Blood Wars!
Talking to Your Doctors About Transfusion

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LifeStream Blood Bank
BBGuy.org
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A Look Ahead...

• History and future with Patient Blood Management
• Production of various blood products
• Evidence-based usage guidelines
• Resource conservation
Evidence-based Medicine

• Application of scientific method to medical practice
• Assesses strength of available evidence to predict outcomes
• Has strengths and weaknesses in general, but applies well to transfusion practices
Era of Blood Management

• What is it?
  - A philosophy designed to improve patient outcomes
    ✓ Includes giving transfusions only when necessary
    ✓ Optimize blood use through a variety of strategies
Era of Blood Management

Source: Public Domain
Equivalent?
Here’s Where We’ve Been…

- Decades of anecdotal practice
- “Blood as a drug” model fails completely
  - Evidence for benefit nearly absent
  - Evidence for lack of harm minimal
- As viral detection got better and better…
- Blood component use spiked dramatically in the 1990’s and early 2000’s
Interdisciplinary Blood Conservation Modalities
Managing Anemia
Optimizing Coagulation
Patient-Centered Decision Making

IMPROVED PATIENT OUTCOMES
SABM© 2018

Source: www.sabm.org
When considering improved patient outcomes, the majority of blood transfusions may be inappropriate.³

PBM has significantly reduced...

Transfusions
Mortality
Average LOS
Reoperation
Readmissions
Complications (composite morbidity)
Complications (infections rate)
Costs

Source: SABM Executive Guide for Patient Blood Management Programs 2019
Drivers of PBM

• Evidence-based decision-making
  - Better outcomes
  - Fewer complications

• Economics of modern medicine
  - Every lab’s #1 budget item: Blood products
  - Dramatic stories of massive savings
Battle!
Train Has Left the Station!
Transfusion-transmitted Infections

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<td>HIV-1</td>
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<tr>
<td>HBV</td>
<td>1 in 2,000,000</td>
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<tr>
<td>HCV</td>
<td>1 in 2,000,000</td>
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<tr>
<td>HTLV-1</td>
<td>1 in 3,000,000</td>
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<tr>
<td>HIV-2, WNV</td>
<td>None</td>
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<tr>
<td>Bacteria (plts)</td>
<td>1 in 75,000 (plt)/500K (rbc)</td>
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</tbody>
</table>
FDA Fatalities (2005-15)

- TRALI: 224
- HTR: 121
- TACO: 82
- Microbial: 39
- Anaphylaxis: 21
- Babesia: 14
- TA-GVHD: 2
Donation Types

Whole Blood

Apheresis
Component Indications

Red Blood Cells

Platelets

Plasma
Red Blood Cells

- 5.9 M units/yr as of 2014 (declining)

**Volume:** 350 mL (incl. additive)

**Contents:**
- RBCs (200-250 mL)
- Plasma (< 50 mL)
- WBCs \((10^9)\) and PLTs
- Anticoagulant/preservative
- Additive solution (110 mL)
- 200-250 mg iron
Red Blood Cells

- “Packed cells”, “pRBCs”
- Many manipulations possible

Leukocyte reduce

Rinse
FREEZE
Irradiate
Wash
Why Use?

• Insufficient O₂ delivery due to carrying capacity
  - Acute hemorrhage (>30% of BV)
  - Hemolysis
  - Marrow failure
• Replace malformed RBCs in Sickle Cell Disease
• Exchange coated RBCs in neonates with HDFN

Seems simple, right?
Not So Much!

- Wide variations in practice
  - Cardiac surgery
  - Orthopedic surgery
- Reports suggesting poor outcomes
- “Standard” doses questioned
  - Two units = One “dose” historically
Red Blood Cells

- Tx Rxns
- Post-op Infxn
- TTDs
- Length of Stay
- Cancer recurs

SAVES LIVES!
Red Blood Cells

SAVES LIVES!
Transfusion Trigger

- Single lab measurement?
- Historic:
  - Hemoglobin 10 g/dl
  - Hematocrit 30%
- Passed down for decades
Red Blood Cells

Clinical Practice Guidelines From the AABB
Red Blood Cell Transfusion Thresholds and Storage

Jeffrey L. Carson, MD; Gordon Guyatt, MD; Nancy M. Heddle, MSc; Brenda J. Grossman, MD, MPH; Claudia S. Cohn, MD, PhD; Mark K. Fung, MD, PhD; Terry Gernsheimer, MD; John B. Holcomb, MD; Lewis J. Kaplan, MD; Louis M. Katz, MD; Nikki Peterson, BA; Glenn Ramsey, MD; Sunil V. Rao, MD; John D. Roback, MD, PhD; Aryeh Shander, MD; Aaron A. R. Tobian, MD, PhD

• Recommendation 1:
  - Restrictive transfusion strategy (transfuse at 7 g/dL) in adult, hospitalized, stable patients
  - Use 8 g/dL for cardiac disease history, cardiac surgery, and orthopedic surgery
  - UNCLEAR for acute cardiac syndrome/chronic tx

Source: Carson JL et al, JAMA 2016
Clinical Investigation

Clinical trials evaluating red blood cell transfusion thresholds: An updated systematic review and with additional focus on patients with cardiovascular disease

Critical Care Study ("TRICC")

- Over 800 patients
- Randomized:
  - Liberal (transfuse if Hgb <10 g/dL)
  - Restrictive (transfuse if Hgb <7 g/dL)
- Startling result!
  - Restrictive equally effective, maybe SAFER!
  - Possible exception: Acute cardiac patients

Summary of Evidence

**Primary Outcome**
- **RBCs if Hb fell to ≤ 7.0 g/dL (n = 418)**
  - 18.7% 30-day mortality, P = .11
  - 22.2% in-hospital mortality, P = .05

**Mean Difference of 3.0 Transfused RBC Units**
- **RBCs if Hb fell to ≤ 10.0 g/dL (n = 420)**
  - 23.3% 30-day mortality
  - 28.1% in-hospital mortality

**Absolute Risk Difference**: 5.8%
**Number needed to treat**: 16.9
Orthopedic Study ("FOCUS")

- 2000+ post-op hip fracture patients
- ALL WITH CAD
- Randomized:
  - Liberal (Hgb <10 g/dL)
  - Restrictive (Hgb <8 g/dL)
- 65% fewer RBCs in restrictive group
- Death and walking rates at 60 days equal

Cardiac Disease

• Cardiac surgery:
  - Data is clear: Restrictive strategies are equal
• Acute Cardiac Syndrome/Acute MI:
  - Data is NOT clear
• Chronic Cardiac Disease:
  - Most data points to no difference with liberal vs restrictive strategies
  - Few small studies raise questions
So, What to Do?

- Don’t transfuse more than necessary
  - “Why use 2 when 1 will do?”
- Don’t transfuse RBCs for iron deficiency without hemodynamic instability
- Don’t perform serial blood counts on clinically stable patients
- Utilize evidence-based guidelines

www.choosingwisely.org
Red Blood Cells

Clinical Practice Guidelines From the AABB
Red Blood Cell Transfusion Thresholds and Storage

 Recommendation 2:
- All patients should receive RBC units selected at any point in their licensed dating period (“fresh” units show no added benefit in multiple prospective studies)

Source: Carson JL et al, JAMA 2016
2018 Frankfurt Conference

Patient Blood Management Recommendations From the 2018 Frankfurt Consensus Conference

Markus M. Mueller, MD; Hans Van Remoortel, PhD; Patrick Meybohm, MD, PhD; Kari Aranlo, MD, PhD; Cécile Aubron, MD, PhD; Reinhard Burger, PhD; Jeffrey L. Carson, MD, PhD; Klaus Cichutek, PhD; Emmy De Buck, PhD; Dana Devine, PhD; Dean Ferguson, PhD; Gilles Fofana, MD, PhD; Craig French, MB, BS; Katherine P. Frey, MD; Richard Gammon, MD; Jerrold H. Levy, MD; Michael F. Murphy, MD, MBB; Yves Ozer, MD; Katerina Pavriki, MD; Cynthia So-Okwan, MD, PhD; Pierre Tisseyre, MD, PhD; Jimmy Valerié, MD, PhD; Jonathan H. Waters, MD; Erica M. Wood, MB, BS; Erhard Selfried, MD, PhD; for the ICC-PBM Frankfurt 2018 Group

Key Points

Questions What is the current evidence base for patient blood management (PBM) in adults, and what international clinical recommendations can be derived for preoperative anemia, red blood cell transfusion thresholds, and PBM implementation strategies?

Findings Diagnosis and management of preoperative anemia is crucial, and iron-deficient anemia should be treated with iron supplementation. Red blood cell transfusion thresholds for critically ill, clinically stable patients (hemoglobin concentration <7 g/dL), patients undergoing cardiac surgery (hemoglobin concentration <7.5 g/dL), patients with hip fractures and cardiovascular disease or risk factors (hemoglobin concentration <8 g/dL), and hemodynamically stable patients with acute gastrointestinal bleeding (hemoglobin concentration 7-8 g/dL) are relatively well defined, although the quality of evidence is moderate to low.

Meaning Further high-quality research to support PBM is required for a range of clinical scenarios and implementation of PBM programs.
Platelets: Two Options

Apheresis Platelets

>90%
Multiple products
Limits exposure

Whole Blood Platelets

<10%
Pooled product
Trauma
Platelets

• Whole blood or apheresis procedure
  - US: 85-90% apheresis
  - “Six packs” no longer used!
• Functions:
  - Baseline vascular integrity
  - Foundation of hemostatic response
Typical Conversions

4-6 of these (Whole blood)

One of these (Apheresis)
Platelet Function
Platelets

• “Normal” count: 150-400,000/μl
• Consequences of deficiency
  - Mucocutaneous bleeding
  - Gastrointestinal hemorrhage
  - Catastrophic CNS hemorrhage
Platelets

• History
  - Gaydos LA et al, NEJM 1962
    ✓ No threshold was predictive
    ✓ Increased bleeding < 20,000/μl
  - Confounded by ASA effect
  - 20K “trigger” was taught for decades
Thrombocytopenia

• “Might bleed" vs. “IS bleeding” debate
  - Answered in Heme/Onc (prophylactic helps)
• Increased risks (? higher threshold):
  - Fever
  - Sepsis
  - Thrombocytopenia
  - Splenomegaly?
  - Coagulopathy?
Thrombocytopenia, No Bleed

• Evidence:
  - For patients without risk factors
    ✓ 5000/µl shown safe in many studies
    ✓ 10,000/µl shown safe clearly (*recommended)
    ✓ 20,000/µl with risk factors (fever, sepsis, bleeding)
    ✓ 50,000/µl for surgery
Thrombocytopenia, Bleeding

- Whether or not to transfuse usually not the issue
  - Exception: Uremia patients
- Amount is more critical
- Clinical judgment and evaluation of efficacy needed
No bleeding or risk factors: <10K
Elective CVC placement: <20K
Elective lumbar puncture: <50K
Major non-neuraxial surgery: <50K
No prophylaxis for CPB

Source: Kaufman RM et al, Ann Int Med 2015
Controversial

• Liver biopsy/endoscopy/regional anesthesia?
  - 50K common (sometimes 100K!)
  - Count is not predictive of bleeding
  - Skill of operator IS predictive!
  - Cranial bleed?
    - Data suggesting worse if on anti-PLT
  - Cranial surg/Pulm or eye hemorrhage?
    - No rec; typically 100K used
Frozen Plasma

• Explosive growth in use 1990-2010
• Whole blood-derived
• Apheresis-derived
Fresh Frozen Plasma

Volume: 200-300 mL
Contents: All coagulation factors
>500 mg fibrinogen
1 IU/mL of all others
Lysed RBCs and WBCs
No QC required
Relationship between INR and coagulation factors

60 ml/kg FFP = 4 L ‘fresh’ plasma

1.5 ml/kg FFP

zone of normal hemostasis

zone of anticoagulation

INR 1 1.3 1.7 2.0 2.2 3.0

100 % 50 % 30 %

Slide courtesy Dr. Jeannie Callum
Diminishing Returns With Low INR

Adapted from Holland and Brooks, AJCP 2006
INR 1.1-1.5!

Each unit is about 7% of total PV
Finally! (June 2010)

TRANFSUION PRACTICE

Evidence-based practice guidelines for plasma transfusion


BACKGROUND: There is little systematically derived evidence-based guidance to inform plasma transfusion decisions. To address this issue, the AABB commissioned the development of clinical practice guidelines to help direct appropriate transfusion of plasma.

STUDY DESIGN AND METHODS: A systematic review

ABBREVIATIONS: ACCP = American College of Chest Physicians; CTMC = Clinical Transfusion Medicine Committee; EBM = evidence-based medicine; GRADE = Grading of Recommendations, Assessment, Development, and Evaluation; FP24 = plasma frozen within 24 hours after phlebotomy; PG(s) = practice guideline(s); SR = systematic review.
FFP “Indications”

• Bleeding-operative patients with coagulopathy from multiple factor deficiencies
  - Hepatic failure (avoid prophylaxis)
  - Dilution, consumption
• Bleeding patients needing urgent reversal of warfarin effect
  - 4 factor PCC may be better choice ($$)
A Quick Word on Liver Failure

CLOT

BLEED

PRODUCTION DECLINES
FFP “Indications”

- Trauma massive transfusion
  - 1:1 RBC:FFP ratio
  - PROPPR study published 2015 (no difference in mortality, less exsanguination)
- Transfusion/exchange in TTP
- Factor-specific coagulopathies without a factor concentrate (V, XI)
FFP Contraindications

• Volume expansion
• Heparin reversal
• Specific concentrate available
• Prophylaxis with mild INR elevations
• Nutrition, wound healing, etc.

Don’t transfuse plasma in the absence of active bleeding or significant laboratory evidence of coagulopathy.
Recent Study

Transfusion of fresh-frozen plasma in critically ill patients with a coagulopathy before invasive procedures: a randomized clinical trial

Marcella C. Müller,1 M. Sesmu Arbous,2 Angelique M. Spoelstra-de Man,3 Roel Vink,4 Atilla Karakus,5 Marleen Straat,1 Jan M. Binnekade,1 Evert de Jonge,2 Margreeth B. Vroom,1 and Nicole P. Juffermans1


CVC, thoracentesis, tracheostomy, abscess drainage
FFP vs. no FFP randomization
No Help...

Blood Conservation and Transfusion Alternatives

Paucity of studies to support that abnormal coagulation test results predict bleeding in the setting of invasive procedures: an evidence-based review

Jodi B. Segal and Walter H. Dzik on behalf of the Transfusion Medicine/Hemostasis Clinical Trials Network

TRANSFUSION 2005;45:1413-1425.
No Help…

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<th>Reference/Procedure</th>
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<th>Normal tests n/N</th>
<th>Risk difference</th>
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Fig. 1. Risk differences (and 95 percent CIs) between patients with abnormal and normal coagulation test results.

TRANSFUSION 2005;45:1413-1425.
O Negative Use in U.S.

Fig. 2. Combined distributions from five American-based blood centres for 2010–2015. The 2015 estimate based on Year to date (YTD).
Wise O Negative Use

• Avoid emergency use for males and postmenopausal females
• Determine blood type rapidly in ED
• Avoid use as “universally compatible”
• Avoid use just to avoid expiration
• Keep just what is needed in the hospital
Thanks!

INCONCEIVABLE!