

PATIENT BLOOD MANAGEMENT / BLOOD CONSERVATION

Aryeh Shander, MD, FCCM, FCCP

Chief, Department of Anesthesiology, Critical Care and Hyperbaric Medicine. Englewood Hospital and Medical Center, Englewood, New Jersey

> Clinical Professor of Anesthesiology, Medicine and Surgery Mount Sinai School of Medicine, New York





Disclosure

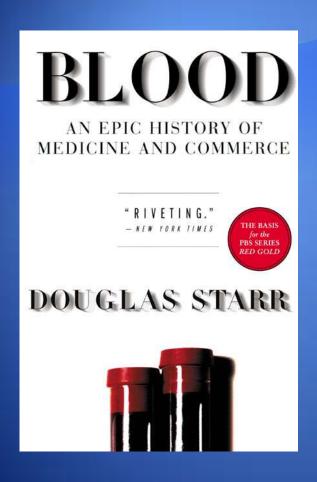
Speakers bureau: Baxter, Zymogenetics, Novartis, CSL, Coviden and Masimo

Grants: Centocor OBI, Zymogenetics, Novartis and Masimo

Consultant: Baxter, Centocor OBI, Novartis, J&J, CSL, AMAG and Vifor



Blood: An Emotional Topic



"...the sweeping story of a substance that has been feared, revered, mythologized, and used in magic and medicine from earliest times — a substance that has become the center of a huge, secretive, and often dangerous worldwide commerce."

—From the publisher's description of the book

Starr D. *Blood: An Epic History of Medicine and Commerce*. New York, NY: HarperCollins Publishers; 2000.

Introduction & objectives

- Issues with blood
- Anemia
- Transfusion
- Patient outcome
- What to do about it

BLOOD TRANSFUSION

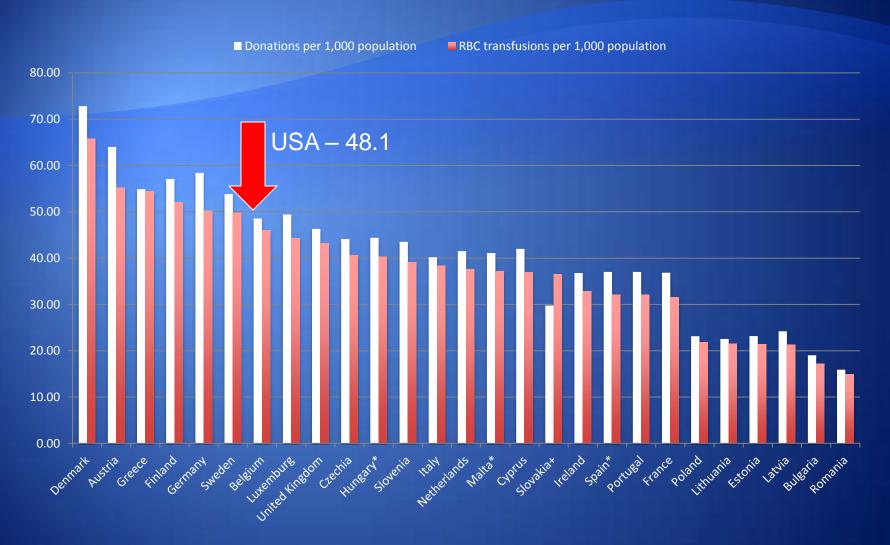
- USDHSS: In 2006, total of 14,650,000 units of RBC/WB transfused in the U.S.
 - 3.3% increase from 2004
 - ~ 20% in cardiac surgery

- AHRQ: in 2007, blood transfusions occurred in 1/10 of all hospital stays that had a procedure
 - A cumulative growth of 140% from 1997
 - One of the fastest growing top-five procedures





Inventory pressure



1. van derPoel, C.L. and M.P. Janssen, Final Report - The collection, testing and use of blood and blood products in Europe in 2002. 2005: Strasbourg. 2. van derPoel, C.L. and M.P. Janssen, Final Report - The collection, testing and use of blood and blood products in Europe in 2003. 2005: Strasbourg. 3. *Rouger P., Blood Transfusion in Europe: The White Book 2005, European Network of Transfusion Medicine Societies

SUPPLY - BLOOD CENTERS

American Red Cross (ARC)^{1,2}

- Responsible for ~45% of US blood supply
- Largest single supplier of US blood supply
- Leader in research and testing
- Implemented the first nationwide hemo- vigilance program
- Protocol development and safer transfusions

American Blood Centers (ABC)^{3,4}

- Conglomerate of smaller blood centers in US and Canada
- 685 donor centers in 45 states
- Responsible for ~55% of US blood supply
- Members represent 77 community-based blood donor centers
- Provide blood products to more than 3500 health care facilities and hospitals

Blood Systems⁵

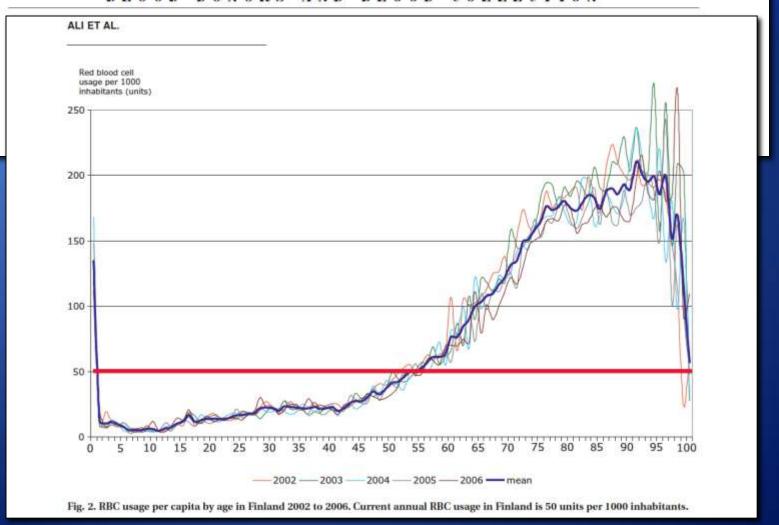
- Represent ~9% of ABC's US share of blood supply³
- Testing divided into laboratories in Arizona and Texas
- Developed UBS
 - Centralized donor testing operation
 - Review and approve SOPs
 - Validate blood product protocol
 - Record quality control records

SOP, standard operating procedure; UBS, United Blood Service.

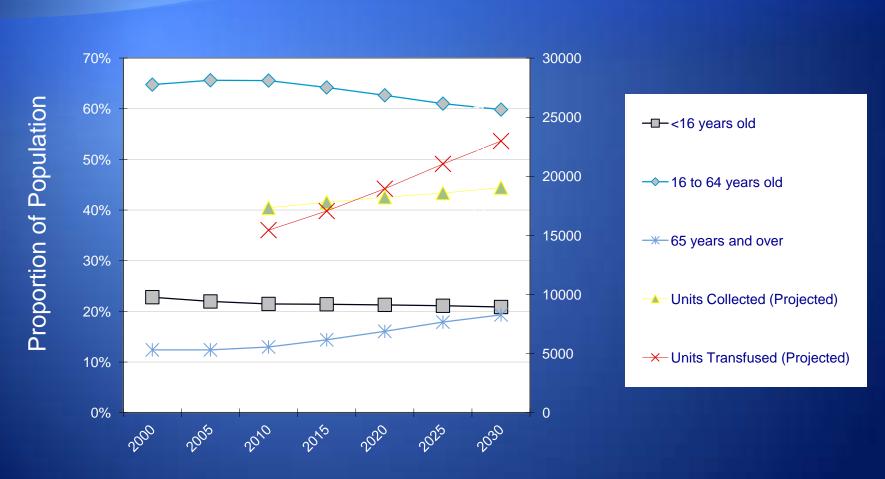
BLOOD DEMAND (Impact of the Ageing Population)

584 TRANSFUSION Volume 50, March 2010

BLOOD DONORS AND BLOOD COLLECTION



Predicted RBC Collections and Transfusions



A CLINICIAN'S PERCEPTIONS

- Safety of BLOOD high
 - Risk of BLOOD low
- Risk of Anemia unknown
- Risk of Surgical Bleeding low
 - Transfusions- rare



TRANSFUSION of Allogeneic Blood

- Past: Considered a therapeutic intervention
- Present/future: A negative outcome

WHY?

TRANSFUSION of Allogeneic Blood

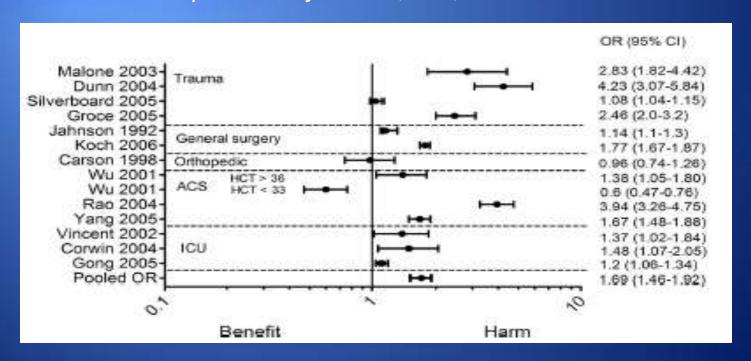
- Transfusion outcome
- Transfusion risks
- Transfusion variability
- Modifiable risk (for transfusion) ignored
- We cannot continue on this journey

Risks and Benefit "Equation"

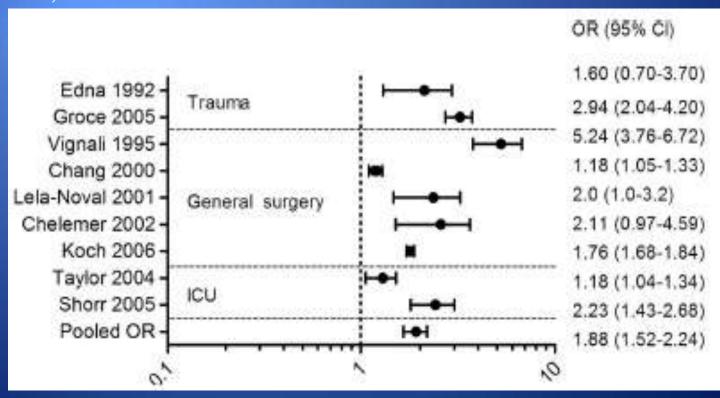
- Variability in transfusion of ALL components
- Immediate risks FDA and blood providers obsession – ZERO R I S K
- Unknown benefit close to 120 years in the dark

- N = 45 articles reviewed
- Outcome measures: Mortality, Infections, MODS, ARDS
- 42 of the 45 studies showed the risks of RBC transfusion outweighed the benefits
- In adult, ICU, trauma, and surgical patients, RBC transfusions are associated with increased morbidity and mortality

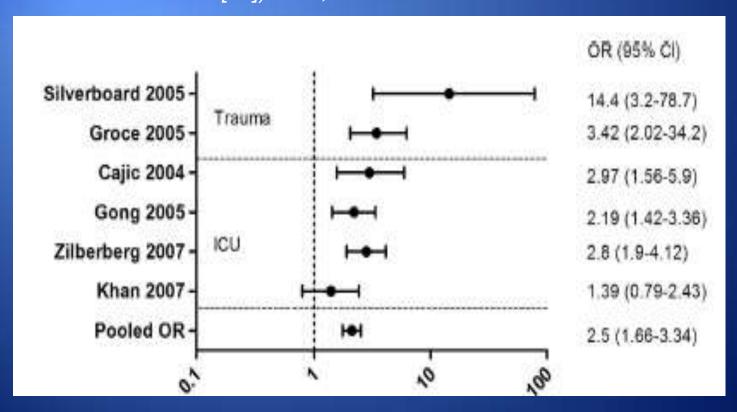
Association between blood transfusion and the risk of death (odds ratio [OR] and 95% confidence interval [CI]). ACS, abdominal compartment syndrome; ICU, intensive care unit



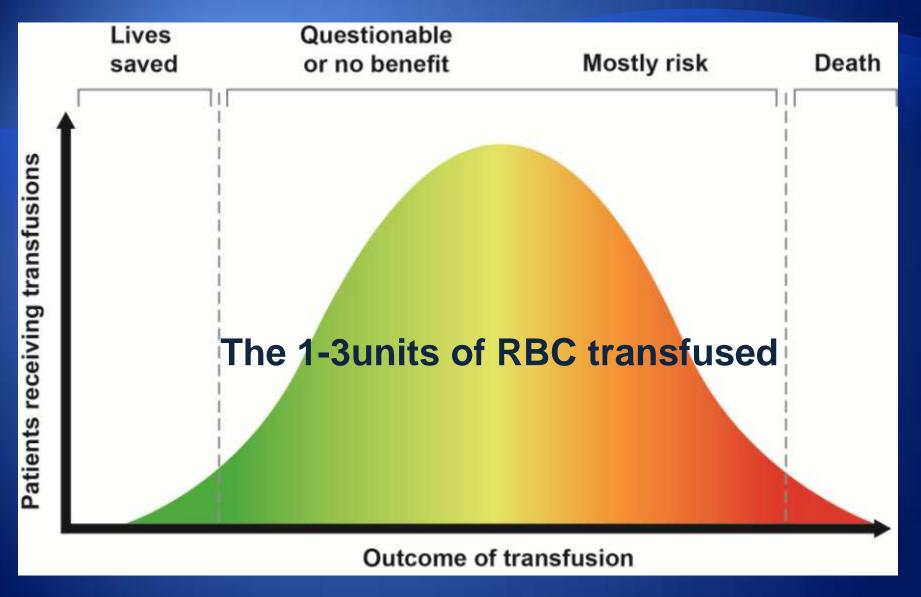
Association between blood transfusion and the risk of infectious complications (odds ratio [OR] and 95% confidence interval [CI]). ICU, intensive care unit



Association between blood transfusion and the risk of developing adult respiratory distress syndrome (odds ratio [OR] and 95% confidence interval [CI]). ICU, intensive care unit



Blood Transfusion: Who is at risk



Side Effects And Hazards For RBC Transfusion

- Acute and delayed hemolytic transfusion reactions
- Transfusion-related acute lung injury (TRALI)
- Administrative errors
- Bacterial contamination
- Storage lesions
- Viral transmission (eg, CMV, HIV, HBV, HCV)
- Alloimmunization
- Volume overload
- Iron overload

The Coming Plague?

"It is sobering to consider that if a new agent with a long silent carrier state and efficient blood transmission (HIV prototype) were to appear, the blood component collectors would be scarcely better prepared to interdict a transfusion transmitted epidemic than they were during the early days of AIDS in 1977."

Klein H. Emerging Infectious Disease and Blood Transfusion TATM 2005;7(1):18



U.S. Department of Health and Human Services



National Institutes of Health

Transfusion Medicine In American Undergraduate Medical Education

- Transfusion is the most common procedure in hospitals
- N = 86 American medical schools surveyed (AAMC)
- 83% administrators reported didactic lectures
- 48% of medical schools providing 1 or 2 hours of lectures
 Handful reported small group sessions on transfusion
 medicine (6%)
- 92% administrators were <u>unfamiliar</u> with the 1989 or the 1995 TMAA curricula.

Transfusion Practice

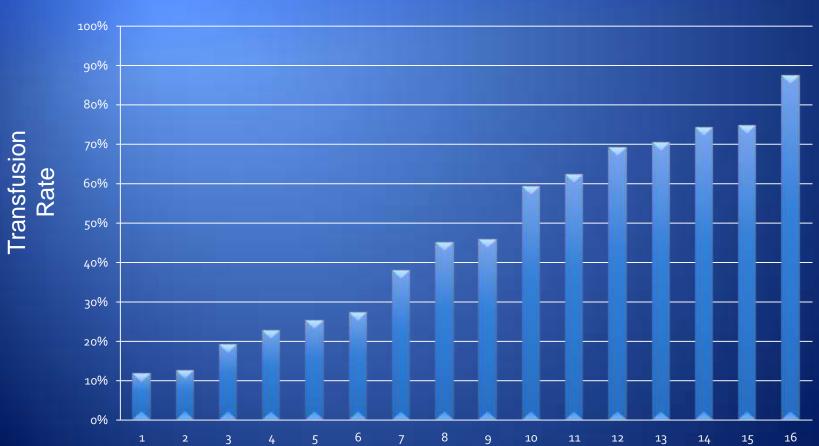
Influence of knowledge and attitudes on the quality of physicians' transfusion practice

- Amount of transfused products was inversely proportional to physician knowledge of transfusion medicine
- Attending MD lower scores, greater confidence than residents
- >60% of residents inappropriate transfusion due attending pressure (once a month)

Variability of Transfusion Rates For Matched Patients

Gombotz H, Rehak P, Shander A, Hofmann A..
Transfusion 2007

TKR – Txn Rate (n=1,401)

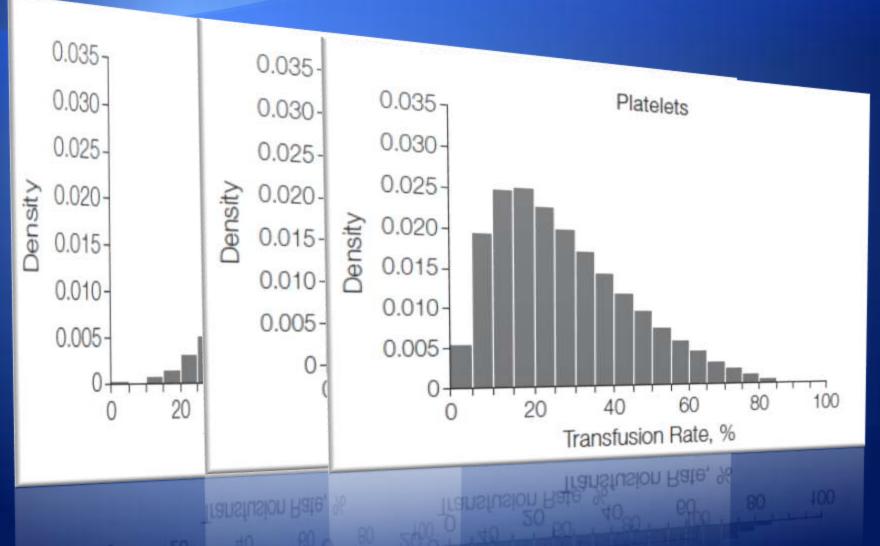


Variation In Use Of Blood Transfusion In CABG Surgery

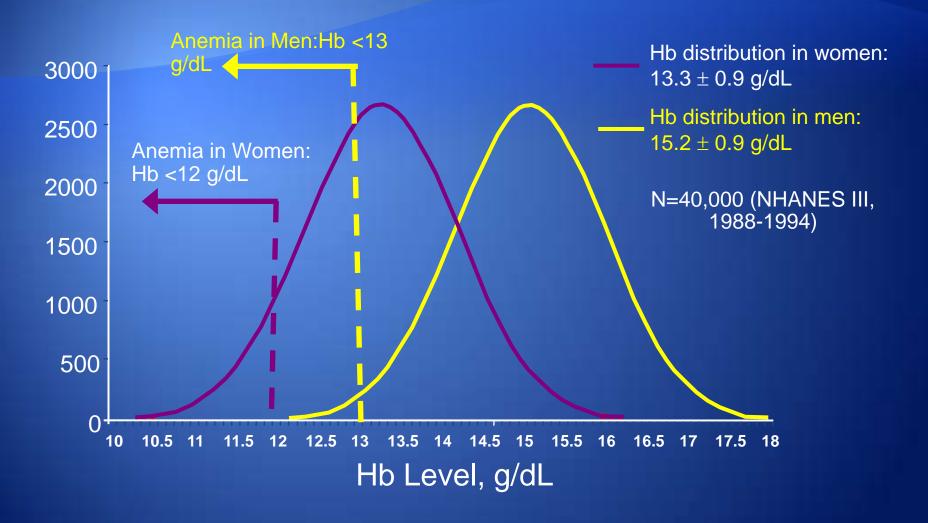
- To assess variation in use of allogeneic red blood cell (RBC), FFP, and platelet transfusions in patients undergoing (CABG) surgery.
- N = 102 470 CABG patients in 2008 at 798 sites in the US (STS Adult Cardiac Surgery Database)
- The rates of transfusions ranged from:
 - 7.8% to 92.8% for RBCs
 - o% to 97.5% for fresh-frozen plasma
 - o.4% to 9o.4% for platelets.
- Multivariable analysis transfusion rates varied by:
 - Geographic location (P=.007), Academic status (P=.03), and Hospital volume (P<.001)
- Wide variability in rates of transfusion of all blood products in CABG operations in US hospitals

Variation in use of blood transfusion in CABG surgery

Bennett-Guerrero E et al. JAMA 2010



WHO Definition of Anemia and Hgb. Distribution in General population



I-b- 1 !bb- ... 0 O- . 4000.0F 74

Anemia Is Often "Accepted" As A Normal Part Of Doing Business

- 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

Anemia: A Potent Multiplier of Mortality

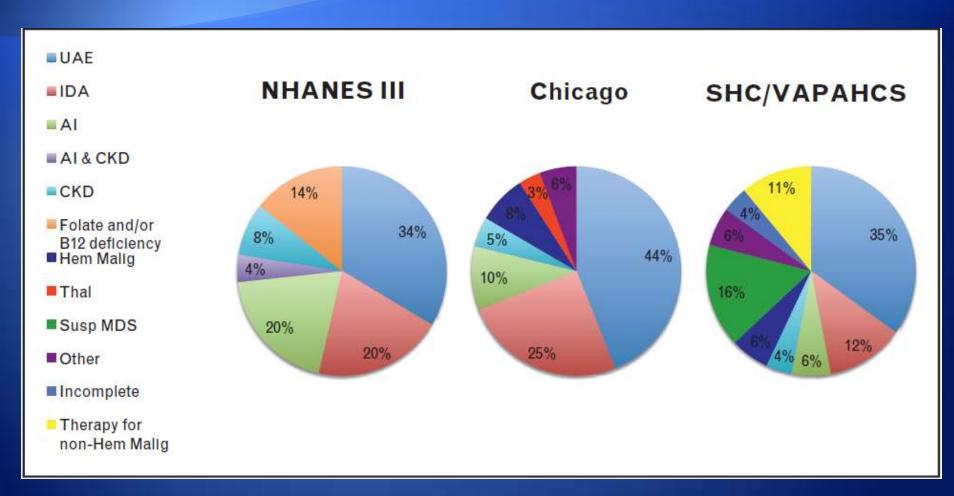


N = 1.1 million (5% Medicare sample, 1996-1997)

Herzog CA, Muster HA, Li S, Collins AJ. Impact of congestive heart failure, chronic kidney disease, and anemia on survival in the Medicare population. J Card Fail 2004; 10:467–472.

ANEMIA IN THE ELDERLY

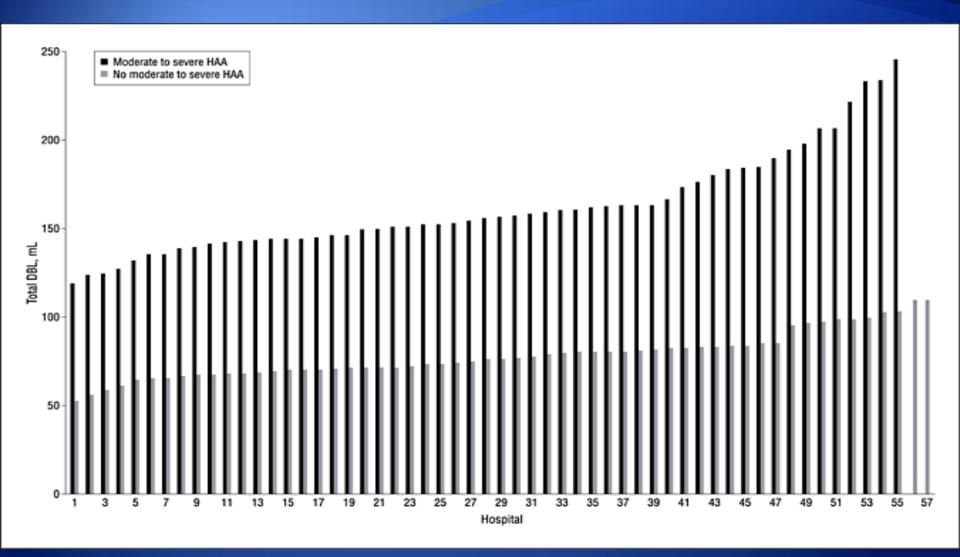
Pang WW et.al



Diagnostic Blood Loss From Phlebotomy and Hospital-Acquired Anemia (HAA) During Acute Myocardial Infarction

- N= 17 676 patients with AMI from 57 US hospitals AMI database (Jan 2000- Dec 2008)
- Moderate to severe HAA developed in 3551 patients (20%).
- The mean (SD) phlebotomy volume was higher:
 - HAA (173.8 [139.3] mL) vs those without HAA (83.5 [52.0 mL]; P < .001)
- There was significant variation in the mean diagnostic blood loss across hospitals
 - For every 50 mL of blood drawn, the risk of moderate to severe HAA increased by 18% (relative risk [RR], 1.18; 95% confidence interval [CI], 1.13-1.22)
- Blood loss from \phlebotomy is independently associated with the development of HAA.

Variation in mean diagnostic blood loss (DBL) across the 57 hospitals



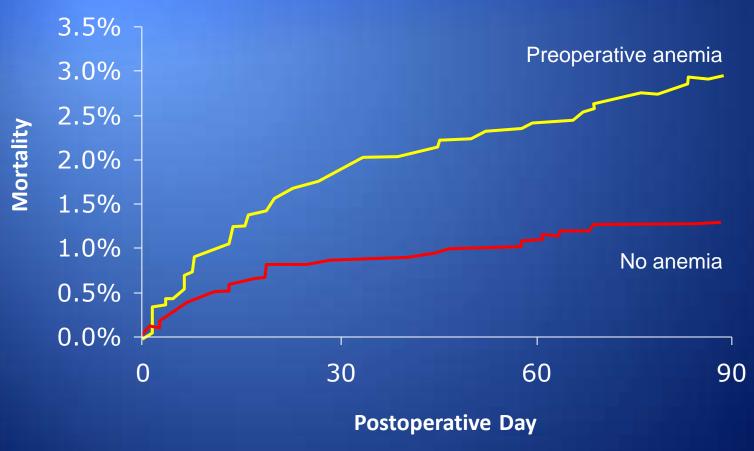
Does Preoperative Anemia Adversely Affect Colon and Rectal Surgery Outcomes?

- 2005-2008 NSQIP (251 hospitals)
- CO MI, CVA, AKI, Mortality and HLOS
- N 23,348 47.4 % Anemic
- Uni, multi, logistic regression and propensity scoring

Anemia	НСТ	N	CO - OR	HLOS
None	(>38%)	12,281	1.0	-
Mild	(30-37%)	9037	1.47	-
Moderate	(26-29%)	1726	1.87	1.2
Severe	(21-25%)	304	2.1	1.6

Preoperative Anemia Is Associated With Postoperative Mortality

N – 7759 2003 – 2006 Hb<12 g/dL for women and <13 g/dL for men



Beattie WS et al. Anesthesiology. 2009;110:574-581.

Association between Intra-operative Blood Transfusion and Mortality and Morbidity in Patients Undergoing Non-Cardiac Surgery

- N= 10,100 patients (general, vascular, or orthopedic surgery)
- Intraoperative blood transfusion associated with an increased risk of death (odds ratio [OR], 1.29; 95% CI, 1.03–1.62)
- Patients receiving one or two units of erythrocytes more likely to have:
 - Pulmonary complications (OR, 1.76; 95% Cl, 1.48 2.09)
 - Sepsis (OR, 1.43; 95% Cl, 1.21–1.68)
 - Thromboembolic complications (OR, 1.77; 95% Cl, 1.32–2.38)
 - Wound complications (OR, 1.87; 95% CI, 1.47–2.37)
- Intraoperative blood transfusion is associated with a higher risk of mortality and morbidity in surgical patients with severe anemia

Impact of Intraoperative Transfusion on 30-Day Mortality and 30-Day Complications

Outcome	Transfusion Group, Outcome Rate %	No Transfusion Group, Outcome Rate (%)	Adj OR Txf <i>vs.</i> No Txf (95% CI)
Mortality	6.44	4.26	1.29 (1.03, 1.62)
Cardiac complications	2.08	1.40	1.40 (0.97, 2.03)
Pulmonary complications	12.6	6.03	1.76 (1.48, 2.09)
Renal complications	2.69	1.85	1.32 (0.93, 1.88)
CNS complications	0.69	0.58	0.84 (0.43, 1.64)
Sepsis complications	16.4	9.81	1.43 (1.21, 1.68)
Wound complications	9.17	4.65	1.87 (1.47, 2.37)
Thrombo-embolic Complications	4.07	1.89	1.77 (1.32, 2.38)

Risk ratios (95% CI) compared with patients receiving no blood products by timing of administration

Outcome	Intra	Within 48 h	After 48 h
	operative	postop	postop
In-hospital	7.71	7.09	10.37
mortality	(4.44–13.38)	(3.95–12.72)	(5.21–20.63)
Acute renal failure	3.98	4.12	10.78
	(2.77–5.74)	(2.82–6.03)	(7.03–16.52)
Sepsis/	3.74	4.11	11.84
DSWI	(1.85–7.57)	(1.99–8.48)	(5.56–25.23)

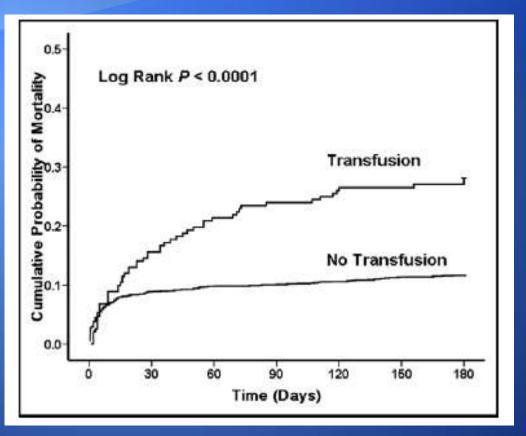
Liberal or Restrictive Transfusion in High-Risk Patients after Hip Surgery FOCUS Trial

- 2016 subjects from 42 Hosp 60% US
- Patients with Hip Fx > 50 y/o ~ 82 y/o
- Randomized to Hb 10 (L) or 8(R) with symptoms
- 1° Death or walk across the room in 60 days
- # 1 reason for Tx in R Tachycardia and Hypotension
- Results show no difference in outcome
- 1. Liberal group received 65% more transfusion

impact of flood Blood Coll Hallordoloff off Climbal

Outcomes in Patients with Acute Myocardial Infarction

Aronson D, Dann EJ, Bonstein L, Blich M, Kapeliovich M, Beyar R, Markiewicz W, Hammerman H.



rospectiv database l=2,358 /ith AMI .1% of atients evd ransfusion

Kaplan- Meier plots showing the crude cumulative incidence of 6-,month mortality among patients who did and those who did not receive RBC

transfusion Am J Cardiol. 2008 Jul 15;102(2):115-9. Epub 2008 May 9

Bleeding and blood transfusion issues in patients with non-ST-segment elevation acute coronary syndromes

Sunil V. Rao1*, John A. Eikelboom2, Christopher B. Granger1, Robert A. Harrington1, Robert M. Califf3, and Jean-Pierre Bassand4

European Heart Journal (2007) 28, 1193–1204



Impact of Blood Transfusion on Short- and Long-Term Mortality in Patients With ST-Segment Elevation Myocardial Infarction

Mehdi H. Shishehbor, Surabhi Madhwal, Vivek Rajagopal, Amy Hsu, Peter Kelly, Hitinder S. Gurm, Samir R. Kapadia, Michael S. Lauer, and Eric J. Topol

J. Am. Coll. Cardiol. Intv. 2009;2;46-53



There Will Be Blood

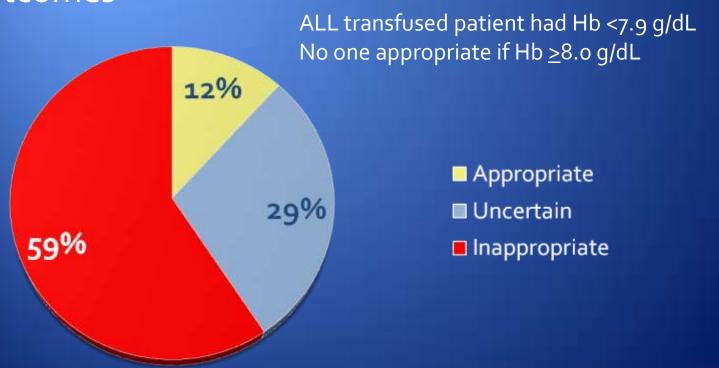
Brendan Doyle

J. Am. Coll. Cardiol. Intv. 2009;2;54-55

For asymptomatic patients, it would seem prudent to avoid the use of arbitrary cutoffs (such as a hemoglobin "8 g/dl) tor trigger transfusion. With minimal potential gain to offset any adverse effects, transfusion could in theory be more likely to cause harm in these circumstances.

ICCTO — International Consensus Conference on Transfusion Outcomes

- > 30,000 citations 494 analysed 450 clinical scenarios
- Appropriateness of ABT based on improving <u>health</u> outcomes

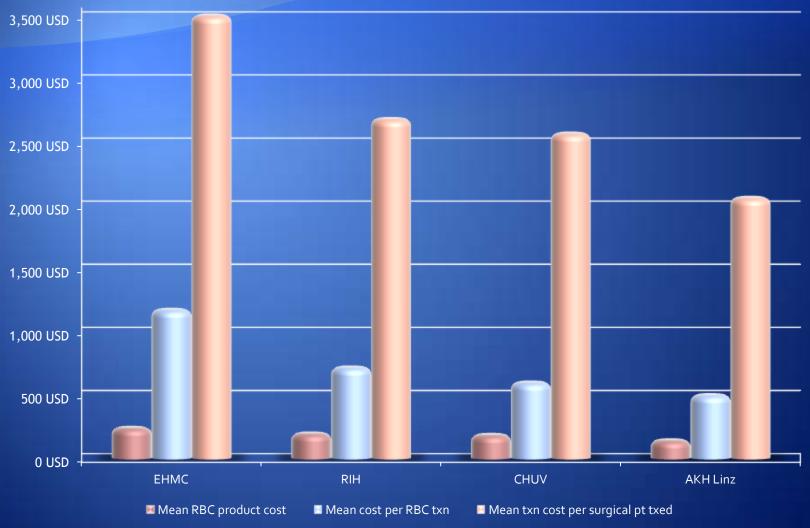


WHY IT MATTERS?

Mean Hospital Amount (\$) Paid per Selected Component Unit in 2006 - 2008

Component	Average Amount Paid (\$)		
	2008	2006	% Change (2006-2008)
Red cells, leukocyte filtered	223.09*	211.50	5.5*
Fresh Frozen Plasma	57.78	100 00 00 00 00 00 00 00 00 00 00 00 00	<u> </u>
Plasma Frozen Within 24 Hours After Phlebotomy	53.85*	52.63	2.3*
Whole-blood-derived platelets, not leukocyte reduced or irradiated	64.98	65.54	-0.9
Apheresis platelets, leukocyte reduced	538.56*	525.05	2.6*
Cryoprecipitate	65.10*	46.67	39.5*
*Significantly different from 2006 data.			

Activity Based Cost of Transfusion

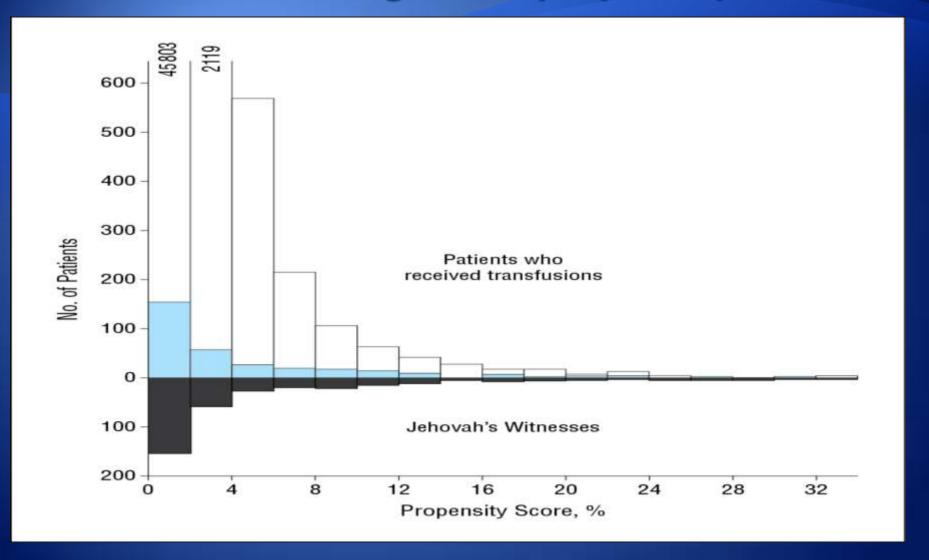


Shander A. et. al. Transfusion 2010

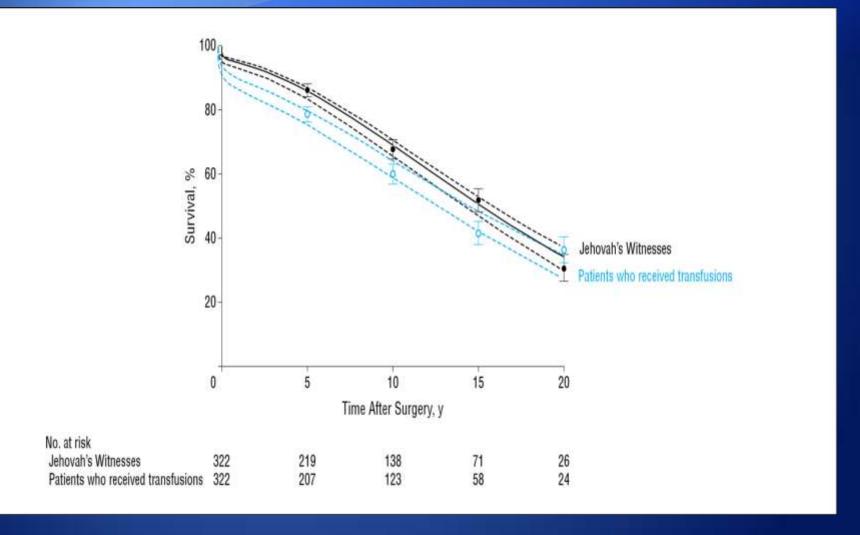
Outcome of Patients Who Refuse Transfusion After Cardiac Surgery

- N= 322 Witnesses and 87 453 non-Witnesses cardiac surgery patients
- Non-Witnesses, 38 467 did not receive blood transfusions and 48 986 did
- Witnesses had fewer acute complications and shorter length of stay than matched transfused patients:
 - myocardial infarction, 0.31% vs 2.8% (P = .01);
 - hospital length of stay (15th, 50th, and 85th percentiles), 5, 7, and 11
 vs 6, 8, and 16 days (P < .001)
 - Witnesses had better 1-year survival (95%; 95% CI, 93%-96%; vs 89%; 95% CI, 87%-90%; P = . 007)
 - Similar 20-year survival (34%; 95% CI, 31%-38%; vs 32% 95% CI, 28%-35%; P = . 90)
- Blood management strategies do not appear to place patients at heightened risk for reduced long-term survival

Mirrored histogram of propensity scores



Survival of matched patients. Error bars indicate Kaplan-Meier estimates at 5, 10, 15, and 20 years after surgery



Is fresh frozen plasma clinically effective? An update of a systematic review of randomised controlled trials

- Primary outcome effect of FFP on survival
- Trials reviewed up to July 2011 (n = 21)
- Trials identified from searches of :
 - MEDLINE, EMBASE, CINAHL, The Cochrane Library, and the UKBTS/SRI Transfusion Evidence Library
- Prophylactic and therapeutic FFP use in:
 - liver disease, cardiac surgery, warfarin anticoagulation reversal, TTP treatment, plasmapheresis
- Results: no significant benefit for FFP use across all the clinical conditions

"New" strategies for the optimal use of platelet transfusions

- Severe thrombocytopenia is presumed to be high risk for bleeding
- Controversy as to the optimal use of platelets (amount and timing)
- Lack of data on different regimens and clinical outcomes
- Platelet Tx strategy needs to be addressed in clinical trials: examples of such trials:
 - The PLADO study (Prophylactic PLAtelet Dose)
 - The SToP study (Strategies for the Transfusion of Platelets)

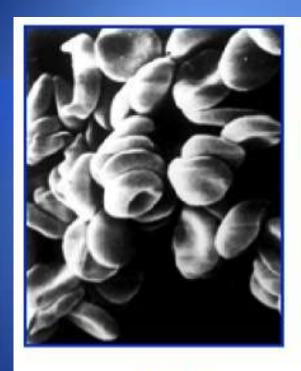
Established Transfusion Risks/Complications – immediate (FDA)

- Acute and delayed hemolytic transfusion reactions
- Transfusion-related acute lung injury (TRALI)
- Administrative errors
- Bacterial contamination
- Storage lesions
- Viral transmission (eg, CMV, HIV, HBV, HCV)
- Alloimmunization
- Volume overload
- Iron overload

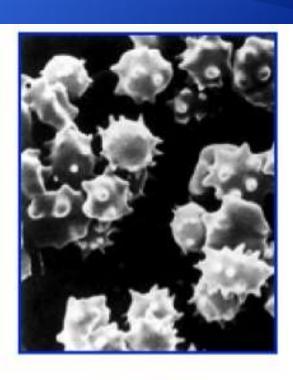
American Association of Blood Banks, America's Blood Centers, and American Red Cross. Available at:

http://www.aabb.org/resources/bct/Documents/coi809r.pdf. Accessed

Morphology of RBCs in Stored Blood







I Day

21 Days

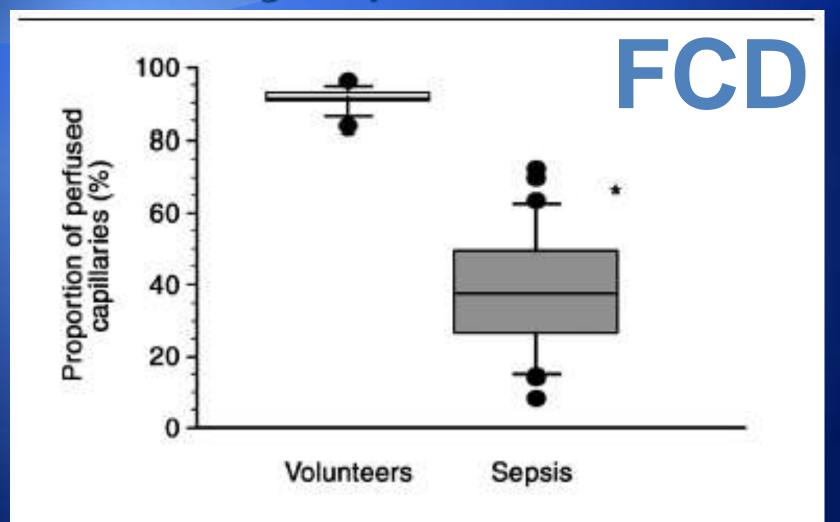
35 Days

Time in Storage

Hb 3.5

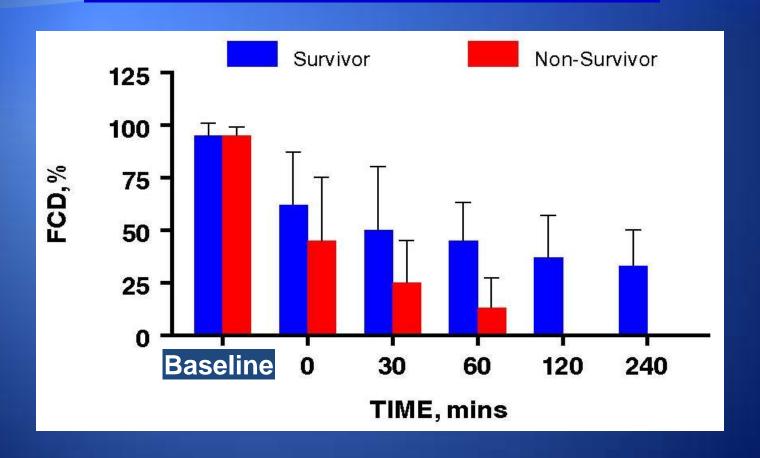


PERFUSION Microvascular Dysfunction as a Cause of Organ Dysfunction

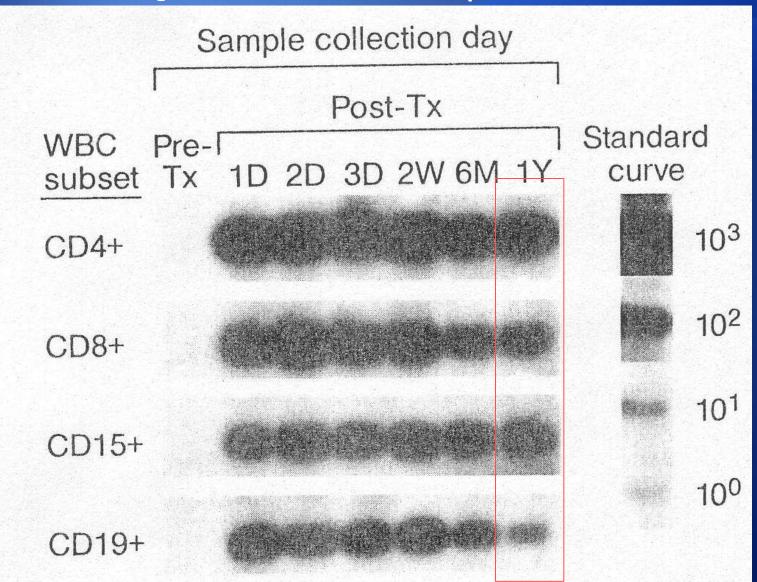


HEMORRHAGIC SHOCK

Functional capillary density predicts survivors vs. non-survivors



Survival of donor WBC in severe trauma patients Quantitative allele-specific PCR

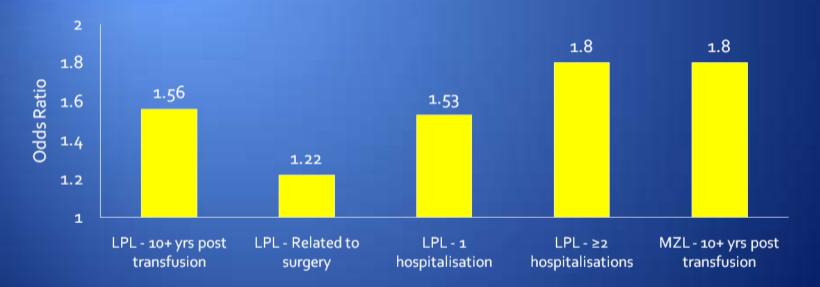


BLOOD TRANSFUSIONS AND THE SUBSEQUENT RISKS – of Hematologic malignancies (HM)

Chang et al. Transfusion 2010; 50: 2249-2257

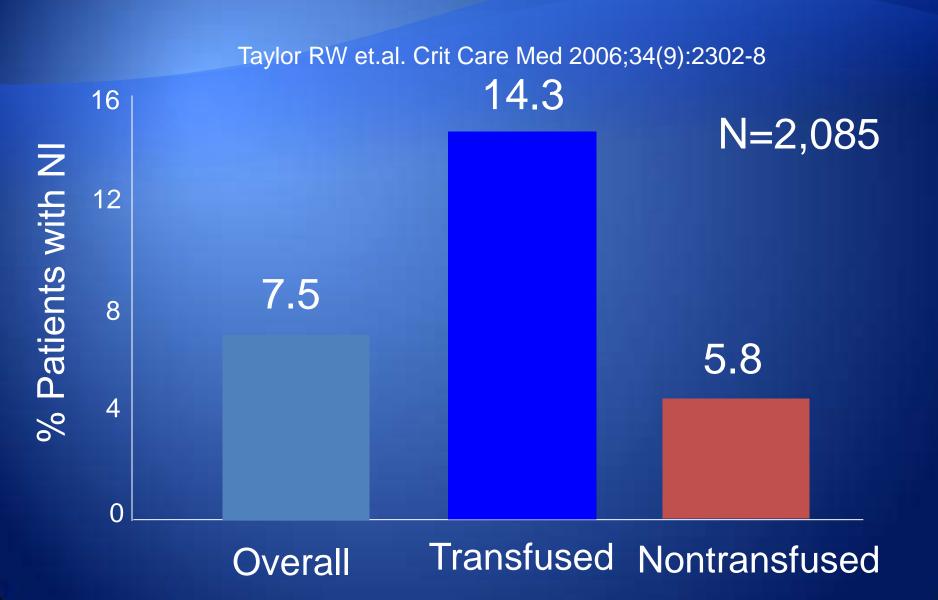
US Case-control study conducted by NCI

- 77,488 elderly HM cases and 154,509 controls
- History of transfusion in 7.9% of HM cases vs. 5.9% of controls



Patterns of elevated risk for lymphoplasmacytic and marginal zone lymphomas suggest an etiologic role for transfusion

Nosocomial Infections in the ICU



Current Solutions

 Guidelines – Hessel EA II. et al. (Anesth Analg. Dec 2010): Guidelines for perioperative blood transfusion and conservation in cardiac surgery: lessons and challenges



- Education
- Blood Management
- Patient Blood Management SABM we have results (see NHA)
- Regulation
- Payment



Red Blood Cell Transfusion: A Clinical Practice Guideline From the AABB

- Guideline to provide recommendations about Hgb concentration thresholds and other clinical variables that "trigger" RBC transfusions
- Systematic review of the literature only RCT (1950 Feb, 2011)
- Examine proportion of patients who received any RBC transfusion and the number of RBC units transfused to describe the effect of restrictive transfusion strategies on RBC use
- To determine the clinical consequences of restrictive transfusion strategies, we examined:
 - overall mortality, nonfatal myocardial infarction, cardiac events, pulmonary edema, stroke, thromboembolism, renal failure, infection, hemorrhage, mental confusion, functional recovery, and length of hospital stay

Recommendations

- Recommendation 1: adhering to a restrictive transfusion strategy (7 to 8 g/dL) in hospitalized, stable patients
 - (Grade: strong recommendation; high-quality evidence)
- Recommendation 2: adhering to a restrictive strategy in hospitalized patients with preexisting cardiovascular disease and considering transfusion for patients with symptoms or a hemoglobin level of 8 g/dL or less
 - (Grade: weak recommendation; moderate-quality evidence)
- Recommendation 3: cannot recommend for or against a liberal or restrictive transfusion threshold for hospitalized, hemodynamically stable patients with the acute coronary syndrome
 - (Grade: uncertain recommendation; very low-quality evidence)
- Recommendation 4: suggests that transfusion decisions be influenced by symptoms as well as hemoglobin concentration
 - (Grade: weak recommendation; low-quality evidence).

Effect of the perioperative blood transfusion and blood conservation in cardiac surgery clinical practice guidelines of the Society of Thoracic Surgeons and the Society of Cardiovascular Anesthesiologists upon clinical practices

- 1402 surveys from 1061 institutions United States (677 institutions) and Canada (34 institutions) [32% response rate]
- 78% of anesthesiologists and 67% of perfusionists reporting having read all, part, or a summary of the Guidelines.
- 26% of respondents reported 1 or more practice changes in response to the Guidelines
- Only 4 of 38 Guideline recommendations were reported by >5% of respondents to have been changed in response to the Guidelines
- Little change in clinical practices was attributed to the STS/SCA Guidelines

Blood Management

> Donor Blood Management

Patient Blood Management

Transfusion

Patient blood management

"Is the timely application of evidence based medical and surgical concepts designed to manage anaemia, optimise haemostasis, and minimise blood loss and blood transfusion in order to improve patient outcomes."

A multimodality approach

SABM – Administrative And Clinical Standards For Patient Blood Management Programs

Administrative and Clinical Standards

for Patient Blood Management Programs



OF BLOOD MANAGEMENT

WWW.SABM.org

Transplante Adjustment of Black Management Inc.

Principles of Patient Blood Management

- 94% of transfusions in surgical patients can be attributed to:
 - low preoperative hemoglobin levels, excessive surgical blood loss, and/or inappropriate transfusion practices
- PBM relies on 3 pillars:
- (1) optimizing hematopoiesis
- (2) minimizing bleeding and blood loss
 - (3) harnessing and optimizing physiological

The impact of blood conservation on outcomes in cardiac surgery: is it safe and effective?

PBM strategies used:

- Pre-op hemoglobin optimization
- Intra-op ANH
- Autologous transfusion (cell salvage)
- Meticulous surgical technique
- Endovascular vein harvesting
- Point-of-care coagulation testing
- Targeted pharmacotherapy
- Tolerance of peri-operative anemia (60–70 g/L depending on patient-specific physiology)

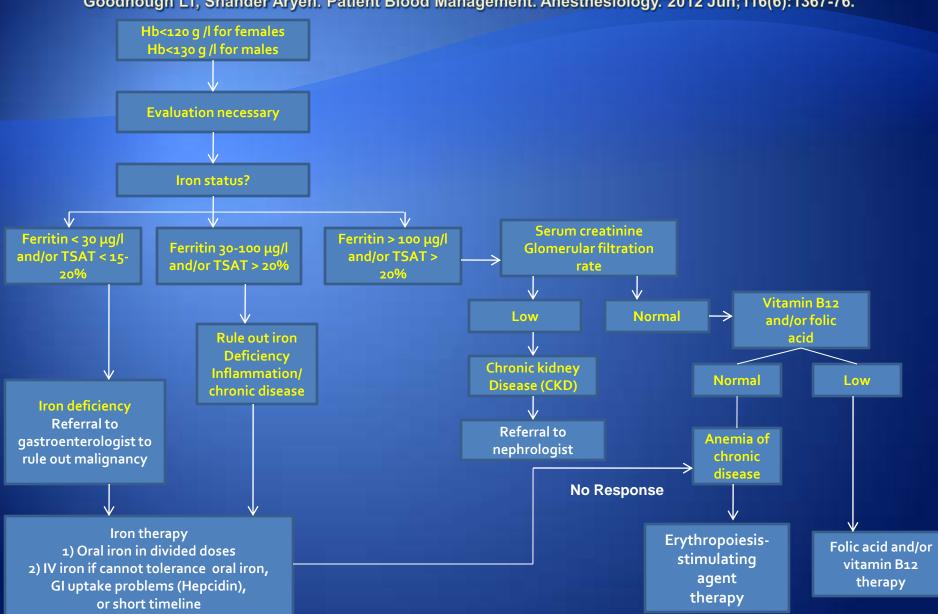
Prin 2

Prin 3

Prin 2

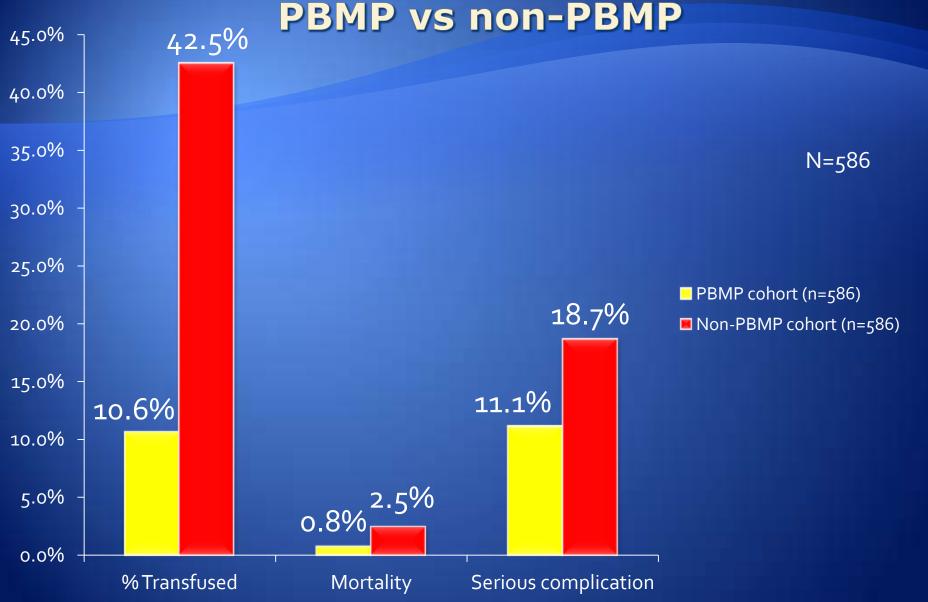
Algorithm For The Detection, Evaluation, And Management Of **Preoperative Anemia**

Goodnough LT, Shander Aryeh. Patient Blood Management. Anesthesiology. 2012 Jun;116(6):1367-76.





CABG outcomes PBMP vs non-PBMP





Executive Board: 126th Session: Provisional Agenda Item 4.16 EB 126/19 Add.1 26th November 2009 Bearing in mind that patient blood management means that before surgery every reasonable measure should be taken to Optimize the patient's own blood volume, to minimize the patient's Blood loss and to harness and optimize the patient-specific physiological Tolerance of anemia following the WHO's guide for optimal clinical use (three pillars of Patient Blood Management)



DHHS Selected Recommendation on PBM:

- Wide variability in transfusion indicated both excessive and inappropriate use of blood transfusion in the U.S.
- PBM programs have shown a significant reduction in blood use without an increase in patient harm

TJC - National Patient Safety Goal (NPSG) overuse of treatments, procedures and tests for the hospital

- Consequences of overuse: tests, treatments and procedures
- Overuse may be defined as:
 - "The use of a health service in circumstances where the likelihood of benefit is negligible and, therefore, the patient faces only the risk of harm."
- The focus is to identify and eliminate overuse
- NPSG provides for incremental implementation and an evaluation of the effectiveness

SUMMARY

- Transfusion not a science
- No demonstration of benefit = all risk!
- Directed therapy RBC, FFP, Platelets and fluid
- Guidelines From Hgb. alone to symptoms
- Reduce or eliminate "overuse"
- Emerging data support that:
- PBM is safe and effective in providing better care and improving patients' outcomes while reducing transfusion of allogeneic blood components

Despite the cost of living, EVEN WHEN APPROPRIATE, TRANSFUSIONIS PREVENTABLE

THANK YOU

2012 ANNUAL MEETING

Society for the Advancement of Blood Management

September 20-22, 2012

SOLDIERS AND SAILORS HALL • PITTSBURGH, PA

