Evidence-based Transfusion Practice and Patient Blood Management Programs

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Disclosures

Haemonetics Corp.
  IMPACT® Online

CSL Behring
  Massive Transfusion Protocols
  Fibrinogen Concentrate

Medtronic
  Blood Management - Hemostasis
  New electrocautery devices
Blood transfusion targeted at the Overuse Summit, as the most commonly performed procedure in US hospitals”*

Five overused procedures:

1. Blood transfusions
2. Heart vessel stents
3. Ear tubes (tympanostomy tubes)
4. Antibiotics for the common cold (viral upper respiratory infections)
5. Early scheduled births (early induction) without medical need

Society of Critical Care Medicine

Don’t transfuse red blood cells in hemodynamically stable, non-bleeding ICU patients with a hemoglobin concentration greater than 7 g/dL.

American Society of Anesthesiologists

Don’t administer packed red blood cells (PRBCs) in a young healthy patient without ongoing blood loss and hemoglobin of ≥ 6 g/dL unless symptomatic or hemodynamically unstable.

American Society of Hospital Medicine

Avoid transfusions of red blood cells for arbitrary hemoglobin or hematocrit thresholds and in the absence of symptoms of active coronary disease, heart failure, or stroke.

American Society of Hematology

Don’t administer plasma or prothrombin complex concentrates for non-emergent reversal of vitamin K antagonists (i.e. outside the setting of major bleeding, intracranial hemorrhage or anticipated emergent surgery).

AABB

Four different initiatives related to blood management and inappropriate transfusion.
Blood Management is one of the few areas in medicine where all three of these can be achieved at the same time:

• Save Cost
• Reduce Risk
• Improve Outcomes
  ↓risk, ↑safety
5% less blood products = over $1 million cost reduction/year
10% less blood products = over $2 million cost reduction/year

$22 million total / year

$/year To Acquire Blood Products at JHH

- All RBC's: $14,000,000
- All FFP: $2 million
- All Platelets: $8,000,000
How much does Medicare pay for transfusion of the first 3 units of red blood cells in a calendar year?

A. $600
B. $900
C. No dollars
How much does Medicare pay for transfusion of the first 3 units of red blood cells in a calendar year?

A. $600  
B. $900  
C. No dollars

“Medicare Blood Deductible”
Dollars to Acquire per Unit at JHH

- Red Cells
- Plasma
- Platelets
“Activity-based costs of blood transfusions in surgical patients at four hospitals”

Actual cost of RBCs is 3-4 times greater than acquisition cost from Red Cross

![Bar chart](image)

Fig. 2. Mean acquisition costs (■) and total ABC model costs ( Arial) per unit of blood.
### Three Categories of Risks / Adverse Effects from Blood Transfusion

<table>
<thead>
<tr>
<th>Clinical Event</th>
<th>Risk / Unit</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Common</strong></td>
<td></td>
</tr>
<tr>
<td>Allergic/Urticaria</td>
<td>1 in 100</td>
</tr>
<tr>
<td>RBC Alloimmunization</td>
<td>1 in 100</td>
</tr>
<tr>
<td>TACO</td>
<td>1 in 100</td>
</tr>
<tr>
<td><strong>Not so Rare</strong></td>
<td></td>
</tr>
<tr>
<td>TRALI</td>
<td>1 in 5,000</td>
</tr>
<tr>
<td>Hemolytic Rxn</td>
<td>1 in 6,000</td>
</tr>
<tr>
<td>Wrong Unit Given</td>
<td>1 in 15,000</td>
</tr>
<tr>
<td><strong>Rare</strong></td>
<td></td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>1 in 200,000</td>
</tr>
<tr>
<td>Hepatitis C</td>
<td>1 in 2,000,000</td>
</tr>
<tr>
<td>HIV 1 and HIV 2</td>
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Hep C and HIV = Death by Lightning Strike
Transfusion Related Immune Modulation (TRIM)
Immunosuppression

“Blood transfusion is actually a tissue of transplant, and as such, it carries a lot of immunologic implications for the recipient”

Mark Ereth MD, May, 2011 Anesthesiology News
Prospective 533 CABG pts. (14% overall bacterial infection rate)

Fig 1. Rates of bacterial infection by site and number of units of red blood cells (RBC) transfused. (SSI = surgical site infection.)
Health Care–Associated Infection After Red Blood Cell Transfusion: A Systematic Review and Meta-analysis

Rohde, et al, JAMA, 2014

RR = 0.88

Hospital-acquired Infection by Transfusion Strategy

% with Infection

Restrictive (Hb 7-8 g/dL) Liberal (Hb 9=10 g/dL)

Rohde, et al, JAMA, 2014
The “Blood is Bad” Papers

Morbidity and mortality risk associated with red blood cell and blood-component transfusion in isolated coronary artery bypass grafting*

Colleen Gorman Koch, MD, MS; Liang Li, PhD; Andra I. Duncan, MD; Tomislav Mihaljevic, MD; Delos M. Cosgrove, MD; Floyd D. Loop, MD; Norman J. Starr, MD; Eugene H. Blackstone, MD

<table>
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<tr>
<th>Risk adjusted OR</th>
<th>Ann Thor Surg. 2006</th>
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<tbody>
<tr>
<td>mortality = 1.77</td>
<td></td>
</tr>
<tr>
<td>renal failure = 2.06</td>
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</tr>
<tr>
<td>vent. support = 1.79</td>
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</tr>
<tr>
<td>serious infection = 1.76</td>
<td></td>
</tr>
<tr>
<td>cardiac comp. = 1.55</td>
<td></td>
</tr>
<tr>
<td>neurol. events =</td>
<td></td>
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*
The “Blood is Bad” Papers
Most are retrospective
“Confoundling by indication”

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Transfusion in Coronary Artery Bypass Grafting is Associated with Reduced Long-Term Survival

Colleen Gorman Koch, MD, MS, Liang Li, PhD, Andra I. Duncan, MD, Tomislav Mihaljevic, MD, Floyd D. Loop, MD, Norman J. Starr, MD, and Eugene H. Blackstone, MD

Crit Care Med. 2006

# of Units
0
1
2
3-5
6+
Risks associated with preoperative anemia in cardiac surgery

Mild preop. anemia – 4-fold increase morbidity

Composite Adverse Outcome Rate (%)

Preoperative Hemoglobin (g/dL)

- 9.5-10.9: N = 43/207
- 11.0-12.4: N = 79/567
- 12.5-13.9: N = 57/1068
- 14.0-15.4: N = 52/1076
- >15.4: N = 16/368
Conclusions:

- Anemia is associated with worse outcome
- Transfusion is associated with worse outcome
- Better off with your own RBCs than someone else’s
Patient Blood Management

“Right dose, right product, right patient, right time”

1. Preop anemia treatment –
   A $5 bottle of iron pills beats $500 of blood IV iron, EPO as needed – preop and postop
2. Good surgery, less invasive -
   The Jehovah’s Witness Phenomenon
3. Blood Salvage -
   Avoiding the “storage lesion”
4. Thromboelestography (TEG)
5. Antifibrinolytics – Aprotonin, Amicar, Tranexamic acid
6. Autologous normovolemic hemodilution
7. MUF, ZBUF, hemoconcentration
8. Minimize phlebotomy
Johns Hopkins Data from Impact Online (Haemonetics)
Past 12 months - 1,188 Cardiac Surgery Patients
Percent Patients Anemic Based on First Recorded Hemoglobin

% of Patients

<table>
<thead>
<tr>
<th>Year, Month</th>
<th>% of Patients</th>
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<tbody>
<tr>
<td>2011 Jan</td>
<td>30.0</td>
</tr>
<tr>
<td>2011 Feb</td>
<td>40.0</td>
</tr>
<tr>
<td>2011 Mar</td>
<td>45.0</td>
</tr>
<tr>
<td>2011 Apr</td>
<td>35.0</td>
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<tr>
<td>2011 May</td>
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</tr>
<tr>
<td>2011 Jun</td>
<td>35.0</td>
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<tr>
<td>2011 Jul</td>
<td>45.0</td>
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<tr>
<td>2011 Aug</td>
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<td>2011 Sep</td>
<td>30.0</td>
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<tr>
<td>2011 Oct</td>
<td>40.0</td>
</tr>
<tr>
<td>2011 Nov</td>
<td>40.0</td>
</tr>
<tr>
<td>2011 Dec</td>
<td>45.0</td>
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<tr>
<td>2012 Jan</td>
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<tr>
<td>2012 Feb</td>
<td>35.0</td>
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<tr>
<td>2012 Mar</td>
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<td>2012 May</td>
<td>40.0</td>
</tr>
<tr>
<td>2012 Jun</td>
<td>40.0</td>
</tr>
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</table>
Impaired red blood cell deformability after transfusion of stored allogeneic blood but not autologous salvaged blood in cardiac surgery patients


Blood Salvage
(Cell Saver)
Recycled blood is better than donated blood for transfusions, Hopkins study finds

BY LENNY BERNSTEIN  ☵  May 9 at 8:45 am

We recycle a lot of things — paper, plastic, metal, blood.

Yes, blood. During some surgeries, operating room personnel try to capture as much blood as possible and return the red blood cells to your system, instead of, or in addition to, donated blood from a blood bank. They find that patients have better outcomes when transfused with their own blood.

A Johns Hopkins University study, published in the June issue of the journal Anesthesia and Analgesia, explains one reason for that. As banked blood sits on shelves for as long as 42 days, the membranes of red blood cells become less able to change shape and squeeze through the smallest capillaries to deliver critical oxygen to tissues.
“Storage Lesion”

What happens to RBCs over 42 days of storage?
“Storage Lesion”

What happens to RBCs over 42 days of storage?

Why your own Hb of 9 is better than a transfused Hb of 9
“Storage Lesion”

What happens to RBCs over 42 days of storage?

Transfused blood may inc. Hb

But does it deliver more $O_2$?
Transfused RBCs, especially during the time period acutely following transfusion, are not “normal.”

Multiple factors may impair oxygen delivery

**Storage of RBCs:**
- Decreases 2,3-diphosphoglycerate levels
- Decreases nitric oxide-Hgb (SNO-Hgb)
- Impairs RBC deformability
- Promotes endothelial adherance
- Increases aggregability (pro-thrombotic effects)

<table>
<thead>
<tr>
<th>Day 1</th>
<th>Day 21</th>
<th>Day 35</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1.jpg" alt="Image" /></td>
<td><img src="image2.jpg" alt="Image" /></td>
<td><img src="image3.jpg" alt="Image" /></td>
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</tbody>
</table>
Decreased Erythrocyte Deformability After Transfusion and the Effects of Erythrocyte Storage Duration


Percent Change in Elongation Index

-30  -25  -20  -15  -10  -5  0

Preop  End  POD 1  POD 2  POD 3

Minimal transfusion

Moderate transfusion

*
Left shift with banked blood (average 21 days storage)
No shift with salvaged blood (Cell Saver)

![Graph showing oxyHb dissociation curves for different types of RBCs]

**Fig. 1.** Comparison of oxyHb dissociation curve plots between fresh, salvage and banked RBCs
Decreased Erythrocyte Deformability After Transfusion and the Effects of Erythrocyte Storage Duration

The Shelf Life of Donor Blood

Red blood cells change in storage, raising questions about efficacy.

By NICHOLAS BAKALAR

How long should blood be stored?

For decades, the Food and Drug Administration has limited storage of refrigerated red blood cells to 42 days. But it has been clear for some time that stored blood degrades in various ways long before that six-week limit, and some research suggests that the changes may be harmful to patients who receive older blood.

Now a study published in the journal Anesthesia & Analgesia has found that after even 21 days, the membranes of stored blood cells have stiffened, apparently the result of damage over time. That’s a problem because red blood cells are about the same diameter as small capillaries, and they have to change shape to get through.

“What we showed is that the cell membranes lose their flexibility,” said the lead author, Dr. Steven M. Frank, an associate professor of medicine at the University of Ottawa and one of the study’s principal investigators. Historically, he said, “the test was whether the cells would survive in a person for 24 hours. That was the benchmark.” As researchers discovered that blood cells survived for longer periods, the storage limit eventually stretched to 42 days. But the effectiveness of stored blood was not fully evaluated.

“It’s as if we tested whether a drug got into your body, but not whether it actually worked,” Dr. Hébert added. “We don’t know whether giving these products old or fresh is just as effective or if both cause harm.”

North Carolina, said that even if the study showed that newer blood was better for seriously ill cardiac patients, it would not mean that all patients needed the freshest blood.

Dr. Richard J. Benjamin, chief medical officer at the Red Cross, said the two trials would provide important information. If older blood turns out to be less effective, he said, “there are a couple of ways we can respond.”

“There are already better storage solutions in development that show drastically improved biochemistry parameters,” he said. “Is the next step to restrict the age of blood for vulnerable populations? That’s possible as well.”

As the system works now, the newest blood goes to hospitals that do transfusions infrequently. This gives them time to store the blood safely until it is needed. But it leaves hospitals that use the most blood — trauma hospitals and academic medical centers — with the older blood. “That would have to change,” Dr. Benjamin said, “and we could have more wastage or..."

Survival

<table>
<thead>
<tr>
<th>Years</th>
<th>Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>100%</td>
</tr>
<tr>
<td>1</td>
<td>95%</td>
</tr>
<tr>
<td>2</td>
<td>90%</td>
</tr>
</tbody>
</table>

*P* < 0.001

**Newer Blood**

**Older Blood**

2519

2251

2029

1820

2136

2278

2392

2521
Thromboelastography-Guided Transfusion Algorithm Reduces Transfusions in Complex Cardiac Surgery

Linda Shore-Lesserson, MD*, Heather E. Manspeizer, MD*, Marietta DePerio, RN*, Sanjeev Francis, BS*, Frances Vela-Cantos, RN*, and M. Arisan Ergin, MD, PhD†

(Anesth Analg 1999;88:312–9)
Ultrafiltration reduces blood transfusions following cardiac surgery: a meta-analysis

Munir Boodhwani\textsuperscript{a}, Kathryn Williams\textsuperscript{b}, Andrew Babaev\textsuperscript{a}, Gurinder Gill\textsuperscript{a}, Nusrat Saleem\textsuperscript{a}, Fraser D. Rubens\textsuperscript{a,*}

Dec. RBC transfusion by 0.73 units ($P = 0.001$)

More pronounced with MUF (modified ultrafiltration)

Dec. postop bleeding as well

We do this for JW patients – why not others

Eur J Cardiothorac Surg, 2006
ICU phlebotomy at Johns Hopkins
Over 1% of blood volume/day (cancels out erythropoiesis)
Cut in half using Safeset blood draw system ($9.45 cost)
Conclusions

• There is general overuse of transfusion
• Transfused blood ≠ your own blood
• Successful blood management includes:
  
  Preop anemia diagnosis and treatment
  Hemostatic surgical techniques
  Cell Salvage (avoids storage lesion)
  Perfusion can drive blood conservation
    ANH, TEG, Ultrafiltration
  Minimize phlebotomy
  Education, audits w/ feedback

• Blood management =
  Reduced Cost, Reduced Risk, Improved Outcome