Why Old Blood is Bad
...tales from the electronic perfusion record

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Disclosure

I have no financial relationship with any of the companies whose products or materials are discussed here within.
Plan of Attack

• Why blood has the potential to be good

• Why old blood can be bad

• What does the electronic perfusion record tell us?

• Would washing donor RBC's help?
Allogeneic Red Blood Cells
Why Blood Can Be Good

- **Oxygen Carrying Capacity**

\[ \text{CaO}_2 = (1.34 \times \text{Hgb} \times \text{SaO}_2) + (0.0031 \times \text{PaO}_2) \]

- Administration of donor RBC's can increase the \text{CaO}_2, thereby increasing oxygenation
Why Blood Can Be Good

- 2,3-Diphosphoglycerate (2,3-DPG)

Lowers affinity of Hemoglobin molecule for oxygen → oxygen released to tissues

![Graph showing the effect of 2,3-DPG on oxygen saturation](image.png)
Why Blood Can Be Good

- **Adenosine Triphosphate (ATP)**
  - Intracellular energy source
  - Intracellular signaling molecule
  - RBC's release ATP in response to hypoxia, pH, and mechanical stress
  - Increase production of nitric oxide (NO)
    - Vasodilator under hypoxic conditions
Why Blood Can Be Good

• **Red Blood Cell shape**
  - Round, elastic, bi-concave discs
    • Large surface area for O$_2$ diffusion
    • Flexibility allows RBC's to pass through capillaries as narrow as 3μm
    • Rouleaux formation
The Storage Lesion
(aka Why Old Blood is Bad)
Why Old Blood is Bad

• **Loss of 2,3 DPG**
  - Decreases quickly in first 2 weeks of storage to almost undetectable levels
  - Increased $O_2$ affinity
  - Levels appear to recover post-transfusion
    • Up to 72 hours
  - Studies suggest minimal physiological impact
Why Old Blood is Bad

- Decreased Intracellular ATP
  - 40% reduction @ 35-42 days
  - Associated with the reduced oxygen-delivery capacity
  - Can induce RBC shape changes
  - Levels recover in-vivo
Why Old Blood is Bad

• **Morphological changes**
  - Biconcave discs
  - Echinocytes with protrusions
  - Spheroechinocytes
  - Formation of microvesicles
    • Loss of membrane phospholipids
Why Old Blood is Bad

- **Morphological changes**
  - Decreased membrane deformability
  - Increased aggregability
  - Increased adhesion to endothelium
    - Minimizes ability to flow through microcirculation
    - Influences RBC transport of O$_2$ to tissues
  - Increased osmotic fragility
    - Hemolysis
Why Old Blood is Bad

• Other Changes
  - ↑ Potassium
  - ↓ Sodium
  - ↓ pH
  - ↑ Lactate
  - ↓ Glucose
Loss in Membrane Deformability

Steady rise in $K^+$

Alteration in corpuscular shape (↑ hemolysis)

Increased extracellular lactate, $K^+$, pCO$_2$

Decreased pH, bicarbonate

Deterioration of gastric intramucosal pH

Independent risk factor for MOF

2,3-DPG, ATP & RBC survivability < 80%

DAYS

0 15 20 42
The Word on the Street
• 2872 patients who received 8802 units of blood ≤ 14 days old
• 3130 patients who received 10,782 units of blood > 14 days old

• Blood older than 2 weeks was associated with a significantly increased risk of postoperative complications as well as reduced short-term and long-term survival
Four groups based on PRBC age:

- <10 days
- 10–14 days
- 15–19 days
- >19 days

Transfusion of RBCs increased cerebral oxygenation except in those transfused with RBCs stored > 19 days.
Two groups: blood ≤ 5 days old, blood ≥ 20 days old

Measured gastric pH as index of gastric oxygenation status

No change in oxygenation with any transfusion

Blood transfusion worthwhile?
Association between duration of storage of transfused red blood cells and morbidity and mortality in adult patients: myth or reality?

Christophe Lelebre, Michael Piagnerelli, and Jean-Louis Vincent

BACKGROUND: The duration of red blood cell (RBC) storage before transfusion may alter RBC function and, therefore, influence the incidence of complications.

STUDY DESIGN AND METHODS: With a computerized literature search from 1993 to 2008, 27 studies reporting the relationship between age of transfused RBCs and physiologic variables or incidence of complications in adult patients were identified.

RESULTS: Three studies (one abstract only, two foreign languages) were excluded. The 24 remaining studies were grouped according to the patient population: cardiac surgery (eight studies), colorectal surgery (three), intensive care unit (ICU; seven), and trauma (six). The studies were too heterogeneous to allow a formal meta-analysis. Twenty-one of the 24 studies were single-center, and 12 were retrospective. The number of patients was highly variable, ranging from 15 to 6002. In cardiac surgery, two studies reported an increased risk of mortality but had statistical limitations. In colorectal surgery, two studies that addressed the effect on postoperative infections in the same database but with different designs yielded conflicting results. In general ICU patients, two retrospective studies reported a significant correlation between length of RBC storage and microcirculatory alterations or mortality, but the results were not confirmed in subsequent prospective, double-blinded studies. In trauma, five studies reported a correlation between RBC age and development of infection, multiple organ dysfunction, or mortality.

CONCLUSIONS: From the currently available published data, it is difficult to determine whether there is a relationship between the age of transfused RBCs and outcome in adult patients, except possibly in trauma patients receiving massive transfusion.

RBC storage lesion, defined as biochemical and biomechanical changes in the RBC and the storage media during ex vivo preservation, may exacerbate this transfusion-associated morbidity and mortality. Biochemical changes occurring during storage include an enhanced susceptibility to oxidative damage, and a decrease in adenosine triphosphate (ATP), 2,3-diphosphoglycerate, and membrane sialic acid. Changes to the storage medium also occur, with a progressive decrease in pH, an increase in plasma potassium, release of free hemoglobin (Hb) from lysed RBCs (binding

ABBREVIATIONS: CA: coronary artery bypass grafting; ICU = intensive care unit; IQR = interquartile range; LOS = length of stay; MOF = multiple organ failure; pHi = gastric mucosal pH; P'O2 = cerebral tissue oxygenation; SAGM = saline-adenine-glucose-mannitol.

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TRANSFUSION **\*\*\*\*.**
“From the currently available published data, it is difficult to determine whether there is a relationship between the age of transfused RBC's and outcome in adult patients, except possibly in trauma patients receiving massive transfusion.”
Loss in Membrane Deformability

Steady rise in $K^+$

Alteration in corpuscular shape (↑ hemolysis)

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Decreased pH, bicarbonate

Deterioration of gastric intramucosal pH

Independent risk factor for MOF

2,3-DPG, ATP & RBC survivability < 80%
Tales from the Electronic Perfusion Record
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Utilization of the EPR

• Use of the third timer on the Sorin S3 pump allows us to track transfusion time

• Three time points:
  - Pre-transfusion
  - Transfusion
  - Post-transfusion

• Data collected every 20 seconds
Utilization of the EPR

• At the end of each case, data is wirelessly exported to a desktop computer

• That data can then be exported from the DMS program as an Excel file for evaluation
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**Miscellaneous timer started**

**Miscellaneous timer stopped**
| Pre-Transfusion Data | Transfusion Data | Post-Transfusion Data |
Data copy and pasted from master Excel file into separate worksheets based on three time points:

- Pre-transfusion (1)
- During transfusion (2)
- Post-transfusion (3)
• We now have information separated by time point (pre-, post-transfusion)

• But what about the different variables?
- Data separated into worksheets for 18 different variables
- Pre-, during, and post-transfusion
Variables

- Cardiac Index
- MAP
- Temperature
- Sweep Rate
- FiO₂
- Hemoglobin
- Invos (Right)
- Invos (Left)
- SVR
- pH
- SvO₂
- SaO₂
- PaCO₂
- PaO₂
- HCO₃
- Oxygen Consumption
- Oxygen Delivery
- Oxygen Extraction Ratio
Variables

- Cardiac Index
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- Oxygen Consumption
- Oxygen Delivery
- Oxygen Extraction Ratio
Oxygen Extraction Ratio ($O_2ER$)

- Index of global oxygenation
- Measure of the fractional tissue uptake of oxygen from the blood at the microcirculation level

$$O_2ER = \frac{VO_2}{DO_2}$$

- Normal value $\leq 30\%$
Data Analysis

- Transfusion data separated into 3 groups based on blood age
  - Group 1: 0 – 15 days old
  - Group 2: 16 – 28 days old
  - Group 3: 29 – 42 days old

- Multiple, concurrent transfusions of same age counted as same event

- Multiple, concurrent transfusions of different ages counted as same event but categorized by oldest unit
Oxygen Extraction Ratio

Graph showing Oxygen Extraction Ratio over time for Group 1, Group 2, and Group 3.
Oxygen Extraction Ratio

- **Group 1**
- **Group 2**
- **Group 3**
Oxygen Extraction Ratio

![Graph showing Oxygen Extraction Ratio over time for three groups: Group 1, Group 2, and Group 3. The graph indicates fluctuations in oxygen extraction percentages across different time points.]
Oxygen Delivery ($DO_2$)

\[ DO_2 = Q \times [(1.34 \times Hgb \times SaO_2)] \]
Oxygen Delivery ($\text{DO}_2$)

\[
\text{DO}_2 = Q \times [(1.34 \times \text{Hgb} \times \text{SaO}_2)]
\]
Cardiac Index

\[ \text{DO}_2 = Q \times [(1.34 \times \text{Hgb} \times \text{SaO}_2)] \]
Cardiac Index

\[ DO_2 = Q \times [(1.34 \times Hgb \times SaO_2)] \]
**Hemoglobin**

- **Hemoglobin Values (g/dL):**
  - Group 1: 7.0, 7.5, 8.0, 8.5, 9.0, 9.5, 10.0
  - Group 2: 0:00, 0:06, 0:13, 0:20, 0:26, 0:03, 0:09, 0:16, 0:23, 0:29

**Equation:**

$$DO_2 = Q \times [(1.34 \times Hgb \times SaO_2)]$$
PaO$_2$
Oxygen Consumption (VO$_2$)
Venous Oxygen Saturation ($SvO_2$)
Mean Arterial Pressure

The graph illustrates the mean arterial pressure over time for three different groups labeled Group 1, Group 2, and Group 3, represented with different line colors and styles.
Points of Interest

• Noticeable and consistent differences between the three groups of blood

• Oxygen extraction least in oldest blood
  - Venous saturation greatest is oldest blood
  - Strongly suggests decreased ability of old blood to release oxygen to microcirculation
Limitations

- **Observational study**

- *Cannot isolate storage lesion variables to determine cause and effect*

- **Limited power of certain variables due to small sample size**
Future Direction

• Continue to collect and analyze data
• Data analysis to show statistical significance
• Compute changes in oxygenation variables
• Correlate data to outcomes
• Compare washed RBC’s to unwashed RBC’s
• Create a multi-institutional data set among other DMS users
To Wash or Not To Wash
pRBCs 3–21 days old

“Washing pRBCs results in very low levels of K+.”
- Free lactate and potassium significantly reduced
- RBC osmotic resistance improved
- RBC aggregation capacity reduced
- Deformability and Free Hgb unchanged

Conclusion: Washing stored blood before transfusion may be of benefit, because the waste products are effectively removed from the stored RBC.

Key words: aggregation, autotransfusion device, deformability, RBCs, transfusion, washing.
The Effect of Preprocessing Stored Red Blood Cells on Neonates Undergoing Corrective Cardiac Surgery

Mean age of RBC's ~ 15 days

blood glucose, [K⁺], and lactate

Table 3. The Differences of Blood Variables in Unprocessed PRBCs in C Group and Processed PRBCs in P Group

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<thead>
<tr>
<th></th>
<th>Hematocrit (%)</th>
<th>Lactate (mmol/L)</th>
<th>Blood Glucose (mmol/L)</th>
<th>Potassium (mmol/L)</th>
<th>Base Excess (mmol/L)</th>
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<tr>
<td>P group</td>
<td>65.7 ± 8.1*</td>
<td>3.2 ± 0.8*</td>
<td>9.3 ± 1.7*</td>
<td>7.3 ± 2.8*</td>
<td>−27.8 ± 3.9</td>
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</table>

Comparing with C group.
*p < 0.01.

The study was approved by Fuwai Hospital, Beijing, China. Before surgery, parents of every patient participating in this investigation gave informed written consent. From May 2005 to December 2006, 16 neonates with congenital heart disease undergoing cardiac surgery with CPB were randomly assigned to two groups: P group (n = 8) received the processed PRBC before priming with CATS (Fresenius, Bad Homburg, Germany); C group (n = 8) received unprocessed PRBC for priming.
To Wash or Not To Wash?

Research has demonstrated:
- Decreased potassium load
- Decreased lactate load
- Increased hematocrit

Within the Geisinger Health System, all donor RBC's are washed prior to transfusion in cases utilizing ATX.
- Exception: emergent need for RBC's

Negatives to this practice?
Take Home Messages

• After 15 days of storage:
  - 2,3 DPG, ATP, and RBC survivability decreases
• Clinical significance is inconclusive based on current studies
• The Electronic Perfusion Record may assist in elucidating these differences
• The age of donor RBC’s has an effect on oxygenation variables