Success in Patient Blood Management: Bloodless Surgery and Beyond

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Medical Director, Center for Blood Conservation

Illinois Association of Blood Banks (ILAAB) Annual Spring Meeting
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Chicago Marriott Southwest, Burr Ridge, Illinois
DISCLOSURES

• Reimbursed for travel by HbO$_2$ Therapeutics, have Expanded Access IND to use HBOC-201 (Hemopure)
Learning Objectives

• Discuss limitations in caring for patients refusing transfusion and review recent outcome data for “bloodless” surgery
• Review the data on restrictive transfusion practices and when is appropriate to transfuse in the perioperative setting
• Discuss the four “Pillars of Blood Management” and how they can be used to decrease the need for transfusion
• Introduce alternate therapies and future directions in blood conservation
History of Transfusion Medicine

1667
Human to Human transfusion

Figure 2. Blundell’s Gravitator in use. Arguably the most famous image of transfusion’s history in nineteenth-century Britain (from James Blundell, “Observations on Transfusion of Blood, with a Description of his Gravitator,” The Lancet 2 [1828–29]: 321–24).
Further Advances...
Why Transfuse?
Low HCT and Adverse Outcome

- Lowest CPB HCT of <14% in low risk patients and <17% in high risk patients associated with doubling of mortality risk (Fang WC, Circulation 1997)

- Below 23%, CPB HCT is inversely related to mortality (Defoe GR, Ann Thorac Surg 2001)

- In postop cardiac surgical pts, inverse relationship exists between hemoglobin and major morbidity (Hardy JF, Br J Anaesth, 1998)

- Perioperative vital organ dysfunction, short- and intermediate-term mortality increased with HCT <22% (Habib RH, J Thorac Cardiovasc Surg 2003)
Anemia and Mortality

Retrospective study of 1958 patients refusing transfusion

Figure: Adjusted odds ratio for mortality by cardiovascular disease and preoperative haemoglobin

Carson et al, Lancet 1996
Why not transfuse?
Transfusion and Outcome

• Observational cohort study at Cleveland Clinic
• 11,963 isolated CABG patients from 1995-2002
• 48.6% were transfused
• RBC transfusion was *single factor most reliably associated* with risk-adjusted perioperative morbidity
• Risk-adjusted odds ratio for in-hospital mortality of 1.77 (95%CI 1.67-1.87; p < 0.0001)
• Risk is *incremental* for each unit of RBCs and persists for at least 10 years

Koch CG et al., Crit Care Med 2006; 34:1608-16
Transfusion and Outcome

- Retrospective, database study of long-term outcome in 1,915 patients after primary CABG
- **5-year** mortality **double** in transfused patients (15% vs 7%)
- 546 patients transfused during hospitalization were matched by propensity score (age, gender, size, LOS, perfusion time and STS risk) with patients not transfused and 5-year mortality compared
- After correction for comorbidity, 5-year mortality remained 70% higher in transfused group (p<0.001)

The belief of Jehovah’s Witnesses

- Genesis 9:4
  - “But flesh with the life thereof, which is the blood thereof, shall ye not eat”

- Leviticus 17:10
  - “And whatsoever man there be of the house of Israel, or of the strangers who sojourn among you, who eateth any manner of blood, I will even set My face against that soul who eateth blood and will cut him off from among his people.”

- Acts 15:29
  - “that ye abstain from meats offered to idols, and from blood, and from things strangled, and from fornication…”
Jessar et al. *Cardiac Surgery in Jehovah's Witness Patients: Ten-Year Experience*  
*The Annals of Thoracic Surgery, 2012*
Procedures involving blood
Advance Medical Directive

No Blood
Outcome of Patients Who Refuse Transfusion After Cardiac Surgery

A Natural Experiment With Severe Blood Conservation

Gregory Pattakos, MD, MS; Colleen G. Koch, MD, MS, MBA; Mariano E. Brizzio, MD; Lillian H. Batisy, MS; Joseph F. Sabik III, MD; Eugene H. Blackstone, MD; Michael S. Lauer, MD

Table 3. In-Hospital Complications: Matched Comparison

<table>
<thead>
<tr>
<th>Variable</th>
<th>Jehovah’s Witnesses</th>
<th>Non-Witnesses Who Received Transfusions</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total No. of Patients</td>
<td>Value(^a)</td>
</tr>
<tr>
<td>Additional operation for bleeding or tamponade</td>
<td>322</td>
<td>12 (3.7)</td>
</tr>
<tr>
<td>Additional operation for graft occlusion(^c)</td>
<td>105</td>
<td>0</td>
</tr>
<tr>
<td>Cardiac reoperation excluding valve dysfunction and graft occlusion</td>
<td>322</td>
<td>0</td>
</tr>
<tr>
<td>Reoperation for valve dysfunction(^c)</td>
<td>102</td>
<td>0</td>
</tr>
<tr>
<td>Other noncardiac operations(^d)</td>
<td>116</td>
<td>0</td>
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<tr>
<td>Permanent stroke</td>
<td>322</td>
<td>7 (2.2)</td>
</tr>
<tr>
<td>Perioperative MI</td>
<td>322</td>
<td>1 (0.3)</td>
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<tr>
<td>Atrial fibrillation</td>
<td>258</td>
<td>64 (24.8)</td>
</tr>
<tr>
<td>Respiratory failure(^d)</td>
<td>322</td>
<td>20 (6.2)</td>
</tr>
<tr>
<td>Postoperative hematocrit(^g)</td>
<td>150</td>
<td>25/31/37</td>
</tr>
<tr>
<td>Renal failure</td>
<td>322</td>
<td>14 (4.3)</td>
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<tr>
<td>Renal failure requiring dialysis(^c)</td>
<td>173</td>
<td>2 (1.2)</td>
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<tr>
<td>Septicemia(^f)</td>
<td>258</td>
<td>3 (1.2)</td>
</tr>
<tr>
<td>Deep sternal wound infection</td>
<td>322</td>
<td>0</td>
</tr>
<tr>
<td>Operative length of stay, 15th/50th/85th percentiles</td>
<td>322</td>
<td>5.1/7.1/11</td>
</tr>
<tr>
<td>ICU length of stay, 15th/50th/85th percentiles, h(^f)</td>
<td>258</td>
<td>24/25/72</td>
</tr>
<tr>
<td>Hospital death</td>
<td>322</td>
<td>10 (3.1)</td>
</tr>
</tbody>
</table>
Costs and outcomes after cardiac surgery in patients refusing transfusion compared with those who do not: a case-matched study

Nicole R. Guinn, Russell S. Roberson, William White, Patricia A. Cowper, Bob Broomer, Carmelo Milano, Antonio Chirico, and Steven Hill

Figure 2: Overall Cost

Figure 1: Treatment Group Costs by Cost Group

Mean of Surg + Postop Costs by Cost Group

Treatment Group = CBC

Treatment Group = Control

Surg $14,652 47.03%
Clin $11,091 35.60%
Supplies $4,008 12.57%

Surg $15,564 45.27%
Clin $11,771 33.34%
Diag $1,796 5.09%

Supplies $5,755 16.30%
Risk-adjusted clinical outcomes in patients enrolled in a bloodless program

Steven M. Frank,1 Elizabeth C. Wick,2 Amy E. Dezern,2 Paul M. Ness,4 Jack O. Wasey,1
Andrew C. Pippa,1 Elizabeth Dackiw,1 and Linda M.S. Resar2

<table>
<thead>
<tr>
<th>Parameter</th>
<th>All inpatients</th>
<th>Bloodless patients (n = 264)</th>
<th>Matched controls (n = 1157)</th>
<th>p value</th>
<th>Bloodless patients (n = 196)</th>
<th>Matched controls (n = 690)</th>
<th>p value</th>
<th>Bloodless patients (n = 98)</th>
<th>Matched controls (n = 467)</th>
<th>p value</th>
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</thead>
<tbody>
<tr>
<td>In-hospital death</td>
<td>2 (0.7)</td>
<td>31 (2.7)</td>
<td>0.046</td>
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<td>2 (1.0)</td>
<td>14 (2.0)</td>
<td>0.54</td>
<td>0</td>
<td>17 (3.6)</td>
<td>0.05</td>
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<td>LOS (days)</td>
<td>6.9 ± 14.4</td>
<td>7.4 ± 10.8</td>
<td>0.66</td>
<td></td>
<td>5.0 ± 6.3</td>
<td>5.5 ± 7.2</td>
<td>0.62</td>
<td>10.0 ± 13.4</td>
<td>10.6 ± 13.6</td>
<td>0.99</td>
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<tr>
<td>Morbidity outcomes</td>
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<td></td>
<td></td>
<td></td>
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<td>Infection</td>
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<td></td>
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<tr>
<td>Renal</td>
<td></td>
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<td></td>
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<td>Respiratory</td>
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<tr>
<td>Myocardial infarction</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any morbid outcome</td>
<td>40 (13.6)</td>
<td>166 (14.4)</td>
<td>0.74</td>
<td>0.003</td>
<td>25 (12.6)</td>
<td>111.0</td>
<td>0.50</td>
<td>15 (15.3)</td>
<td>90 (19.3)</td>
<td>0.35</td>
</tr>
<tr>
<td>Any morbid outcome or death</td>
<td>40 (13.6)</td>
<td>178 (15.4)</td>
<td>0.44</td>
<td>0.003</td>
<td>25 (12.6)</td>
<td>81 (11.7)</td>
<td>0.70</td>
<td>15 (15.3)</td>
<td>97 (20.8)</td>
<td>0.21</td>
</tr>
</tbody>
</table>

* Data are reported as number (%), median (IQR), or mean ± SD.

LOS = length of stay.

Univariate predictors of the composite outcome (any morbidity or death) were receipt of any ABT (p = 0.0001), APR-DRG complexity score (p = 0.0001), increased patient age (p = 0.0001), and obesity (p = 0.04, Table 5). Male sex was associated with less composite outcome (p = 0.003), but only for the medical subgroup of patients. Bloodless care was not associated with a difference in occurrence of the composite outcome for the entire cohort (p = 0.45) or for the medical (p = 0.70) or surgical (p = 0.22) subgroups.
When to transfuse? (What hb level?)
TRICC Trial

Hebert PC, et al., NEJM 1999
Restrictive Vs. Liberal Strategies  
The Level 1 Evidence

<table>
<thead>
<tr>
<th>Patient Population</th>
<th>Year Published</th>
<th># Enrolled</th>
<th>Hb Threshold</th>
<th>Outcome Measured</th>
<th>Outcome difference</th>
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<tbody>
<tr>
<td>ICU patients</td>
<td>1999</td>
<td>838</td>
<td>7 vs 10</td>
<td>30-day mortality</td>
<td>Improved in restrictive*</td>
</tr>
<tr>
<td>Cardiac Surgery</td>
<td>2010</td>
<td>502</td>
<td>8 vs 10</td>
<td>30-day mortality</td>
<td>Equivalent</td>
</tr>
<tr>
<td>Hip Replacement</td>
<td>2011</td>
<td>2016</td>
<td>8 vs 10</td>
<td>Death/ inability to walk independently</td>
<td>Equivalent</td>
</tr>
<tr>
<td>GI Bleeding</td>
<td>2013</td>
<td>921</td>
<td>7 vs 9</td>
<td>6-week mortality</td>
<td>Improved in restrictive</td>
</tr>
<tr>
<td>TBI</td>
<td>2014</td>
<td>200</td>
<td>7 vs 10</td>
<td>Glasgow Outcome Scale</td>
<td>Improved in restrictive</td>
</tr>
<tr>
<td>Cardiac Surgery</td>
<td>2015</td>
<td>2007</td>
<td>7.5 vs 9</td>
<td>Infection or ischemic event (3 mo)</td>
<td>Equivalent</td>
</tr>
</tbody>
</table>
How much blood should I give?

Or…

What hemoglobin/hematocrit does MY patient need?
\[ DO_2 = CO \times (1.39 \times [Hb] \times SaO_2 + (0.003 \times PaO_2)) \]

- **Rate of oxygen delivery (ml per minute)**
- **Haemoglobin concentration (grams per litre)**
- **Cardiac output (litres per minute)**
- **Oxygen binding capacity of haemoglobin: 1.39 ml per gram**
- **Haemoglobin oxygen saturation expressed as a fraction (i.e. 97% is expressed as 0.97)**
- **Amount of dissolved oxygen in the blood, in ml.**
  - For every 1 mmHg of oxygen tension, 0.003ml of oxygen gas is dissolved in 100ml of blood.
How low to go?

• Consider the physiologic response to anemia
  – Increased Cardiac Output
    • Predominantly by \( \uparrow \) Stroke Volume in anesthetized patients
  – Increased oxygen extraction
    • Critical hemoglobin
What is the critical hemoglobin?

- Hgb of 5.0 gm/dL does not compromise global tissue oxygenation in conscious, healthy, resting humans (Weiskopf RB, JAMA 1998)
Cognitive function impaired at Hgb >5.0 and <6.0 gm/dL

Weiskopf RB, Anesthesiology, 2000
Outcomes:

• Retrospective cohort study of 10,179 consecutive patients with normal preop hgb for on-pump cardiac surgery

• Composite outcome of death, stroke or renal failure

• Increased risk assoc with ≥50% drop in hemoglobin concentration (adjusted OR 1.53, 95% CI 1.12-2.08, p=0.007)

Fig. 2. Spline function plots of the relationship between maximum decrease in Hb concentration and probability of the composite adverse outcome in the entire sample and the selected subgroups (superimposed).

A. "Why give 2 when 1 will do?"

Single Unit RBC Transfusion

Choosing Wisely

Single unit red cell transfusions should be the standard for non-bleeding, hospitalized patients.

- 7 g/dL threshold for stable patients
- 8 g/dL threshold for stable patients with cardiovascular disease

Don't transfuse more units of blood than absolutely necessary.

http://www.choosingwisely.org/societies/american-association-of-blood-banks/


B. RBC Orders: 1 vs. 2 Unit Orders

All Hospitals - RBC Orders: 1 vs. 2 Unit Orders

[Graph showing data distribution over years]
What else can we do?
Diagnose and Treat Anemia
Minimize Blood Loss
Optimize Coagulation
Patient-Centered Decision Making

Improved Patient Outcomes
**Diagnose and Treat Anemia**

**Minimize Blood Loss**

**Optimize Coagulation**

**Patient-Centered Decision Making**

**PATIENT BLOOD MANAGEMENT**

**Improved Patient Outcomes**
Preoperative Anemia

• WHO definition: Hgb< 13g/dL in males, <12g/dL in females

• Common: 5-75% pre-surgical population

[Diagram: Incidence of Preop Anemia]

The Problem

- Independent predictor of morbidity and mortality
- Strongest predictor of perioperative transfusion


Arch Intern Med 2005,165;2214-20
Circulation 2008;117:478-84
The Solution

• Assess and treat patients with anemia before surgery to improve outcomes and reduce both costs and length of stay
Hemoglobin Optimization

• Delay surgery to allow for treatment of anemia
  – Early evaluation (need 4-6 weeks to treat)
  – Delay after catheterization (radial preferred)
Laboratory Evaluation

• Complete Blood Count
• Iron studies
  – Ferritin, Iron, TIBC
• Reticulocyte Count
• B12, Folate levels
• Creatinine
# PAC Testing and Treatment Algorithm

**Hb < 11 g/dL for primary knee replacement, Hb < 11.5 for knee revision or primary hip replacement, or Hb < 12 g/dL for hip revision?**

- **Yes**
  - Evaluation necessary
    - Thorough H & P looking for source of anemia. Lab data: CBC, iron studies, B12/folate, serum creatinine/GFR
  - Evidence of:
    1) existing oncologic or hematologic disease,
    2) severe unexplained anemia (hb < 8), or
    3) anemia with decrease in multiple cell lines?
      - **Yes**
        - Referral to hematology/oncology
      - **No**
        - Iron status?
          - Ferritin < 100 µg/L and/or TSAT < 20%
            - Iron deficiency. Referral to PCP or gastroenterologist to rule out malignancy (form letter to PCP)
            - Iron therapy:
              - (i) Oral iron in divided doses
              - (ii) IV iron if intolerance to oral iron, GI uptake problems/deficiency, or chronic inflammatory disease, post gastric bypass, or < 21 days before surgery
          - Ferritin > 100 µg/L and/or TSAT > 20%
            - Chronic kidney disease
              - Consider referral to nephrologist
              - Serum creatinine/GFR
                - GFR > 60 mL/min
                  - No response
                - GFR < 60 mL/min
                  - B12 and/or folic acid
                    - Normal
                      - Reticulocyte count
                        - Low
                          - Consider anemia of chronic disease
                        - High
                          - Consider hemolysis or blood loss source and refer to hematology and/or PCP
                    - Low
                      - Folic acid and/or vitamin B12 therapy

Anemia Treatment

- Erythropoietin Stimulating Agents (ESAs)
  - EPO 600 Units/kg weekly with IV iron
  - EPO 300 Units/kg daily with IV iron

- Iron supplementation
  - Intravenous versus oral
  - Treat to Ferritin>100, Iron sat>20%

- Vitamin B12, Folate
“Black Box Warning” on ESAs

• Issued by FDA in 2007
• “Increase the risk for death and serious cardiovascular events when administered to a target hgb>12g/dL”
• “Physicians and patients should carefully weigh the risks of ESAs against transfusion risk”
A single dose of erythropoietin reduces perioperative transfusions in cardiac surgery: Results of a prospective single-blind randomized controlled trial
## Intravenous Iron

<table>
<thead>
<tr>
<th>Formulation</th>
<th>Brand Name</th>
<th>Dose</th>
<th>Advantage</th>
<th>Disadvantage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Iron Sucrose</td>
<td>Venofer</td>
<td>300mg</td>
<td>Safe, short infusion time, inexpensive</td>
<td>Requires multiple doses</td>
</tr>
<tr>
<td>LMW Dextran</td>
<td>InFed</td>
<td>1000mg</td>
<td>Total dose repletion, inexpensive</td>
<td>Long infusion time, requires test dose</td>
</tr>
<tr>
<td>Ferric gluconate</td>
<td>Ferrlecit</td>
<td>125mg</td>
<td>May be given as IV push</td>
<td>Requires multiple doses</td>
</tr>
<tr>
<td>Ferumoxytol</td>
<td>Feraheme</td>
<td>510mg</td>
<td>Short infusion time</td>
<td>May affect MRI imaging</td>
</tr>
<tr>
<td>Ferric carboxymaltose</td>
<td>Injectafer</td>
<td>750mg</td>
<td>Short infusion time</td>
<td>Expensive</td>
</tr>
</tbody>
</table>
Ferric carboxymaltose reduces transfusions and hospital stay in patients with colon cancer and anemia

José Luis Calleja1, Salvador Delgado2, Adolfo del Val3, Antonio Hervás4, José Luis Larraona5, Álvaro Terán6, Mercedes Cucala7, Fermín Mearin8, on behalf of the Colon Cancer Study Group
Pre-Autologous Donation

• Reduced exposure to pathogens
• Increased cost
• Reduces allogeneic transfusion but increases transfusion overall
• Not recommended for cases with low likelihood of transfusion
• Fallen out of favor

Gunter et. al. Blood Transfusion, 2011
Diagnose and Treat Anemia

Minimize Blood Loss

Optimize Coagulation

Patient-Centered Decision Making
Intraoperative Treatment

- Surgical techniques
  - Minimally invasive techniques, tissue coagulants, minimize cooling

- Perfusion Techniques
  - RAP, smaller circuit volume

- Minimize phlebotomy

- Cell salvage

- Acute Normovolemic Hemodilution (ANH)
Retrograde Autologous Prime

Fig. 1 – Schematic representation of the retrograde autologous priming circuit (Adapted from Eising et al., 2003)

Rgies et al. *Brazilian Journal of Cardiovascular Surgery*, 2011
Cell Salvage

- Cochrane review of 75 trials
- Overall, the use of cell salvage reduced the rate of exposure to allogeneic RBC transfusion by a relative 38% (RR=0.62; 95% CI 0.55 to 0.70).
- Orthopedic surgery: RR of exposure to RBC transfusion was 0.46 (95% CI 0.37 to 0.57)
- Cardiac surgery: RR of exposure to RBC transfusion was 0.77 (95% CI 0.69 to 0.86)
- The use of cell salvage resulted in an average saving of 0.68 units of allogeneic RBC per patient (WMD=-0.68; 95% CI -0.88 to -0.49).

Cell salvage for minimizing perioperative allogeneic blood transfusion.
Carless PA¹, Henry DA, Moxey AJ, O'Connell D, Brown T, Fergusson DA.
Acute Normovolemic Hemodilution (ANH)

• Definition: Removal of whole blood prior to surgery with replacement of an appropriate volume of crystalloids and/or colloids to maintain normovolemia

• Indications: Patients undergoing cardiac surgery with cardiopulmonary bypass, or major surgery with expected blood loss >20% of blood volume, as a technique to reduce the need for allogeneic blood transfusion
Benefits of ANH

• Blood lost during the procedure has proportionately fewer RBCs per mL
• Whole blood available for re-transfusion
  – Improved coagulation
• Improvement of microvascular blood flow
• Inexpensive
  – No testing, no storage required
• Safe
  – Infectious risks, avoid administration errors
Data supporting hemodilution

- Meta-analysis of normovolemic hemodilution including 42 randomized controlled trials (2233 patients)
- Similar risk of exposure to transfusion, but ANH patients were transfused 1-2 fewer units
- Less total blood loss in ANH groups

Segal JB et al., Transfusion 2004
Limitation of ANH

• Unusual to get more than 3-4 whole blood units (<3.0x10^{11} PLTs)
• Contraindicated with severe coronary disease or critical AS
• Requires pre-operative euvoolemia
• Requires adequate baseline hemoglobin (>12g/dL)
How to do it?

• Set-up:
  – Dedicated observer for harvest
  – Adequate IV access and monitoring
  – Connect citrated bags to central line via tubing
  – Determine harvest volume:

Predicted Body Weight:
  Males=50kg + (2.3X inches over 5’) Females=45.5kg+ (2.3X inches over 5’)

Weight = PBW + 0.33(actual weight – PBW)

Harvest Volume = \( \frac{\text{Weight} \times 70 \ (\text{Hgb} - \text{target Hgb})}{\text{Hgb}} \)
Beginning INH Circuit

DUKE
Prime

Patient Connection End
Continuous INH Circuit
Key Points

• Maintain strict aseptic technique
• Do not overfill or under-fill citrate collection bags
• Ensure adequate speed of collection to avoid stasis
• Maintain euvoolemia
• Utilize appropriate monitoring to avoid risk of myocardial ischemia
Diagnose and Treat Anemia
Minimize Blood Loss
Optimize Coagulation
Patient-Centered Decision Making
Coagulopathy

• Preoperative
  – Hold non-ASA anti-coagulants appropriately
  – Stop herbal supplements that may contribute to coagulopathy
Coagulopathy

• Intraoperative
  – Minimize crystalloid
  – Temperature management
  – ANH

• Intra and Postoperative
  – Pharmacotherapy
  – Point-of-Care testing
ROTEM-Guided Algorithm

Lab-Based Decisions

- **HB < 7 g/dl**
  - 1-2 Units PRBC
  - Target HB 8g/dL

- **Platelets < 50K OR A10Ex <45 mm AND A10Fib >= 13**
  - 1U Platelets

- **Platelets < 50K AND A10Ex<45 mm AND A10Fib <13 mm**
  - 1U Platelets + 5U Cryoprecipitate OR 2g Fibrinogen Concentrate

- **Platelets >50K AND Fibrinogen <200 mg/dl OR A10Ex< 45mm AND A10 Fib <13 mm**
  - 5U Cryoprecipitate OR 2g Fibrinogen Concentrate

- **PT/INR >1.5 x OR CTex >80s.**
  - FFP 10 - 15 ml/Kg

- **IF A10Ex < 45 AND A10Fib<10:10U Cryoprecipitate OR 4 g Fibrinogen Concentrate**

- **IF Fibrinogen < 150mg/dl OR A10Ex <45 AND A10Fib <10: 10U Cryooperationate OR 4g Fibrinogen Concentrate**
Table 4. Bleeding and Transfusion Requirements

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<th>Intraoperative</th>
<th></th>
<th></th>
<th>Postoperative</th>
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<tr>
<td></td>
<td>TEG</td>
<td>Control</td>
<td>(P)</td>
<td>TEG</td>
<td>Control</td>
<td>(P)</td>
<td>TEG</td>
<td>Control</td>
<td>(P)</td>
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<tr>
<td>Packed red blood cells (mL)</td>
<td>267 ± 423</td>
<td>346 ± 449</td>
<td>0.4</td>
<td>103 ± 252</td>
<td>177 ± 318</td>
<td>0.27</td>
<td>354 ± 487</td>
<td>475 ± 593</td>
<td>0.12</td>
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<tr>
<td>Fresh-frozen plasma (mL)</td>
<td>22 ± 101</td>
<td>113 ± 407</td>
<td>0.4</td>
<td>33 ± 169</td>
<td>146 ± 378</td>
<td>0.13</td>
<td>36 ± 142</td>
<td>217 ± 463</td>
<td>&lt;0.04</td>
</tr>
<tr>
<td>Platelet concentrates (mL)</td>
<td>22 ± 75</td>
<td>41 ± 122</td>
<td>0.6</td>
<td>11 ± 46</td>
<td>42 ± 107</td>
<td>0.3</td>
<td>34 ± 94</td>
<td>83 ± 160</td>
<td>0.16</td>
</tr>
<tr>
<td>Autologous reinfusion volume (mL)</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>128 ± 145</td>
<td>141 ± 290</td>
<td>0.19</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>6-h MTD + reinfusion volume (mL)</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>362 ± 274</td>
<td>469 ± 637</td>
<td>0.63</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>24-h MTD + reinfusion volume (mL)</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>702 ± 500</td>
<td>901 ± 847</td>
<td>0.27</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Packed red blood cells</td>
<td>17/53</td>
<td>23/52</td>
<td>0.2</td>
<td>10/53</td>
<td>16/52</td>
<td>0.16</td>
<td>22/53</td>
<td>31/52</td>
<td>0.06</td>
</tr>
<tr>
<td>Fresh-frozen plasma</td>
<td>3/53</td>
<td>8/52</td>
<td>0.1</td>
<td>2/53</td>
<td>11/52</td>
<td>&lt;0.007</td>
<td>4/53</td>
<td>16/52</td>
<td>0.002</td>
</tr>
<tr>
<td>Platelet concentrates</td>
<td>5/53</td>
<td>8/52</td>
<td>0.4</td>
<td>3/53</td>
<td>9/52</td>
<td>0.06</td>
<td>7/53</td>
<td>15/52</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

Values are mean ± sd or proportion of patients transfused.
Nonparametric statistics performed for all data not conforming to normal distribution.

TEG = thromboelastography, MTD = chest tube drainage.

Thromboelastography-Guided Transfusion Algorithm Reduces Transfusions in Complex Cardiac Surgery
Shore-Lesserson, Linda; Manspeizer, Heather E.; DePerio, Marietta; Francis, Sanjeev; Vela-Cantos, Frances; Ergin, M. Arisan
Pharmacotherapy and PBM

- **Anti-fibrinolytics (TXA, aminocaproic acid)**
- **DDAVP**
  - Stimulates release of von Willebrand factor from endothelial cells
  - Useful for treating acquired von Willebrand disease, thrombocytopenia, impaired platelet function
- **Fibrinogen Factor Concentrate**
  - Preservative free concentrate of fibrinogen made from pooled human plasma
  - Used off-label for acquired hypofibrinogenemia and dilutional coagulopathy in multiple studies of patients for orthopedic, cardiac, obstetric, urologic, and trauma surgeries
  - Prepared faster than cryoprecipitate and in a smaller volume, causing less hemodilution
- **Prothrombin Complex Concentrates**
  - Kcentra contains vitamin K-dependent coagulation Factors II, VII, IX, and X and antithrombotic Proteins C and S, Profilnine contains factors II, IX and X
- **Recombinant Factor VII**
Diagnose and Treat Anemia

Minimize Blood Loss

Optimize Coagulation

Patient-Centered Decision Making

Improved Patient Outcomes

PATIENT BLOOD MANAGEMENT
Blood Conservation at Duke

Mission Statement:
The Center for Blood Conservation was designed to serve the medical and surgical needs of those patients wishing to refuse or avoid blood transfusion. By utilizing innovative techniques and treatments and through education, we endeavor to reduce unnecessary transfusions. We assist with the coordination and optimization of patients for elective surgery and provide consultation services for inpatients at Duke Hospital.
What We Do

CBC Team responsibilities:

• Advocate for the declared wishes of the patient regarding treatment with blood or blood products
• For patients undergoing non-emergent treatment, ensure completion of the required documentation
  – Consents in Red Chart, note in EPIC
  – FYI flag
  – Add to Problem List
  – Armbands
• Inform Transfusion Services (TS) of the patient's refusal
  – Block placed preventing release of products
• Optimize hemoglobin prior to major blood loss surgery
• Inform attending physician or his or her designee of patient's refusal of transfusion therapy with blood products.
• Maintain continual pager coverage for consultation
• “A” Patients
  – “… will not accept treatment with allogenic blood/blood products, such as whole blood, red cells, white cells, unfractionated plasma, or platelets, EVEN if, in the opinion of my physician, such measures are necessary to prolong the continuation of my life and/or avoid damage to tissues, organs, or body functions. I do request that all applicable non-blood medical management strategies be used and exhausted.”

• “B” Patients
  – “…will accept the use of blood/blood products ONLY if, in the opinion of my attending physician (or designee), such measures are necessary to sustain my life and/or avoid damage to tissue, organs, or body functions. Under these circumstances, all applicable non-blood medical management strategies will have been exhausted.”
Duke University Hospital

DIRECTIONS FOR MINOR FRACTIONS OF BLOOD AND BLOOD CONSERVATION EQUIPMENT FOR ADULT PATIENTS REFUSING BLOOD OR BLOOD PRODUCTS

The following are my wishes and directions regarding procedures, treatments, minor fractions of blood and blood conservation equipment:

<table>
<thead>
<tr>
<th>MINOR FRACTIONS OF BLOOD</th>
<th>ACCEPT</th>
<th>REFUSE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Interferon</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Immunoglobulins or Immune Globulins (example: RhoGAM, Vaccinations)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recombinant Protein Preparations (example EPO - may contain albumin)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Albumin, Plasmanate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cryoprecipitate (contains Fibrinogen)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tissue adhesives, fibrin glue</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clotting Factors (minor fraction of pooled plasma)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cryo-poor-plasma (cryosupernatant)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>PROCEDURES</th>
<th>ACCEPT</th>
<th>REFUSE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intraoperative blood salvage (Cell Saver) without blood storage</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Perioperative surgical drain reinfusion device</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intraoperative hemodilution without blood storage</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dialysis and Heart-Lung equipment (non-blood primed closed circuit)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Therapeutic Apheresis (similar to dialysis)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>TRANSPLANTS</th>
<th>UNDECIDED</th>
<th>ACCEPT</th>
<th>REFUSE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tissue transplant (non-blood tissue transplants)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Patient's Signature

Healthcare Power of Attorney Document in Medical Record □ Yes □ No

If no, explain:

Signature of Witness CBC Practitioner or Attending ID# Date/Time
ASA PBM Committee Form

|_whole Blood Components (some people call these Major Fractions)_

Blood carries oxygen and nutrients throughout the body. It is made of 4 main parts:

- **Red Blood Cells** (Other Names: Erythrocytes, RBCs) take oxygen from your lungs to your organs and tissues. They also take carbon dioxide back to your lungs to breathe out. We give RBCs if your blood count is too low.
- **White Blood Cells** (Other Names: Leukocytes, WBCs) are one of your body’s defenses against bacteria, viruses, and diseases the body produces. We give WBCs to help you fight certain diseases.
- **Platelets** (Other Name: Thrombocytes) are small pieces of cells. They help your blood make clots that prevent or stop bleeding. We give Platelets if your bleeding is hard to stop or if your Platelet count is very low.
- **Plasma** is the liquid part of blood. It is made of water, albumin, clotting factors, salts, sugars, fats, vitamins, and hormones. We give Plasma if you do not have enough or if you need more clotting factors.

**Types of Plasma**

- Frozen (or thawed) plasma (FFP) is plasma removed from whole blood. It is frozen so it can be used later.
- Solvent detergent-treated plasma is plasma that is cleaned to reduce the chance of infection or allergic reaction.

|_fractionated Components (some people call these Minor Fractions)_

_Cryosupernatant_ is plasma that has most of the solid parts taken out. The leftover liquid is called Cryosupernatant. We give Cryosupernatant to replace plasma.

_Cryoprecipitate_ is plasma that has the liquid part taken out. The leftover clotting factors are called Cryoprecipitate. We give Cryoprecipitate to help stop bleeding.

_Prothrombin Complex Concentrate_ is a mix of many clotting factors. We give this mix to help stop bleeding or to reverse the effects of blood thinning medicine.

_CONCENTRATED CLOTTING FACTORS_ are single clotting factors. We give them to help stop bleeding.

_Albumin_ is the main protein in plasma. We give Albumin to increase blood volume.

_Antibodies (Other Name: Immune Globulins)_ are proteins your body makes to fight disease. We can also give you Antibodies to help your body fight some types of infections.

|_Your Own Blood_ can be used in the procedures below in a closed system. Your blood is not mixed with any other blood.

- **Apheresis** (Other Names: Plasma exchange, Plasmapheresis) is when a closed-system machine replaces bad plasma with a good plasma substitute. It is used if your plasma has antibodies that are attacking your body.
- **Auto-Transfusion** (Other Names: Cell Saver, Cell Salvage, Salvaged Autologous Blood) is when your blood is collected during surgery, washed and filtered, and then given back to you in a closed system during surgery.
- **Hemodilution** is when your blood is replaced with IV fluids during surgery. After surgery, we give your blood back to you in a closed system.
- **Heart and Lung Machine** is when your blood flows into a machine that adds oxygen. Your blood then flows back into your body in a closed system primed with non-blood fluid. It can be used during some surgeries.
- **Dialysis** (Other Names: Renal Dialysis, Hemodialysis) is when your blood flows into a machine that filters and cleans it, then flows back into your body in a closed system. It is used if your kidneys are not working well or harmful substances need to be taken out of your blood.
- **Epidural Blood Patch** is some of your blood injected around your spinal cord to stop a spinal fluid leak.
- **Platelet Gel** is made of your platelets and white blood cells. We use it to cover wounds and help stop bleeding.
Benefits of Transfusion Avoidance

- Infectious risks
- TRALI/ TACO
- Immune suppression
- Administration error/ transfusion reactions
- Limited resource
- Cost
Cost of Blood Products

• Acquisition Costs (from American Red Cross)
  – PRBCs $212.73
  – Plateletpheresis $514.00
  – FFP $49.98
  – Cryoprecipitate pool (5 bags) $315.67
Cost of Transfusion

- Tasks and resource consumption (materials, labor, third-party services, capital) related to blood administration identified prospectively at two US and two European hospitals
- Activity-based costing used to calculate cost of blood
- RBC-unit costs averaged $761 ± 294
- Did not include treatment of complications associated with transfusion-transmissible disease, litigation or reimbursement/indemnification for adverse events

Shander, A et al. Transfusion, 2010; 50: 753-765
Cost of Transfusion Alternatives

• ESAs, IV iron
  – EPO 40,000 unit dose - $455
  – Iron sucrose 200mg dose - $99
  – LMW Iron Dextran 1000mg- $250
  – TXA 1gm- $31

• ANH

• Pediatric phlebotomy tubes
## Future Directions... HBOCs

### Table 1. Biochemical and Biophysical Properties of Hemoglobin-based Oxygen Carriers in Development

<table>
<thead>
<tr>
<th>Hemoglobin Name, Brand Name, Company Source</th>
<th>Molecular Size (kDa)</th>
<th>% Tetramer</th>
<th>Chemical Modifier</th>
</tr>
</thead>
<tbody>
<tr>
<td>HbA (Normal Human Hb)</td>
<td>64</td>
<td></td>
<td>None</td>
</tr>
<tr>
<td>DCLHb (Hemase®) Baxter (development terminated)</td>
<td>64&lt;sup&gt;117&lt;/sup&gt;</td>
<td>66-68 (0-1% deoxygen) (&lt;1% unroached tetramer)&lt;sup&gt;118&lt;/sup&gt;</td>
<td>Bio-O (chromosomal) fumurate + immunoabsorbent crossing</td>
</tr>
<tr>
<td>MP4 (Hemase®) Sargent</td>
<td>92&lt;sup&gt;119&lt;/sup&gt;</td>
<td></td>
<td>None</td>
</tr>
<tr>
<td>Pyrrotilated Hb FOX - conjugate (HPH) - Catexa &amp; SQ3</td>
<td>106 (peak average weight by size chromatography)</td>
<td></td>
<td>None</td>
</tr>
<tr>
<td>O-M-PyridylHb (Hemase®, Hemex) - Hemex (development terminated)</td>
<td>32 to &gt;500&lt;sup&gt;119&lt;/sup&gt;</td>
<td></td>
<td>None</td>
</tr>
<tr>
<td>Polybutyl (polyurethane) Biopure (Bovine Hb)</td>
<td>130-500&lt;sup&gt;120&lt;/sup&gt;</td>
<td>&lt;1%&lt;sup&gt;121,122&lt;/sup&gt;</td>
<td>Pyridoxal phosphate immunobead crossing</td>
</tr>
<tr>
<td>HBO® (Polyurethane) Northfield Human Hb</td>
<td>Average 256&lt;sup&gt;123&lt;/sup&gt;</td>
<td>&lt;1%&lt;sup&gt;121,122&lt;/sup&gt;</td>
<td>Glutathione + Intramolecular/Intermolecular creasing</td>
</tr>
<tr>
<td>hHb-1 (Gran®) Sargent (development terminated)</td>
<td>64&lt;sup&gt;124&lt;/sup&gt;</td>
<td></td>
<td>Glutathione + Intramolecular creasing</td>
</tr>
<tr>
<td>PEG-Hemoglobin Ezon (development terminated)</td>
<td>&lt;133 (NA)</td>
<td></td>
<td>Succinimidyl carbonate PEG-modified bovine Hb</td>
</tr>
</tbody>
</table>

### Table 2. Summary of Adverse Events Reported in the Literature or Publicly Available

<table>
<thead>
<tr>
<th>Event</th>
<th>Apex</th>
<th>Baxter</th>
<th>Biopure</th>
<th>Enox</th>
<th>Hemex</th>
<th>Northfield</th>
<th>Sargent</th>
<th>Semagen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of subjects</td>
<td>Not reported</td>
<td>965</td>
<td>695</td>
<td>709</td>
<td>618</td>
<td>Not reported</td>
<td>209</td>
<td>170</td>
</tr>
<tr>
<td>1. Death</td>
<td>-</td>
<td>78</td>
<td>61</td>
<td>25</td>
<td>14</td>
<td>-</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>2. Hypotension</td>
<td>-</td>
<td>76</td>
<td>34</td>
<td>160</td>
<td>59</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>3. Pulmonary hypertension</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>1</td>
<td>3</td>
<td>0</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>4. Chest pain/pleurisy</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>0</td>
<td>1</td>
<td>54</td>
<td>22</td>
<td>-</td>
</tr>
<tr>
<td>5. Congestive heart failure</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>0</td>
<td>1</td>
<td>54</td>
<td>22</td>
<td>-</td>
</tr>
<tr>
<td>6. Cardiac arrest</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>1</td>
<td>14</td>
<td>9</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>7. Myocardial infarction</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>6</td>
<td>14</td>
<td>4</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>8. Cardiac arrhythmias/conduction abnormalities</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>23</td>
<td>175</td>
<td>100</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>9. Cerebrovascular accident</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>16</td>
<td>3</td>
<td>3</td>
<td>-</td>
<td>2</td>
</tr>
</tbody>
</table>

## Normal Blood Flow vs. Anemic Blood Flow

- **Normal Blood Flow**: Blood flows smoothly through the blood vessels, providing oxygen and nutrients to the body tissues.
- **Anemic Blood Flow**: Blood flow is impaired due to a lower oxygen-carrying capacity, leading to reduced oxygen delivery to tissues.

### Normal Blood Flow

- Blood flows smoothly through the blood vessels.
- Oxygenated blood is delivered to body tissues.
- Nutrients are efficiently distributed.

### Anemic Blood Flow

- Reduced oxygen-carrying capacity.
- Impaired blood flow through vessels.
- Oxygen deprivation affects tissue function.

**Clinical Impact**

- **Cardiac Arrest**: Life-threatening heart failure.
- **Myocardial Infarction**: Severe heart muscle damage.
- **Arterial Hypertension**: Elevated blood pressure.
- **Atrial Fibrillation**: Abnormal heart rhythm.
- **Pulmonary Hypertension**: High pressure in the lungs.
- **Cerebrovascular Accident**: Stroke.

**Note**: The table provides a summary of adverse events reported in the literature or publicly available. The clinical significance of each event is not detailed in the table. For more detailed information, consult the original reports or clinical trials.
Artificial Oxygen Carriers (HBOCs)

Weiskopf et. al. Transfusion 2017.
How can “We” decrease transfusions?

- Delay Elective Surgery and Treat Anemia
  - IV iron, ESAs
- Use Blood Conservation Techniques to Avoid Transfusion
  - Cell salvage and ANH
  - Routine use of anti-fibrinolytics
- When transfusion is necessary, use restrictive thresholds
  - Give single units a time, reassess if stable
- Recognize coagulopathy and treat early
  - Use TEG or ROTEM for rapid assessment of clot strength
- Don’t perform serial blood counts on hemodynamically stable patients
  - Excessive phlebotomy can lead to unnecessary transfusions

It Takes a TEAM!
Questions?

Thank you to:
Cathleen Peterson-Layne
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Evelyn Lockhart
Kevin Collins
Nick Bandarenko
Jessica Poisson
Holly Muir
Dhanesh Gupta
Joseph Mathew