THOUGHTS ON BLOOD MANAGEMENT:
CONCERNS OF ONE ANESTHESIOLOGIST-
DO WE FOLLOW SCIENCE OR BELIEFS?
THE RELIGION OF TRANSFUSION!

Bruce D. Spiess, MD, FAHA
Professor of Anesthesiology and Emergency Medicine
Senior Fellow VCURES
Virginia Commonwealth University Medical Center
Richmond, Virginia
USA
I have a few observations!

“If you don’t have anything profound to say, don’t say anything at all.”
General Observations- A little history and philosophy! Can we change Culture?
Anemia- Pre-op prep- what can we do?
Hgb- O₂ Delivery- What Product?
Euvolemic Hemodilution/ Fluid Management
Aprotinin/Amicar,TXA, PCC, Fib-concentrate, VIIa
Coagulation Management
Future Technologies
ICU Transfer and Education of a TEAM!
FIRST EVER DROP IN TX. RATE/UTILIZATION!

US ALLOGENEIC RBC TRANSFUSIONS FROM NBCUS DATA

Affects of Bld Mgmt?

Millions of Units Transfused

10.6 M 14.9 M 13.8 M
40.3/1000Pts. 48.9 RBC/1,000 44.2 RBC/1000


Years

10 11 12 13 14 15 16

Units Transfused (Millions)
THE BIG QUESTIONS - WE ASSUME THINGS IN THE PRACTICE OF MEDICINE!

- Does transfusion improve or worsen outcome?
- Are the findings real or just associations?
- What mechanisms might be responsible?
- When should we, or must we transfuse?
- Are we damned if we do, damned if we don’t?
- What about those not transfused-JW.?
- We cannot let people bleed to death!
Outcomes Using Lower vs Higher Hemoglobin Thresholds for Red Blood Cell Transfusion

Clinical Question: Is a lower vs higher hemoglobin threshold best for minimizing both red blood cell use and adverse clinical outcomes when used to trigger red blood cell transfusions in anemic patients in critical care and acute care settings?

Bottom Line: Compared with higher hemoglobin thresholds, a hemoglobin threshold of 7 or 8 g/dL is associated with lower red blood cell units transfused without adverse associations with mortality, cardiac morbidity, functional recovery, or length of stay.

**Background:** This report analysis of transfusion occurring hospital and aims to date threatening transfusion safe of safety measures.

**Study Design and Methods:** Systematically identified from 2004 to 2011 on a number of databases. Each patient from established outcomes. Questions were identified. A complementary database was used to complement results.

**RESULTS:** A total of 15,134 median number of 215 per 100,000. Overall, 9832 (60% transfusion services and 66% in fatal). In total, 29% of elderly patients were older than 65 years of age and more than 50% of elderly patients were older than 75 years of age. In total, 22% of elderly patients were older than 85 years of age.

**Cardiac Surgery**

Cardiac surgery patients with a history of cardiac surgery had a higher risk of death (28.8%) and a lower risk of death (18%). This cost of product to error was $693,337.

**Summary of Findings:**

The hemoglobin transfusion threshold used in the study groups testing lower thresholds for transfusion varied from 7.0 to 10.0 g/dL. In the comparison groups, the mortality rate was significantly lower in the lower threshold group. The risk ratio for mortality was 0.83 (95% CI, 0.70 to 1.03). This calculation of patients randomized to a higher threshold for transfusion was associated with a reduced mortality rate (mean difference, −1.48 g/dL; 95% CI, −1.92 to −1.03).

A lower hemoglobin threshold for transfusion was associated with reduced mortality rate (mean difference, −1.92 to −1.03). The reduction in mortality rate was 0.83 (95% CI, 0.70 to 1.03). Figure 1: Hospital mortality was lower in patients randomized to a lower hemoglobin threshold for transfusion vs those randomized to a higher threshold for transfusion (RR, 0.77; 95% CI, 0.62 to 0.93).

Figure 2: Association of a higher vs lower hemoglobin threshold on 30-Day Mortality in Patients With Anemia

**Figure:** Association of a higher vs lower hemoglobin threshold on 30-Day Mortality in Patients With Anemia.
The Association of Perioperative Red Blood Cell Transfusions and Decreased Long-Term Survival After Cardiac Surgery


BACKGROUND: Exposure to red blood cell (RBC) transfusions has been associated with increased mortality after cardiac surgery. We examined long-term survival for cardiac surgical patients who received one or two RBC units during index hospitalization.

METHODS: Nine thousand seventy-nine consecutive patients undergoing coronary artery bypass graft, valve, or coronary artery bypass graft/valve surgery at eight centers in northern New England during 2001–2004 were examined after exclusions. A probabilistic match between the regional registry and the Social Security Administration’s Death Master File determined mortality through June 30, 2006. Cox Proportional Hazard and propensity methods were used to calculate adjusted hazard ratios.

RESULTS: Thirty-two percent of patients (n = 2254) were exposed to one or two RBC transfusions during index hospitalization for cardiac surgery compared with those who received none (p < 0.001). After adjustment for patient and disease characteristics, patients exposed to 1 or 2 U of RBCs had a 16% higher long-term mortality risk (adjusted hazard ratios = 1.16, 95% CI: 1.01–1.34, P = 0.035).

CONCLUSIONS: Exposure to 1 or 2 U of RBCs was associated with a 16% increased hazard of decreased survival after cardiac surgery.

Surgenor SD, Kramer RS, Olmstead EM, et al
Blood product conservation is associated with improved outcomes and reduced costs after cardiac surgery

Damien J. LaPar, MD, MSc, Ivan K. Crosby, MD, Gorav Ailawadi, MD, Niv Ad, MD, Elmer Choi, MD, Bruce D. Spiess, MD, Jeffery B. Rich, MD, Vigneshwar Kasirajan, MD, Edwin Fonner, Jr, DrPH, Irving L. Kron, MD, and Alan M. Speir, MD, Investigators for the Virginia Cardiac Surgery Quality Initiative

(J Thorac Cardiovasc Surg 2013;145:796-804)

The Virginia Cardiac Surgery Quality Initiative (VCSQI) is a voluntary consortium of 17 different collaborating cardiac surgical centers, both academic and private, within the Commonwealth of Virginia. This group exchanges and

Study is being widely heralded!
### Complications of Blood Use: CABG Only, Non-Emergent, First CV Surgery, July 2008 - June 2010

<table>
<thead>
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</thead>
<tbody>
<tr>
<td>OpMortality</td>
<td>3.2%</td>
<td>0.4%</td>
<td>3.6%</td>
<td>1.1%</td>
<td>3.6%</td>
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<td>5.1%</td>
<td>0.8%</td>
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<td>1.0%</td>
<td>6.7%</td>
<td>2.6%</td>
<td>7.8%</td>
<td>1.2%</td>
<td>3.4%</td>
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<tr>
<td>Stroke Perm</td>
<td>2.5%</td>
<td>0.6%</td>
<td>1.8%</td>
<td>1.3%</td>
<td>2.8%</td>
<td>0.6%</td>
<td>1.4%</td>
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<tr>
<td>Readmission*</td>
<td>10.3%</td>
<td>7.3%</td>
<td>10.8%</td>
<td>7.9%</td>
<td>10.6%</td>
<td>7.4%</td>
<td>8.4%</td>
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<tr>
<td>Mediastinitis</td>
<td>0.7%</td>
<td>0.3%</td>
<td>0.6%</td>
<td>0.4%</td>
<td>0.8%</td>
<td>0.3%</td>
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<tr>
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<td>15.8%</td>
<td>23.9%</td>
<td>18.4%</td>
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<td>0.9%</td>
<td>6.8%</td>
<td>2.6%</td>
<td>8.2%</td>
<td>0.9%</td>
<td>3.3%</td>
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<tr>
<td>No Complications or Mortality</td>
<td>53.2%</td>
<td>76.6%</td>
<td>54.9%</td>
<td>70.1%</td>
<td>50.7%</td>
<td>75.7%</td>
<td>67.4%</td>
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<td>4,272</td>
<td>1,247</td>
<td>5,775</td>
<td>2,335</td>
<td>4,688</td>
<td>7,023</td>
</tr>
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* <=30 Days from DOP

** p<0.001  ** p=0.02

### US Government will not pay for readmissions!
### Cost of Complications of Blood Use: CABG Only, Non-Emergent, First CV Surgery, July 2008 - June 2010

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<td>OpMortality</td>
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<td>$45,505</td>
<td>$95,487</td>
<td>$81,591</td>
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<td>$46,531</td>
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<td>$44,381</td>
<td>$88,393</td>
<td>$80,195</td>
<td>$96,486</td>
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<tr>
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<td>$45,437</td>
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<td>$107,008</td>
<td>$43,518</td>
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<td>$55,713</td>
<td>$34,769</td>
<td>$61,197</td>
<td>$40,924</td>
<td>$57,259</td>
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<td>Any Re-Op</td>
<td>$106,763</td>
<td>$73,540</td>
<td>$122,098</td>
<td>$89,542</td>
<td>$106,818</td>
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<td>$101,368</td>
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<td>No Complications or Mortality</td>
<td>$34,990</td>
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<td>$36,533</td>
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<td>$31,167</td>
<td>$49,151</td>
<td>$34,938</td>
<td>$48,820</td>
<td>$31,805</td>
<td>$37,462</td>
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</tbody>
</table>

* <=30 Days from DOP

![Graph showing cost comparison between patients who received any blood transfusion and those who did not for various complications.](image)
“MY CHALLENGE IS THAT BY THE YEAR 2020, NO PATIENT WILL DIE DUE TO HUMAN ERROR”...
PRESIDENT BILL CLINTON, JAN 14, 2013

With malice towards none and charity for all…. Abe Lincoln

Unnecessary Red Cell Transfusion is a Human Error Problem!- Pres. Clinton!
TRALI/ TACO VERY COMMON

- TRALI: 1/73 to 1/193 patients transfused. 50% mortality!
- TACO: 1/50 patients transfused. 20% mortality

- 25-50,000 deaths per year!


Post Op Prolonged Ventilation in cardiac??
Why is that every retrospective study finds a high degree of correlation between intra-op transfusion and prolonged ventilation/pneumonia
77 yo F with chronic myelodisplastic syndrome underwent CABG. 2 months later she presented to the hospital with dyspnea and mild CHF. A surface echo showed a 45% EF. She was given diuretics and discharged to a skilled nursing home.

At the nursing home she was found to have a Hgb of 7.1 gm/dl. No evidence of bleeding. Her oncologist arranged for the patient to be transferred to the ED for transfusion.

On arrival she had normal VS, no dyspnea and a repeat Hgb of 8.1 gm/dl was found.

She was transfused 2 units of PRBCs.

30 minutes after Tx. she became lethargic and her PaO₂ sat went to 60%. Hospitalized for 2 weeks intubated for 2 days!

TRALI V. TACO?

Agency for Healthcare Research and Quality: Spotlight Case- M/M
Effect of Hospital Culture on Blood Transfusion in Cardiac Procedures

Ruyun Jin, MD, MCR, Edy S. Zelinka, CCP, Julie McDonald, BSN, Thomas Byrnes, BS, Gary L. Grunkemeier, PhD, and James Brevig, MD on behalf of Providence Health & Services Cardiovascular Disease Study Group

Medical Data Research Center, Providence Health & Services, Portland, Oregon; Providence Regional Medical Center Everett; Providence Physician Group, Providence Health & Services, Everett, Washington

(Ann Thorac Surg 2012;xx:xxx)
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What is the “culture of Tx? Who has better outcomes?

Fig 5. Timing of red blood cells (RBC) transfusion by surgeon. Surgeons are grouped by hospital, indicated by the alternating vertical shaded panels. The widths of the bars represent surgeon volumes. (CABG = coronary artery bypass grafting.)
**Transfusion in Medicine: A Faith Based Pillar of Medicine**

- **Religion**
  - Belief in an un-provable series of teachings.
  - The teachings form the foundation for how the believer approaches life (medicine) and many situations.
  - There is a dogma taught
  - There is a resistance to questioning the dogma
  - The choir sings when something supports dogma.
  - When something does not support dogma it is discarded.
  - Attacking dogma is heresy!

- **Transfusion**
  - No/Limited Level 1 Evidence
  - No Randomized controlled trials showing improved morbidity/mortality.
  - Belief that “blood is good” and that store blood = circulating red cells.
  - Belief that “give a unit save 4 lives”.
  - Institutionalized public relations campaign to attract donors.
  - An industry set up to support the dogma.
  - Discreditation of evidence that disagrees
  - Resistance to JW data (better outcomes)!
  - Similar sound bites today compared to 1600-1850’s when “bleeding patients” was the standard!!
Based upon the teachings of one physician (John Lundy) and promoted until 1986 (the HIV crisis)!
Blood usage has taken on a religious level of worship.
Those who “believe” remember when vital signs were improved or the last big bleeding case.
Those who deny the evidence based literature criticize it as being “largely retrospective”
Cause and effect is not all RCT’s only
Those who believe invoke- “anxiety about being sued”!
Just which profession are the leeches?

The word leech comes from an Old English word "laece" meaning physician.
A tradition of several thousand years dies hard.

_Austin Flint_, M.D., in 1881 gave the following advice:

A great change has taken place with respect to bloodletting in the treatment of acute inflammations. This measure was formerly thought to be highly important, and was rarely omitted. It is now considered by many as seldom, if ever, called for. The infrequent use of the lancet now, contrasted with its frequent use forty years ago, constitutes one of the most striking of the changes in the practice of medicine which have occurred during this period. It can hardly be doubted that this measure was formerly adopted too indiscriminately, and often employed too largely, but the natural tendency being to pass from one extreme to another, the utility of blood letting in certain cases, at the present time, is perhaps not sufficiently appreciated.
Karl Landsteiner – Nobel lecture 1930

“The number of transfusions given is surprisingly large, and it may well be that the use of this technique has been taken too far.”
We have a long tradition of accepting anemia as a relatively harmless problem that can be corrected easily with transfusion.

For the medical community, transfusion as treatment for anemia remains a default position.

**New paradigm** - Anemia is an independent risk of morbidity and mortality regardless of the level of hemoglobin.

*Isbister J. Shander A. TMR 2011*
No Evidence that Transfusion mitigates these risks!
ANEMIA IS BAD!
DOES TRANSFUSION MITIGATE THAT?

- Ranucci M et al. Lowest hematocrit on cardiopulmonary bypass impairs the outcome in coronary surgery: an Italian multicenter study from the National Cardiothoracic Database. Tex Heart Inst J 2006; 33: 300-5.
Transfusion is associated with increased risk of ventricular failure, inability to wean from bypass, and use of two or more inotropes.

16% increase in mortality per unit transfused!!!

Prior work from this same group claimed it was low-Hct that was associated with adverse events.

ANEMIA CLINIC: MAKES A DIFFERENCE!

Detection, Evaluation, and Management of Anemia in the Elective Surgical Patient

Lawrence T. Goodnough, MD, Meryl Shander, MD, Jerry L. Sprinkle, MD
Jonathan H. Warden, MD, Arnold J. Friedman, MD, Jeffrey L. Carson, MD
E. Michael Keating, MD, Thomas Maddox, MD, and Richard Spencer, MD

Department of Pathology and Medicine, Stanford University, Stanford, California Department of Anesthesiology, Critical Care Medicine, Burn Management, and Reproductive Medicine, Brigham and Women's Hospital, Boston, Massachusetts, Department of Anesthesiology, Columbia University Medical Center, New York, New York:

Division of General Internal Medicine, University of Medicine and Dentistry of New Jersey, Robert Wood Johnson Medical School, New Brunswick, New Jersey; Center for Hip and Knee Surgery, St. Francis Hospital, Roslyn, New York; Department of Family Practice, Winthrop-University Hospital, Mineola, New York; Department of Family Practice, W. Lake Hospital Medical Center, Rockville Centre, New York; Hospital of the University of Pennsylvania, Philadelphia, Pennsylvania; Department of Obstetrics and Gynecology, Beth Israel Medical Center, New York, New York.

Aims: To determine the prevalence of preoperative anemia and the effect of transfusion on blood loss and surgical time.

Methods: A prospective cohort study of all patients undergoing major orthopedic surgery was performed. Preoperative anemia was defined as a hemoglobin level of less than 13 g/dL in men and less than 12 g/dL in women. The primary outcome was the incidence of blood transfusion and the effect on blood loss and surgical time.

Results: Of the 100 patients included in the study, 60% had preoperative anemia. The incidence of blood transfusion was 50%, with a mean blood loss of 1.5 units and a mean surgical time of 1.5 hours. No significant difference was found between the transfused and non-transfused groups in terms of blood loss and surgical time.

Conclusion: Preoperative anemia is common in elective surgical patients, and transfusion is associated with increased blood loss and surgical time. Further research is needed to explore strategies for reducing blood transfusion in this population.

Figure 1. Clinical care pathway for identification and evaluation of anemia in elective surgical patients. MCV, mean corpuscular volume.

**Clinical Practice**

Transfusion strategy for primary knee and hip arthroplasty: impact of an algorithm to lower transfusion rates and hospital costs

V. Martinez1, A. Moisioinou-Lorre1, K. Charras2, T. Judd3, M. Chauvin4 and D. Fletcher4

1Department of Anaesthesiology and Intensive Care, 2Department of Transfusion and 3Department of Orthopaedic Surgery, Assistance Publique–Hôpitaux de Paris, Raymond Poincaré Hospital, Paris, France

2Corresponding author. E-mail: dominique.fletcher@ap-hp.fr

Background: Blood transfusion strategies should reduce both blood transfusion and costs. Possible solutions include autologous donation for selected patients and the prescription of erythropoiesis-stimulating agents (ESCs).

Methods: We conducted a quality improvement program to examine the effect of a transfusion strategy algorithm in primary knee (TKA) and hip arthroplasty (THA). Our algorithm is presented as a diagram and is based on preoperative and postoperative blood loss. Patient characteristics, blood loss, transfusions given, autologous blood storage, and costs were examined during an initial evaluation and after implementation of the algorithm.

Results: Analysis of 302 patients (initial evaluation) and 173 post-implementation) arthroplasties demonstrated a 55% reduction in the prescription of autologous blood donation. The proportion of ESC prescriptions increased from 6.6% to 17.3% (P<0.05). There was a 56% overall reduction in transfusions to fewer autologous (12% vs 2%, P<0.001) and allogeneic transfusions (21% vs 13%, P<0.05). There were 50% fewer transfused autologous blood units (P<0.002) and a 56% reduction in hospital costs (€345 to €169) with no significant change in overall costs (€425 vs €407). Autologous donors applied the algorithm in 97% of patients, and it is still in use 1 year after evaluation.

Conclusions: In this study, the implementation of an algorithm for transfusion strategy changed practice and improved quality of care. The costs for ESC, its administration, and monitoring outside hospital were offset by the reduction in hospital transfusion costs.

[Accepted for publication: June 28, 2007]
WHEN SHOULD WE POSTPONE A CASE DUE TO ANEMIA?

- I predict- the day will come when we regard pre-operative anemia as important as a “full stomach” or not taking anti-hypertensives etc!

- Blood Tx avoidance is a key part of an overall hospital campaing to decrease peri-operative infection. Perhaps almost as important as timing and dosage of the right anti-biotic!
BLOOD STORAGE

RBC Shape Change During Storage

Day 1

Day 21

Day 35

Hovav T et al. Transfusion 1999;39:277
THE STORAGE LESION!

- Increased Potassium - Pediatric Deaths!
- Low Potassium and Mg.
- No 2,3 DPG - very low $P_{50}$ - perhaps 6-10mmHg
- Acidosis
- High levels of cytokines
- Microparticles - inflammatory lipids
- CD-40-L
- Plasma from RBC - blocks leukocyte bacterial recognition.
- ETC, ETC.
Blood Transfusion and Infection After Cardiac Surgery

Keith A. Horvath, MD, Michael A. Acker, MD, Helena Chang, MS, Emilia Bagiella, PhD, Peter K. Smith, MD, Alexander Iribarne, MD, MS, Irving L. Kron, MD, Pamela Lackner, Michael Argenziano, MD, Deborah D. Ascheim, MD, Annette C. Gelijns, PhD, Robert E. Michler, MD, Danielle Van Patten, John D. Puskas, MD, Karen O’Sullivan, MPH, Dorothy Kliniewski, RN, BSN, Neal O. Jeffries, PhD, Patrick T. O’Gara, MD, Alan J. Moskowitz, MD, and Eugene H. Blackstone, MD

Cardiothoracic Surgery Research Program, National Heart, Lung, and Blood Institute, National Institutes of Health, Bethesda, Maryland; Department of Surgery, Division of Cardiovascular Surgery, University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania; International Center for Health Outcomes and Innovation Research (InCHOIR), Department of Health Evidence and Policy, Icahn School of Medicine at Mount Sinai, New York, New York; Division of Cardiovascular and Thoracic Surgery, Department of Surgery, Duke University Medical Center, Durham, North Carolina; Division of Thoracic and Cardiovascular Surgery, University of Virginia School of Medicine, Charlottesville, Virginia; Department of Thoracic and Cardiovascular Surgery, Heart and Vascular Institute, and Department of Quantitative Health Sciences, Research Institute, Cleveland Clinic, Cleveland, Ohio; Division of Cardiothoracic Surgery, Department of Surgery, College of Physicians and Surgeons, Columbia University, New York, New York; Department of Cardiovascular & Thoracic Surgery, Montefiore Medical Center/Albert Einstein College of Medicine, New York, New York; Clinical Research Unit, Division of Cardiothoracic Surgery, Emory University School of Medicine, Atlanta, Georgia; Office of Biostatistics Research, National Heart, Lung, and Blood Institute, Bethesda, Maryland; and Cardiovascular Division, Brigham and Women’s Hospital, Boston, Massachusetts

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WHY IS IT SO IMPORTANT?

- 10 major institutions- USA- Cardiothoracic Surgical Trials Network.
- Sponsored by NIH and Health Canada!
- 5158 prospective patients all comers to cardiac.
- Predetermined definitions for infection, independent blinded adjudication.
- Followed for 65 days after surgery
- Complex statistical analysis (Kaplan-Meier, Cox proportional hazard,
TX, DIRECTLY LINKED TO PERIOPERATIVE INFECTION

Fig 2. Risk of major infection as a function of number of packed red blood cell (PRBC) units transfused.

29% increase risk of infection per unit transfused!
Duration of Red-Cell Storage and Complications after Cardiac Surgery

Colleen Gorman Koch, M.D., Liang Li, Ph.D., Daniel I. Sessler, M.D., Priscilla Figueroa, M.D., Gerald A. Hoeltge, M.D., Tomislav Mihaljevic, M.D., and Eugene H. Blackstone, M.D.
**RANDOMIZED TRIALS SHOW INCREASED ADVERSE OUTCOMES WITH “OLD BLOOD”**

STOP THE DEBATE!

---

**Transfusion of older stored blood and risk of death: a meta-analysis**

Dong Wang¹,², Junfeng Sun¹, Steven B. Solomon¹, Harvey G. Klein², and Charles Natanson¹

¹Critical Care Medicine Department, National Institutes of Health, Bethesda, MD, USA
²Department of Transfusion Medicine, National Institutes of Health, Bethesda, MD, USA
³Anesthesiology and Critical Care Medicine Department, West China Hospital of Sichuan University, Cheng Du, China

**Abstract**

BACKGROUND—Blood for transfusion is stored for up to 42 days. Older blood develops lesions and accumulates potentially injurious substances. Some studies report increasing toxicity as blood ages. We assessed the safety of transfused older versus newer stored blood.

STUDY DESIGN AND METHODS—PubMed, Scopus, and Embase were searched using terms new and old and red blood cell and storage through May 6, 2011 for observational and randomized controlled studies comparing outcomes using transfused blood having longer and shorter storage times. Death was the outcome of interest.

RESULTS—Twenty-one studies were identified, predominantly in cardiac surgery (n=6) and trauma (n=6) patients, including 40,966 patients. A test for heterogeneity of these studies’ results was not significant for mortality (I²=3.7%, p=0.41). Older blood was associated with a significantly increased risk of death [odds ratio (OR) 1.16; 95% confidence interval (CI) (1.07, 1.26)]. Using available mortality data, 97 (83, 199; 95% CI) patients need to be treated with only new blood to save one life. Subgroup analysis of these trials indicated the increased risk was not restricted to a particular type of patient, size of trial, or amount of blood transfused.

CONCLUSION—Based on available data, use of older stored blood is associated with a significantly increased risk of death.
Experimental Evidence: Older Blood Causes More/Worse Immunosuppression - Bacterial Infections!

Transfusion Complications

Transfusion of older stored blood worsens outcomes in canines depending on the presence and severity of pneumonia

Dong Wang,1 Irene Cortés-Puch,2 Junfeng Sun,1 Steven B. Solomon,1 Tamir Kanatas,2
Kenneth E. Bemis,1 Jing Feng,1 Meghana Almeida-Dandari,1 Martha Quezado,1 Christine Helms,1
Andreas Pellega,1 Mark T. Cladera,1 2 Daniel B. Kim-Shapiro,1 Harvey G. Klein,1 and
Chester C. Ransone2

Background: In experimental pneumonia we found that transfused older blood increased mortality and lung injury that was associated with increased in vivo hemodynamic and neutrophilic pulmonary macrophage counts, non-transformed blood (NTB), and plasma basic iron (PtI) levels. In this study, we additionally analyze hematologically relevant animals that located lower or higher bacterial dose.

Study Design and Methods: Two-week-old purebred beagles (n = 45) challenged intratracheally with Staphylococcus aureus (M11, 0.5 x 10^9 cfu). 7-30 days post-transfusion with either 7- or 42-day-old canine universal donor blood (80 ml/kg in four divided doses).

Results: The greater increases in CFU with older blood over time after exchange proved to be independent of bacterial dose. The slower increase in CFU with NTB transfused with human blood were bactericidal dosedependent potentially related to bacterial hemodynamics. Without bacterial challenge, levels of CFU, NTB, and PtI were significantly higher with older versus truer stored blood but there was no significant increase in the convalescent phase. The elevated PtI and NTB were observed more evenly and for a shorter duration after transfusion with older versus fresh blood, and older blood was associated with significantly worse shock, lung injury, and mortality.

Conclusion: These observations in vivo haematology of transfused older red blood cells (RBCs) appear to result in excess plasma cytokine and neutrophil, which required the presence of disturbances in relation to anastomotic ulcers. This indicates that transfused older RBCs increase the risk of infection in septic insults.

Fig. 6. Survival curves for each S. aureus challenge dose. Kaplan-Meier plots over the 96-hour study comparing old (---) and new blood (-----) groups at the different bacterial doses studied are represented (A-B).
Washing older blood units before transfusion reduces plasma iron and improves outcomes in experimental canine pneumonia

Irene Cortés-Puch, Dong Wang, Junfeng Sun, Steven B. Solomon, Kenneth E. Remy, Melinda Fernandez, Jing Feng, Tamir Kania, Landon Bellavia, Derek Sinchar, Andreas Perlegas, Michael A. Solomon, Walter E. Kelley, Mark A. Popovskiy, Mark T. Gladwin, Daniel B. Kim-Shapiro, Harvey G. Klein, and Charles Natanson

1Critical Care Medicine Department, Clinical Center, National Institutes of Health, Bethesda, MD; 2Vascular Medicine Institute, University of Pittsburgh, Pittsburgh, PA; 3Department of Physics and the Translational Science Center, Wake Forest University, Winston-Salem, NC; 4Cardiovascular and Pulmonary Branch, National Heart, Lung and Blood Institute, National Institutes of Health, Bethesda, MD; 5Oklahoma Blood Institute, Oklahoma City, OK; 6Haemotronics Corporation, Braintron, MA; 7Department of Medicine, Division of Pulmonary, Allergy and Critical Care Medicine, University of Pittsburgh School of Medicine, Pittsburgh, PA; and 8Department of Transfusion Medicine, National Institutes of Health, Bethesda, MD

Key Points

- Washing older blood before transfusion reduces plasma iron, improving outcomes from established infection in canines.
- In contrast, washing fresh blood before transfusion increases in vivo plasma CFH release, worsening outcomes.

In a randomized controlled blinded trial, 2-year-old purpose-bred beagles (n = 24), with *Staphylococcus aureus* pneumonia, were exchanged-transfused with either 7- or 42-day-old washed or unwashed canine universal donor blood (60 mL/kg in 4 divided doses). Washing red cells (RBC) before transfusion had a significantly different effect on canine survival, multiple organ injury, plasma iron, and cell-free hemoglobin (CFH) levels depending on the age of stored blood (all, P < .05 for interactions). Washing older units of blood improved survival rates, shock score, lung injury, cardiac performance and liver function, and reduced levels of non-transferrin bound iron and plasma labile iron. In contrast, washing fresh blood worsened all these miscal clinical parameters and increased CFH levels. Our data indicate that transfusion of fresh blood, which results in less hemolysis, CFH, and iron release, is less toxic than transfusion of older blood in critically ill infected subjects. However, washing older blood prevented elevations in plasma circulating iron and improved survival and multiple organ injury in animals with an established pulmonary infection. Our data suggest that fresh blood should not be washed routinely because, in a setting of established infection, washed RBC are prone to release CFH and result in worsened clinical outcomes. (*Blood*. 2014;123(9):1403-1411)
Thromboelastography-TEG: whole Blood Visco-elastic test!

This is a standard test!- **my opinion**

It was invented in 1947 and there are almost 3000 articles in the literature!- **Fact**

It is not best as a “bed-side or point of care test”- **my opinion**- convince me otherwise!
ROTEM
TEG- A “ROUTINE TEST?”

>1700 Pub Med Citations (as of 2011).

90 specific to cardiac surgery

- Chen A, Teruya. Global hemostasis testing thromboelastography: old technology, new applications.

Why is it that only 20% of cardiac centers use this test and we still call it “non-routine”?
Thrombelastography (TEG) or thromboelastometry (ROTEM) to monitor haemotherapy versus usual care in patients with massive transfusion (Review)

Afshari A, Wikkelso A, Brok J, Møller AM, Wetterslev J
# Coagulation Treatment Algorithm

## Pre-CPB

**ORDER**
1. kTEG (or hTEG if on Hep)
2. Fibrinogen
3. Platelet Count
4. PT/INR (if on Coumadin)

**INTERPRETATION & PLAN**
- INR>2.0 on Coumadin or R>10:
  - Order Kcentra 25U/kg
- Fibrinogen<200 or K>6mins or α<50:
  - Order 1 pack cryo*
- Platelets<100 and/or MA<50:
  - Order 1 unit platelets*
- Platelets<50
  - Order 2 units platelets*

* DO NOT RELEASE ANY PRODUCTS AT THIS TIME

## CPB Pre-Weaning

**ORDER**
1. hTEG
2. Fibrinogen
3. Platelet Count

**INTERPRETATION & PLAN**
- Fibrinogen<200 or K>6mins or α<50:
  - Release 1 pack cryo*
- Platelets<100 or MA<50:
  - Release 1 unit platelets*
- Platelets<50
  - Release 2 units platelets*
- R>10:
  - Order Kcentra 25U/kg
- MA 50-65:
  - Order DDAVP 0.3mcg/kg

## 5 Mins Post Protamine

**ORDER**
1. kTEG
2. hTEG
3. Fibrinogen
4. Platelet Count
5. PT/INR (if on Coumadin)

**INTERPRETATION & PLAN**
- Fibrinogen<200 or K>6mins or α<50:
  - Give 1 pack cryo*
- Platelets<100 or MA<50:
  - Give 1 unit platelets*
- R>10 on both hTEG and kTEG and INR >2.0:
  - Give Kcentra 25U/kg
- MA 50-65:
  - Give DDAVP 0.3mcg/kg
- kTEG R - hTEG R >2mins:
  - Give 50mg protamine

* ONLY GIVE PRODUCTS IF PATIENT IS ACTIVELY BLEEDING

* DO NOT RELEASE ANY PRODUCTS AT THIS TIME
Gentlemen (sarcastically)- can we get anything done?
Or: Do we let the bleeding/dying continue?
Use of prothrombin complex concentrate for excessive bleeding after cardiac surgery

Vërgina Améziane, Julien Camou, Solys Fattal, Salda Rézaigui-Delcaux, Rémi Nottin and François Stéphane

Abstract

OBJECTIVES: Prothrombin complex concentrates (PCCs) are sometimes used as off-label for excessive bleeding after cardiopulmonary bypass (CPB). The main objective of this study was to retrospectively evaluate the clinical and biological efficacy of PCC in this setting.

METHODS: We reviewed the charts of all patients who had undergone cardiac surgery under CPB in our institution for 2 years. Patients treated for active bleeding with haemostatic therapy were identified. Chest tube blood loss was quantified postoperatively in the first 24 h. Coagulation parameters were recorded at intensive care unit admission and in the patients’ first 24 h. Thromboembolic complications were also assessed.

RESULTS: Seventy-seven patients aged 67 years, 33 (49.2%) were included: PCC was solely administered in 24 patients (group 1), fresh frozen plasma in 26 (group II) and both in 27 (group III). Three cases were of PCC dosed at 10.0, 10.0, and 11.0 U/kg for group I, 13.5, 13.5, and 11.0 U/kg for group II, and 13.0, 13.0, and 11.0 U/kg for group III. The dose of PCC was 10.0 U/kg (P < 0.05) for group I vs 13.5 U/kg (P = 0.05) for group II. The initial blood loss in the first hour was different between the three groups (P < 0.05): 224 ± 131 ml for group I, 369 ± 295 ml for group II and 454 ± 398 ml for group III. Only group I was significantly different from group III (P < 0.05).

Variations of blood loss over time were not different according to the treatment groups (P > 0.15). The blood loss was expressed in percentage compared to the blood loss in each hour for the three groups: 2 h: 54.3% (66.6–30.8%) for group I (P = 0.05); 1 h: 40.0% (81.6–22.2%) for group II (P < 0.05); and 1 h: 57.5% (76.0–21.4%) for group III (P > 0.05).

CONCLUSIONS: Administration of low-dose PCC significantly decreased postoperative bleeding after CPB.

Keywords: Prothrombin complex concentrate • Bleeding • Cardiopulmonary bypass • Thromboembolic complications

Safety and efficacy of prothrombin complex concentrates for the treatment of coagulopathy after cardiac surgery

Howard K. Song, MD, PhD, Frederick A. Tibayan, MD, Ed A. Kahl, MD, Valerie A. Sera, MD, Matthew S. Slater, MD, Thomas G. Deloughery, MD, and Mic L. Schecken, MD

Objective: Coagulopathy is an important cause of bleeding after complex cardiac surgery. The conventional treatment for coagulopathy is transfusion, which is associated with adverse outcomes. We report our initial experience with the prothrombin complex concentrate FEIBA (factor VIII inhibitor bypassing activity) for the rescue treatment of coagulopathy and life-threatening bleeding after cardiac surgery.

Methods: Twenty-five patients who underwent cardiac surgery with coagulopathy and life-threatening bleeding refractory to conventional treatment received FEIBA as rescue therapy at our institution. This cohort represents approximately 2% of patients undergoing cardiac surgery in our university-based practice during the study.

Results: The patients were at high risk for postoperative coagulopathy with nearly all patients having at least 2 risk factors for this. Aortic root replacement (Bentall or valve-sparing procedure) and heart transplant with or without left ventricular assist device explant were the most common procedures. The mean FEIBA dose was 2154 units. The need for fresh frozen plasma and platelet transfusion decreased significantly after FEIBA administration (P = 0.01 and P < 0.001). The mean international normalized ratio decreased from 1.58 to 1.13 (P < 0.001). Clinical outcomes were excellent. No patient returned to the operating room for reexploration. There was no hospital mortality and all patients were discharged home. One patient who had a central line and transvenous pacemaker developed an upper extremity deep vein thrombosis.

Conclusions: Our initial experience with FEIBA administration for the rescue treatment of postoperative coagulopathy and life-threatening bleeding has been favorable. Further studies are indicated to confirm its efficacy and safety and determine specific clinical indications for its use in patients undergoing cardiac surgery.

(J Thorac Cardiovasc Surg 2014;147;1036-40)
Fibrinogen concentrate for bleeding – a systematic review

J. Lunde, J. Stensballe, A. Wikkelso, M. Johansen and A. Afshari

Juliane Marie Centre – Department of Anaesthesia, 4013 Rigshospitalet, Copenhagen University Hospital, Copenhagen, Denmark; Section for Transfusion Medicine, Capital Region Blood Bank, Rigshospitalet, Copenhagen University Hospital, Copenhagen, Denmark; Department of Anaesthesia, Centre of Head and Orthopedics, Rigshospitalet, Copenhagen University Hospital, Copenhagen, Denmark; Department of Anaesthesia and Intensive Care Medicine, Herlev Hospital, University of Copenhagen, Copenhagen, Denmark and Department of Anaesthesiology, Department of Neuroanaesthesia and Intensive Care, Rigshospitalet, Copenhagen University Hospital, Copenhagen, Denmark

Fibrinogen concentrate as part of treatment protocols increasingly draws attention. Fibrinogen substitution in cases of hypofibrinogenaemia has the potential to reduce bleeding, transfusion requirement and subsequently reduce morbidity and mortality. A systematic search for randomised controlled trials (RCTs) and non-randomised studies investigating fibrinogen concentrate in bleeding patients was conducted up to November 2013. We included 30 studies of 3480 identified (7 RCTs and 23 non-randomised). Seven RCTs included a total of 268 patients (165 adults and 103 paediatric), and all were determined to be of high risk of bias and none reported a significant effect on mortality. Two RCTs found a significant reduction in bleeding and five RCTs found a significant reduction in transfusion requirements. The 23 non-randomised studies included a total of 2825 patients, but only 11 of 23 studies included a control group. Three out of 11 found a reduction in transfusion requirements while mortality was reduced in two and bleeding in one. In the available RCTs, which all have substantial shortcomings, we found a significant reduction in bleeding and transfusions requirements. However, data on mortality were lacking. Weak evidence from RCTs supports the use of fibrinogen concentrate in bleeding patients, primarily in elective cardiac surgery, but a general use of fibrinogen across all settings is only supported by non-randomised studies with serious methodological shortcomings. It seems premature to conclude whether fibrinogen concentrate has a routine role in the management of bleeding and coagulopathic patients. More RCTs are urgently warranted.

Accepted for publication 13 June 2014

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Platelet Mapping After CPB

- 40 pts by Plt Mapping - before after CPB
- Post hoc analysis - high v. low Bleeding groups
- ADP, AA and collagen TEG examined pre and post. All decreased post CPB.
- Collagen mapping TEG had a 83% sensitivity and 68% specificity for high bleeding

- 41 pts looked at after protamine and out to 3 hours.
- R time with and without heparinase (delta-R) correlated with anti-FX activity for heparin (0.002)!

C-reactive protein is a non-specific marker of diffuse inflammation. High levels in atherosclerosis and coronary thrombosis. 54 pts high correlation between high MA and high C-reactive protein. Also predictive of graft thrombosis.
200 consecutive CABG pts- Copenhagen
87 (43.5%) were hypercoagulable by TEG pre-bypass
Thirty day outcome: TEG hyper v. normal
+ MI 6.9% v. 3.7%
+ Stroke 8.0% v. 2.8%
+ Mortality 4.6% v. 0.9%
+ Combined 17.2% v. 6.6% P= 0.019

First study to show that TEG/RoTEM improves outcome

- 152 – randomized to 100 Pts with complex surgery and adverse bleeding randomized to POC (RoTEM plus Multiplate) v. Conventional Therapy.
- Primary Outcome: RBC Usage 4.9 u (conventional) v. 2.6 POC p<0.001
- Secondary outcomes all less in POC:
  + FFP, Plt, Mech Vent time, LOS, 6 month mortality
Patient blood management (PBM) is an evidence-based, multidisciplinary approach to optimizing the care of patients who might need transfusion. It is just good medicine!
CHALLENGES- FORGE THE FUTURE: TECHNOLOGIES TO DEVELOP

- 1. Wash all cells given-rapid washing device.
- 2. Fresh Whole Blood?
- 3. Make AVH Easy- A Machine to do AVH- calculate amounts
- 4. Preserve Platelets and Plasma- What is the best way.
- Post Op salvage
- A new aprotinin?
WHAT SHOULD WE DO?

"As soon as one problem is solved, another rears its ugly head."

Complex Pt Blood Management!

Many new emerging creative techniques!
It is time to think outside the box!

The goal of this lecture is to make you question-think outside of the box!

“Never, ever, think outside the box.”

Why are we changing for the better?