

Blood Utilization/Blood Management SEABB March 18, 2010

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Outline

- 1. Current Data on Blood Utilization in the United States
- 2. Reasons for Blood Utilization/Blood Management
 - Infectious and Non-infectious Complications of Transfusions
 - Quality and Compliance
 - Economic

Outline

- 3. Current Research and Evidence-based guidelines for Blood Transfusions
 - RBCs
 - Platelets
 - Plasma
 - 4. Implementation of effective blood utilization/blood management programs
 - Policy development
 - Education
 - Audits
-

Blood Utilization: Current Data

- Approximately 30 million blood products used annually in U.S.
 - Highest compared to averages in Europe, Australia and Canada.
 - Blood transfusions up 140% from 1997-2007 in U.S.
 - Knee surgeries - up 86%
 - Hemodialysis - up 66%
 - Respiratory intubation and mechanical ventilation - up 48%
 - Percutaneous transluminal coronary angioplasty (PTCA) - up 24%
 - Blood transfusions increased out of proportion.

Blood Utilization

- 10-15% of patients use blood in hospitals
 - 21% in hospitals with 300 or more beds
 - 18.6% of surgical patients
 - 8.1% of medical patients
- 20%-25% of transfusions are associated with cardiac surgery.
- 40% of critically ill patients receive transfusions (5 units, pretransfusion Hgb: 8.5g/dL)
- Hospitals' blood bill nearly doubled between 1999-2007.

Blood Utilization

- Not all blood transfusions are appropriate
- Study at Brigham and Women's Hospital in Boston.
 - ER, OR, PACU orders excluded, used liberal criteria.
 - 73% of transfusion orders inappropriate for all medical staff, 72% for junior house staff.
- Audit of 2 New York City hospitals.
 - 62% of transfusion orders inappropriate.
 - 49% inadequately documented.

Outline

- 1. Current Data on Blood Utilization in the United States
- **2. Reasons for Blood Utilization/Blood Management**
 - Increase Patient Safety: Infectious and Non-infectious Complications of Transfusions
 - Quality and Compliance
 - Economic

Blood Management

- Increase Patient Safety
 - Decrease Transfusion reactions/complications, mistransfusions.
 - Decrease patients exposure to unnecessary transfusions.

Transfusion Reactions

- Infectious Complications
 - HIV 1 and 2
 - NAT, Ab
 - 1 in 2 million residual risk
 - HCV
 - NAT, Ab
 - 1 in 1,800,000 residual risk
 - HBV
 - Ag, Ab
 - 1 in 205,000 to 1 in 488,000 residual risk

Transfusion Reactions

- Infectious Complications
 - HTLV I and II
 - Ab
 - 1 in 3 million residual risk
 - West Nile Virus
 - NAT (MP-NAT, ID-NAT)
 - CMV
 - Ab
 - 2.4% risk with LR (CMV-safe) vs. 1.3% with seronegative components

Transfusion Reactions

- Infectious Complications:
 - T. cruzi (Chagas)
 - Ab
 - T. pallidum (Syphilis)
 - Ab, treponemal, non-treponemal
 - Last reported case in 1996
 - Bacteria
 - Risk of Sepsis ~1:108,000 products transfused.
 - Risk of Fatality:~1:500,000 products transfused.
 - Bacterial testing of platelet products.

Transfusion Reactions

- Infectious Complications: Screen donors with questions only
 - Malaria: 1 in 4 million
 - vCJD: 4 cases in UK
 - Babesiosis:
 - FDA Summary paper
 - 52 possible transmissions 1997-2007
 - 12 fatalities, 9 occurred 2004-2007
- Hepatitis A: <1 in million
- HHV-8: 0.082% per transfused product
- Parvovirus B19: rare cases

Non-infectious Complications

- Acute hemolytic
- Delayed hemolytic: 1 in 1500 transfusions
- Febrile non-hemolytic:
 - 0.1-7.0/100 RBC products (↓50% ps LR)
 - 0.2-30% of all platelets transfusions (↓90% ps LR)
- Anaphylactic: 1 in 20,000-47,000
- Allergic: 0.03-0.61% RBC, 0.3-6.0% platelet, 1-3% plasma
- Transfusion associated volume overload: 1-8%
- Transfusion Related Acute Lung Injury: 0.014-0.08%/product transfused

Non-infectious Complications

- Alloimmunization
- Iron overload: 50-100 transfusions
- T-GVHD: rare, universally fatal
- Post-transfusion Purpura: rare
- Transfusion related immunomodulation
- Transfusion associated microchimerism

Acute Hemolytic

- Mistransfusion: wrong blood to patient
 - 1:14,000 units in US
 - WBIT: 0.1-0.5/1000 samples
 - Lab errors: 30% of mistransfusions
 - Transfusing wrong blood to recipient: 38% of mistransfusions
 - Fatality of 1:500,000 units transfused
 - 47% of ABO-incompatible mistransfusion events have no adverse effect.
- FDA: Mistransfusions account for >2x those due to all infectious hazards combined.

Blood Management

- Quality and Compliance
 - TJC, CAP, AABB, FDA, CMS
 - Transfusion Complications: Starting October 1, 2008 Medicare and other commercial health insurance companies are not paying for transfusion errors.

TJC-Blood Management Performance Measures Project

- 02/07: Phase I: Key stakeholders met, proceed with developing Blood Management Performance Measures: blood conservation, appropriate transfusion, patient-centered focus
- 01/08: Phase II: Identify, develop and test set of standardized measures to assess blood management in hospital setting. Decided on 12 of 19 performance measures.

TJC-Blood Management Performance Measures Project

- 08/09: “Call for hospitals” to participate in alpha testing. Ten measures evaluated in alpha testing
- 12/09: Reviewed alpha results and decided that seven measures move forward with modifications in pilot testing.

TJC- Seven Measures

- 1. RBC Transfusion Indication
- 2. Plasma Transfusion Indication
- 3. Platelet/Prophylactic Platelet Transfusion Indication
- 4. Blood Administration Documentation
- 5. Transfusion Consent
- 6. Preoperative Anemia Screening
- 7. Preoperative Blood Type Screening

TJC: Performance Measures

- 02/10- 07/10: Pilot testing at hospitals
- TAP will meet in late 2010 to review test results and recommend final measure set.

Blood Management- Economic

- Economic
 - Estimated that a single unit of RBCs with an acquisition cost of \$200.00 costs \$1,600.00-2,400.00 to transfuse to a patient.
 - Acquisition costs predicted to rise 5-10%/year
 - Legal costs
 - Inventory Management

Blood Management- Economic

- Cardiac Surgery Patients:
 - If a hospital that performs 300 cardiac procedures a year decreased their average per patient blood use by only one unit they would save \$480,000-\$720,000 per year (\$60,000 in acquisition costs).

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RBC Utilization: TJC

- Blood products/RBCs transfused per DRG.
 - Hospitals can decrease the percentage of patients transfused and blood unit requirements by use of conservation strategies.
- Patients with a pre-transfusion Hgb $>9\text{g/dL}$ that receive >1 unit
- Patients with a pre-transfusion Hgb $>10\text{g/dL}$

RBC Transfusion in Critical Care

- 40% critical care patients receive transfusion, 85% of patients with hospital stay >1 week
- In CRIT studies in U.S. 90% of these transfusions were to treat anemia based on a transfusion trigger
- Studies suggest that anemia increases risk of death after surgery in patients with cardiac disease and in critically ill patients.
- Recent research demonstrates that RBC transfusions may be associated with worse outcomes with little documented efficacy.

RBC in Critical Care: TRICC

- 838 critical patients Hgb <9.0g/dL
 - 323 patients with CV disease
 - 418 Restrictive group
 - Transfused Hgb < 7.0 g/dL
 - Maintained between 7 and 9 g/dL
 - 420 Liberal group
 - Transfused when Hgb <10.0 g/dL
 - Maintained between 10 and 12 g/dL

“A multicenter, randomized, controlled clinical trial of transfusion requirements in critical care” Hebert et. Al, New England Journal of Medicine, February 11, 1999



RBC in Critical Care- TRICC

- Average Hgb and RBC units transfused lower in restrictive group.
- Trend towards decreased 30-day mortality among patients treated with restrictive transfusion strategy.
- No statistically significant differences in all survival measures.
- Use of 7.0 g/dL threshold with maintenance between 7-9g/dL was at least as effective and possibly superior to a liberal transfusion strategy in critically ill patients with normovolemia.
 - Possible exception of patients with active coronary ischemic syndromes.

“A multicenter, randomized, controlled clinical trial of transfusion requirements in critical care” Hebert et. Al, New England Journal of Medicine, February 11, 1999



RBC in Critical Care- European

- Vincent et al study 2002 JAMA: Benefits and risks associated with transfusion in critical care, multicenter, prospective study with 3534 patients.
- Significant association between transfusion and mortality, organ failure, length of stay
 - Patients receiving the most transfusions had highest mortality

RBC in Critical Care- European

- Match patients: propensity scores to adjust for differences in the background characteristics so only estimate the effects of transfusion
 - 516 patients in transfused, 516 in nontransfused groups
 - 22.7% mortality vs. 17.1% mortality
- Impact of blood draws: communication, education, guideline development

RBC in Critical Care- Cardiac

- Rao et. al (2004): Large (24,112) retrospective study, Blood transfusion in the setting of ACS is associated with higher mortality after adjustment for other predictive factors and timing of events.
- Yang et. al (2005): Large (74,271) retrospective study, Blood transfusion in patients with non ST-elevated MI 67% more likely to die and 44% more likely to experience either death or MI than those who were not transfused.

RBC in Critical Care- Cardiac

- Wu et. al (2001): Retrospective study of blood transfusions in elderly patients (78,974) with AMI.
- Blood transfusion is associated with a lower short-term mortality rate among elderly patients with acute myocardial infarction if the hematocrit on admission is 30.0 percent or lower and may be effective in patients with a hematocrit as high as 33.0 percent on admission.

RBC in Cardiac- FOCUS

- The overall goal is to determine whether a more aggressive transfusion strategy in patients with cardiovascular disease undergoing surgery for repair of hip fracture is associated with improved functional recovery and decreased risk of adverse postoperative outcomes.
 - RCT, 47 centers in US and Canada, 2600 patients, >50 y/o
 - Patients with cardiovascular risk factors (DM, HTN, lipidemia, cigarettes) and cardiovascular disease (CHF, CAD) plus hip surgery with post-operative Hgb <10 g/dL within 3 days of surgery.
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RBC in Cardiac- FOCUS

- Randomized to transfusion when symptomatic anemia or Hgb <8.0g/dL vs. transfusion permitted when Hgb <10g/dL.
- No meaningful differences in outcomes that were clinically significant.
 - Risk of postoperative myocardial infarction after surgery
 - Risk of in-hospital postoperative non-infectious morbidity (delirium, stroke, and thromboembolism.)
 - Risk of in-hospital postoperative pneumonia.
 - Risk of composite outcome of 30-day mortality, myocardial infarction, pneumonia, stroke, and thromboembolism.
- Large differences in the amount of blood used.

RBC in Critical Care

- Clinical Practice Guidelines: (12/09) by American College of Critical Care Medicine of the Society of Critical Care Medicine and the Eastern Association for the Surgery of Trauma Practice Management Workgroup.

Recommendations Regarding Indications for RBC Transfusion in the General Critically Ill Pt.

- RBC transfusion is indicated for patients with evidence of hemorrhagic shock.
- RBC transfusion may be indicated for patients with evidence of acute hemorrhage and hemodynamic instability or inadequate oxygen delivery.
- A “restrictive” strategy of RBC transfusion (transfuse when Hb 7 g/dL) is as effective as a “liberal” transfusion strategy (transfusion when Hb 10 g/dL) in critically ill patients with hemodynamically stable anemia, except possibly in patients with acute myocardial ischemia.

Recommendations Regarding Indications for RBC Transfusion in the General Critically Ill Pt.

- The use of only Hb level as a “trigger” for transfusion should be avoided. Decision for RBC transfusion should be based on an individual patient’s intravascular volume status, evidence of shock, duration and extent of anemia, and cardiopulmonary physiologic parameters.
- In the absence of acute hemorrhage RBC, transfusion should be given as single units.

Recommendations Regarding Indications for RBC Transfusion in the General Critically Ill Pt.

- RBC transfusion should not be considered as an absolute method to improve tissue oxygen consumption in critically ill patients.
- RBC transfusion may be beneficial in patients with acute coronary syndromes (ACS) who are anemic (Hb \leq 8 g/dL) on hospital admission.

Recommendations Regarding Indications for RBC Transfusion in the General Critically Ill Pt.

- Consider transfusion if Hb \geq 7 g/dL in critically ill patients requiring mechanical ventilation (MV). There is no benefit of a “liberal” transfusion strategy (transfusion when Hb \geq 10 g/dL) in critically ill patients requiring MV.
- Consider transfusion if Hb \geq 7 g/dL in resuscitated critically ill trauma patients. There is no benefit of a “liberal” transfusion strategy (transfusion when Hb \geq 10 g/dL) in resuscitated critically ill trauma patients.

Platelet Utilization

- Platelet transfusions: 50 years
- Still unclear on platelet threshold for transfusion and what is an appropriate platelet dose for both therapeutic and prophylactic transfusions.
- Studies are ongoing....

Platelet Utilization: TJC

- Patients with pre-transfusion platelet count $\geq 10,000/\mu\text{L}$.
 - In absence of bleeding and fever a threshold of 10,000 platelets/ μL was as safe as 20,000 platelets/ μL to prevent mortality as well as major or severe bleeding events

Platelet Utilization: TJC

- Surgical patients with pre-transfusion platelet count $\geq 50,000/\mu\text{L}$.
 - Major surgery requires platelet count of $50,000\mu/\text{L}$. Unlikely to benefit if platelet count is at least $50,000\ \mu/\text{L}$ and thrombocytopenia is only abnormality.

Platelet Utilization: Trigger

- 255 patients, 16-70 y/o with AML in 21 centers
- 135 patients: Transfused platelet count $<10,000$ or between 10,000-20,000 with fever $>38^{\circ}\text{C}$, active bleeding, invasive procedure
- 120 patients: Transfused platelet count $<20,000$
- Risk of major bleeding during induction chemotherapy with AML was similar in both groups.
- Use of lower threshold decreased platelet use by 21.5%.

“The Threshold for Prophylactic platelet transfusions in Adults with Acute Myeloid Leukemia” Rubella et.al, NEJM 12/25/1997



Platelet Utilization- Trigger

- Numerous studies (Rubella, Heckman, Zumberg, Wandt) demonstrated platelet count of 10,000 could be used for prophylactic trigger
- Problems: did not clearly define what a major or minor bleeding was, bleeding events categorized differently in the studies

Platelet Utilization- Dose

- Tinmouth (2004): Main finding: low dose prophylactic regimen as effective as standard dose in treating hemorrhage.
- Other studies have demonstrated that higher platelet doses decrease number of platelet transfusions, increase interval between transfusions, decreased donor exposure.
- Current trials
 - SToP: randomized controlled trial comparing standard and low-dose strategies for transfusion of platelets to patients with thrombocytopenia, outcome: bleeding events.
 - PLADO: randomized controlled trial comparing different doses of platelets (high, moderate, low) in patients with thrombocytopenia, outcome: bleeding events.

Platelet Administration

- Plateletpheresis: raise platelet count 30,000-50,000
- WBD platelets: raise platelet count 5,000-10,000

American Society of Anesthesiologists Task Force on Perioperative Blood Transfusion Practice and Adjuvant Therapies: Practice Guidelines for perioperative blood transfusion and adjuvant therapies. *Anesthesiology*. 2006;105:198-208.

Transfusion alert indications for the use of red blood cells, platelets, and fresh frozen plasma. National Heart Lung Blood Institute.

<u>Prophylactic</u>	<u>Therapeutic</u>
10,000	<50,000 if acutely bleeding and with a platelet function disorder.
20,000 with fever, sepsis, bleeding	
50,000 Procedure (LP, catheter, liver biopsy, thoracentesis, transbronchial biopsy) Surgery	
100,000 CNS, eye surgery	

Plasma Utilization- TJC

- Patients with pre-transfusion $INR \leq 1.5$ who received plasma.
 - If the PT and PTT are < 1.5 times normal, FFP is rarely needed.
- > 3 million units of plasma transfused in U.S. every year.

Plasma Utilization- Indications

- 1. Active bleeding due to deficiency of multiple coagulation factors, or risk of bleeding due to deficiency of multiple coagulation factors.
- 2. Severe bleeding due to warfarin therapy, or urgent reversal of warfarin effect.
- 3. Massive transfusion with coagulopathic bleeding.
- 4. Bleeding or prophylaxis of bleeding for a known single coagulation factor deficiency for which no concentrate is available.
- 5. Thrombotic thrombocytopenic purpura (Plasma or Plasma, cryoprecipitate reduced).
- 6. Rare specific plasma protein deficiencies for which no concentrate is available.

Plasma Utilization- Indications

- Massive Transfusion (plasma upfront): recent trends in the literature based on retrospective studies advocate using a high plasma to RBC ratio to improve survival.
- DIC: Transfusion of plasma should be reserved for patients with active bleeding or non bleeding patients with abnormal coagulation tests awaiting an invasive procedure.

Plasma Administration

- Substantial portion of plasma transfused to patients with mild coagulation abnormalities.
 - INR <1.85
 - PT <17 seconds
- Study to determine the effect of FFP transfusion on PT and INR.

Plasma Administration

- Prospective audit of all transfusions at Mass. General between 09/02/04 to 06/30/05
 - Recorded any patient that received FFP with pretransfusion PT of 13.1-17 seconds (INR 1.1-1.85)
 - 121 patients
 - Demonstrated that regardless of the number of units transfused or the number of hours after FFP transfusion, FFP resulted in only trivial changes of the PT.

“Effect of FFP transfusion on prothrombin time and bleeding in patients with mild coagulation abnormalities.” Ardel-Wahab et. al, Transfusion 2006;46:1479-1285.



Plasma Administration

- Mild-to-moderate elevations of PT corrected by FFP in almost no patients.
 - Median decrease in PT 0.20 seconds
 - Median decrease in INR 0.07
- Only 15.0 percent of patients achieved 50% normalization of pretransfusion PT (<13.1 seconds).
- No significant correlation between PT-INR value and estimated extent of bleeding (Hgb concentration corrected for RBC administration).

Plasma Administration

- Studied effect of 1 L of plasma on 27 healthy, nonbleeding volunteers anticoagulated with coumadin (INR 1.5-2.0).
 - None experienced full correction of PT.

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Blood Management Programs

- Given the known and hypothetical risks of transfusion, as well as the cost, liability and workload involved with this therapy, there are many reasons to move the basis of transfusion practice in a particular institution away from anecdotal experience and tradition, and toward expert advice and clinical evidence.

Blood Management Programs

- Most difficult but most effective way to reduce transfusions is to have protocols based on evidence-based guidelines- Involves changing physician practice.

Blood Management Programs

- An important factor: Transfusion Committee
 - Key stakeholders
 - Hematology, Transfusion Medicine, Surgery, etc.
 - Developing and implementing transfusion guidelines.
 - Review/Audit of transfusion practices.
- Hospital-based peer review mechanism to ensure appropriate use of blood products requirement by CAP and TJC since 1982.

Blood Management Programs

- Policy Development
 - Indications for transfusions
 - Locally agreed upon guidelines for ordering blood components.
 - “Maximum Surgical Blood Ordering Schedule”
 - C:T ratio
 - Agreed upon method of physician feedback

Blood Management Programs

- Education
 - Little transfusion medicine education in medical school, residency, fellowship.
 - In reviews it has been demonstrated that the identity of the ordering physician and not any feature of the patient, diagnosis or treatment, is the primary predictor of which types and how many units of blood components will be transfused.

Blood Management Programs

- Education
 - Formal CME/CE: either web-based or face-to-face presentations
 - Reminders: posters, indications on ordering forms
 - Computerized decision support system
 - Printed materials
- Printed materials and dissemination of consensus statements: ineffective if alone.
- Targeted, professionally based, face-to-face have been successful.
- Need continuous education with audit and peer review.

Blood Management Programs

- Audit
 - Evaluation of ongoing practice and comparison to “standard”
 - Feedback when deviation from “standard” / “average”
 - Continue to update standard
 - Prospective > retrospective audits
 - Needs to be continuous and ongoing or might have relapse.

Summary

- Given the numerous complications of transfusions, both infectious and non-infectious, the need for stewardship of the blood supply, and for economic and regulatory reasons the decision to transfuse a patient is moving towards more evidence-based indications and guidelines.
- Many studies are ongoing to provide more evidence-based guidelines for transfusion indications and better evidence on the consequences of blood transfusions.

Summary

- Blood management programs, although difficult to implement, may be effective in decreasing unnecessary transfusions.
- Blood management programs may increase patient safety, decrease cost, and improve quality and compliance (TJC).