td>25.2</td>
</tr>
<tr>
<td>Multiple organ dysfunction syndrome</td>
<td>319</td>
<td>13.1</td>
</tr>
<tr>
<td>Nosocomial Infections</td>
<td>789</td>
<td>42.7</td>
</tr>
<tr>
<td>Thrombosis</td>
<td>72</td>
<td>3.0</td>
</tr>
<tr>
<td>Acute transfusion reaction</td>
<td>10</td>
<td>0.4</td>
</tr>
</tbody>
</table>
### Primary outcome

<table>
<thead>
<tr>
<th>90-day mortality</th>
<th>N</th>
<th>Absolute risk reduction</th>
<th>(95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intention to treat</td>
<td>2420</td>
<td>1.57%</td>
<td>-2.25%, 5.40%</td>
</tr>
<tr>
<td>Per protocol</td>
<td>2313</td>
<td>2.70%</td>
<td>-1.20%, 6.59%</td>
</tr>
</tbody>
</table>
Planned subgroup analyses

✓ Exposure to RBC: 1 to 3 units vs >3 units
✓ Trauma vs non-trauma
✓ Severe sepsis/septic shock vs other
✓ Severity of illness: APACHE II <20 vs ≥ 20
✓ Admission type: perioperative vs medical
Conclusions

Fresh red cells do not appear superior to standard issue red cells in critically ill patients
Conclusions

• Red cells undergo significant change during storage
• Do not know if old blood toxic
• Several other trials will be published in the coming years
Acknowledgements

Principal investigators
• Jacques Lacroix
• Paul Hébert
• Dean Fergusson
• Alan Tinmouth

Co-investigators
• Morris Blajchman
• Jeannie Callum
• Deborah Cook
• Lauralyn McIntyre
• John Marshall
• Alexis Turgeon

International investigators
• Gilles Capellier (France)
• Pierre Tiberghien (France)
• Timothy Walsh (uk).
• Helen Campbell (uk).
• Simon Stanworth (uk).
• Leo van de Watering (Netherlands).
• Dr Nardo van der Meer (Netherlands
• Belgium: Dr Michael Piagnerelli
Financial support

- CIHR
- Research program on blood products FRSQ
- Établissement Français du Sang (EFS).
- Ministère Français (PHRC #12.01, 2011)
- Health Technology Assessment, NIHR, UK.
- Sanquin, Netherlands