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 $CaO_2 = (1.34 \times Hgb \times SaO_2) + (0.0031 \times PaO_2)$ 100%

 Administration of donor RBC's can increase the CaO₂, 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



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



ATP (µmol/g Hb)



<u>Source</u>: Salzer U, et al. Vesicles generated during storage of red cells are rich in the lipid raft marker stomatin. Transfusion 2008; 48: 451-62.

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 O₂ to tissues
 - Increased osmotic fragility
 - Hemolysis

Hemolysis (%)



Salzer U, et al

Why Old Blood is Bad

- Other Changes
 - 🛧 Potassium
 - **√Sodium**
 - 🕹 pH
 - 🛧 Lactate
 - 🗸 Glucose



\mathbf{K}^{+} (mmol/L)



Na⁺ (mmol/L)



Salzer, et al



Glucose (mmol/L)



Salzer U, et al



The Word on the Street

ORIGINAL ARTICLE

 •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

> duration of storage on outcomes. Survival was estimated by the Kaplan-Meier method and Elackstone's decomposition method.

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.

Measurements and Main Results: Ptio₂, cerebral perfusion pressure, mean arterial pressure, intracranial pressure, peripheral oxygen saturation, CO₂ pressure at the end of expiration, and intracerebral KEY WORDS: brain hypoxia; cerebral oxygenation; erythrocytes; neurotrauma; brain tissue oxygen pressure; red blood cells; severe brain injury; transfusion Does the storage time of transfused red blood cells influence

- 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?

days was 2 days (first and third quarble, 2, 2.25; range, 2–3); red cells stored \geq 20 days had a mean age of 28 days (first and third quartile, 27, 31; range, 22–32). Hemoglobin concentration in-

KEY WORDS: blood transfusion; critical illness; oxygenation; gastric tonometry; anemia; storage lesion

ORIGINAL ARTICLE

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

Christophe Lelubre, 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 1983 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 language) 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. ed blood cell (RBC) transfusion can be associated with adverse events, including the transmission of infective agents (e.g., human immunodeficiency virus, hepatitis B and C viruses, and bacteria), acute and delayed hemolytic transfusion reactions, transfusion-related acute lung injury, transfusion-associated graft-versus-host disease, and so-called transfusion-related immunomodulation. Numerous studies have indicated that RBC transfusions may be associated with an increased risk of morbidity (postoperative infection,¹⁻³ longer duration of hospital or intensive care unit [ICU] stay,⁴⁵ duration of mechanical ventilation,⁴ multiple organ failure [MOF]⁶) and/or mortality.⁵⁷

RBC storage lesion, defined as biochemical and biomechanical changes in the RBC and the storage media during ex vivo preservation,^{8,9} may exacerbate this transfusion-associated morbidity and mortality.¹⁰ Biochemical changes occurring during storage include an enhanced susceptibility to oxidative damage,^{11,12} and a decrease in adenosine triphosphate (ATP), 2,3diphosphoglycerate,¹³ and membrane sialic acid.¹⁴ Changes to the storage medium also occur, with a progressive decrease in pH, an increase in plasma potassium, release offree hemoglobin (Hb) from lysed RBCs¹⁵ (binding

ABBREVIATIONS: CABG – coronary artery bypass grafting; ICU – intensive care unit; IQR – interquartile range; LOS – length of stay; MOF – multiple organ failure; pHI – gastric mucosal pH; PHO₂ – cerebral tissue oxygenation; SAGM – saline-adenine-glucose-mannitol.

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Received for publication November 6, 2008; revision received February 16, 2009; and accepted March 6, 2009. doi: 10.1111/j.1537-2995.2009.02211.x 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."



Tales from the Electronic Perfusion Record



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Graphs Timer Gain/Loss Table Gas flow CPlegia Totals Actual Time Case no. Patient Time Name Quantity/ Unit E -5 12:31:49 12:31:39 ACT 559.0 sec Туре 12:11:54 Heparin 1000units/ml 24000.0 units 00:00:00 Bypass O Drug Comment Output ○ Volume 10:14:10 Cardiac Index 00:00:00 X-Clamp F-keys 10:05:55 RBC/PRP(ml) ACT Isoflurane 0:05:50 PRP(ml) F1 F7 D:05:45 PPP(ml) SIII INPUT Cooling Rewarm F2 F8 0:05:39 Whole B **CDI 500** Vacuum on Vacuum off F3 F9 Car. Flow: 4.872 Labs Sent/CDI Stored F4 • Flow/PressureDownF F5 **ANESTHESIA** MONITOR **Poor Venous Return** ٠ F6 Actual Time < INVOS Additional Selection Store Enter blood gas time (hh:mm) free Input / Comment : actualize Time Arterial BP Art Line/mmHg Blood Qb VAVD Sweep FiO2 NASO Art Temp Ven Tem rSO2 L rSO2 R 12:31:40 36.2 22.3 22.2 80 83 -.0874 144 -1 12:31:20 82 36.2 22.3 22.2 76 73 0 144 -.08 12:31:00 75 83 144 0 36.2 22.3 22.2 74 -.07 12:30:40 22.3 22.2 76 73 84 144 -.08-1 36.2 preoperative data 12:30:20 22.2 77 86 142 -.08 0 36.2 22.3 74 12:30:00 22.3 22.3 79 86 144 -.08 0 36.2 73 12:29:40 85 143 -.080 36.2 22.3 22.3 78 73 12:29:20 85 0 36.2 22.3 22.3 79 74 144 -.08

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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32	105.33	43.67	8,0	154.7	104.8	105.8		135.4	98.4	46.4	36.3	210.6	24.9	130.9	172.8	
33	104.74	40.87	3:00	148.6	94.2	105,7		134.2	93.5	48.5	45	210.9	24.7	132.3	191.7	<u> </u>
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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

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• SvO₂ • SaO₂

pH

- · Paco₂
- PaO₂
- HCO3

Oxygen Extraction Ratio (O_2 ER)

- Index of global oxygenation
- Measure of the fractional tissue uptake of oxygen from the blood at the microcirculation level
- O_2 ER = VO_2/DO_2
- Normal value ≤ 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 Delivery (DO_2)



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

Oxygen Delivery (DO_2)



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

Cardiac Index



 $DO_2 = \mathbf{Q} \times [(1.34 \times \text{Hgb} \times \text{Sa}O_2)]$

Cardiac Index



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

Hemoglobin



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





Oxygen Consumption (VO_2)



Venous Oxygen Saturation (SvO_2)



Mean Arterial Pressure



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

Somanetics



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

A comparative study of reducing the extracellular potassium concentration in red blood cells by washing and by reduction of additive solution 248 TRANSFUSION Volume 47, February 2007

Ila Bansal, Beverly W. Calhoun, Cherilyn Joseph, Mohammad Pothiawala, and Beverly W. Baron

pRBCs 3-21 days old

"Washing pRBCs results in very low levels of K+."

0.0005). Washing, however, was significantly better than AS reduction in reducing K* in stored pRBCs (p < 0.05).

CONCLUSIONS: Washing pRBCs results in very low levels of K*. AS reduction also significantly reduces K* levels. Selection of the method of K* reduction will depend on the stringency of K* reduction needed, the time constraints, and the availability of facilities and staff for washing. cedure, AS reduction, results in reduction of K* in pRBCs comparable to that achieved by washing, we compared the K* levels in blood units subjected to both methods.

ABBREVIATION: pRBCs- packed red blood cell units.

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ORIGINAL PAPER

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Washing of stored red blood cells by an autotransfusion device before transfusion

•Free lactate and potassium siginificantly reduced RBC osmotic resistance improved RBC aggregation capacity reduced •Deformability and Free Hgb unchanged

Received: 13 April 2006, revised 30 August 2006, accepted 8 September 2006, published online 12 December 2006 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.

ASAIO Journal 2007

The Effect of Preprocessing Stored Red Blood Cells on Neonates Undergoing Corrective Cardiac Surgery

Mean age of RBC's ~ 15 days

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

	Hematocrit (%)	Lactate (mmol/L)	Blood Glucose (mmol/L)	Potassium (mmol/L)	Base Excess (mmol/L)
C group	42.4 ± 3.5	10.5 ± 2.1	17.2 ± 2.1	15.2 ± 3.5	-28.4 ± 4.2
P group	65.7 ± 8.1*	3.2 ± 0.8*	9.3 ± 1.7*	7.3 ± 2.8*	-27.8 ± 3.9

Comparing with C group. p < 0.01.

blood glucose, $[K^+]$, and lactate blood glucose, $[K^+]$, and lactate CPB (p < 0.01), and lower than that of C group at the end of Before surgery, parents of every patient part

CPB (p < 0.01), and lower than that of C group at the end of CPB (p < 0.05). The total priming of PRBCs in P group was significantly less than that in C group (p < 0.01). Perioperative processing with CATS provided a high-quality RBC concentration, decreased the total priming of PRBCs, providing increased high-quality blood salvage during neonatal CPB procedure. ASAIO Journal 2007; 53:680–683. 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 prim-

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