



# Blood Management and Conservation in the Cardiac Patient

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## Why Blood Management is Vital



Blood transfusion remains a precious resource that saves lives

Emerging evidence is redefining blood's narrow therapeutic window

Blood transfusion is an inherently hazardous process that causes measurable harm with every exposure

Stored blood is an imperfect substitute  
Blood is a liquid transplant



## Issues Regarding RBC Transfusion Risks



- I. RBC transfusion is associated with **increased nosocomial infection (wound infection, pneumonia, sepsis) rates independent of other factors. (Level 2)**
- II. RBC transfusion is an independent risk factor for **MOF and SIRS. (Level 2)**
- III. RBC transfusions are independently associated with longer ICU and hospital length of stay, increased complications, and increased mortality. (Level 2)
- IV. There is a relationship between transfusion and **ALI and ARDS. (Level 2)**

Crit Care Med 2009 Vol. 37, No. 12:Journal of Trauma-Injury Infection & Critical Care. 67(6): 1439-1442; Dec 2009

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

Colleen Gorman Koch, MD, MS  
Delos M. Cosgrove, MD, FRCPC

**Objective:** Our objective was to evaluate the association between transfusion of packed red blood cells and morbidity after coronary artery bypass grafting.

**Setting:** This investigation took place in a tertiary care referral center.

**Patients:** A total of 11,963 patients who underwent isolated coronary artery bypass grafting from 1995 to 2002.

**Measurements and Main Results:** Among patients who underwent isolated coronary artery bypass grafting, 48.6% were transfused. Risk-adjusted in-hospital mortality and morbidity were significantly higher in transfused patients. Transfusion of red blood cells was associated with increased mortality and morbidity.

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

Colleen Gorman Koch, MD, MS, Farah Khandwala, MS, Liang Li, PhD, Fawzy G. Estafanous, MD, Floyd D. Loop, MD, and Eugene H. Blackstone, MD  
Departments of Cardiothoracic Anesthesia, Quantitative Health Sciences, and Thoracic and Cardiovascular Surgery, and Division of Anesthesia and Critical Care, The Cleveland Clinic Foundation, Cleveland, Ohio

**Background:** Perfusion has been associated with outcomes, but risk has been associated with morbidity, mortality, and cost. The influence of PRBC on long-term survival after bypass grafting after cardiac surgery has not been previously explored. Our objective was to investigate the relationship between perioperative red blood cell and component transfusion and functional health-related quality of life 6 to 12 months after cardiac surgery.

### Persistent Effect of Red Cell Transfusion on Health-Related Quality of Life After Cardiac Surgery

Colleen Gorman Koch, MD, MS, Farah Khandwala, MS, Liang Li, PhD, Fawzy G. Estafanous, MD, Floyd D. Loop, MD, and Eugene H. Blackstone, MD  
Departments of Cardiothoracic Anesthesia, Quantitative Health Sciences, and Thoracic and Cardiovascular Surgery, and Division of Anesthesia and Critical Care, The Cleveland Clinic Foundation, Cleveland, Ohio

**Background:** Although red blood cell transfusion has been associated with an increase in early morbid outcomes and reduced long-term survival after cardiac surgery, its relationship to functional quality of life after surgery has not been previously explored. Our objective was to investigate the relationship between perioperative red blood cell and component transfusion and functional health-related quality of life 6 to 12 months after cardiac surgery.

**Methods:** Of 12,536 patients undergoing cardiac surgical procedures between May 1995 and January 1999, 7,221 completed a self-administered Duke Activity Status Index (DASI) survey preoperatively and least one follow-up survey at nominally 6 or 12 months postoperatively. The influence of baseline DASI, preoperative risk factors, clinical status, laboratory values, operative events, and postoperative morbidities on follow-up DASI were examined with ordinal regression modeling.

**Results:** After adjustment for preoperative DASI, demographic, cardiac and noncardiac comorbidity, type of surgery, postoperative complications, and interval between follow-up DASI, during which patients continued to improve ( $p < 0.0001$ ), postoperative functional status after cardiac surgery was incrementally worse the more perioperative red cells ( $p < 0.0001$ ) and platelets ( $p = 0.02$ ) that had been transfused.

**Conclusions:** Red blood cell and platelet transfusion have an unintended persistently negative risk-adjusted effect on health-related quality of life after cardiac surgery that extends well beyond initial hospitalization. Reductions in functional recovery paralleled increasing units of red blood cells transfused.

(Ann Thorac Surg 2006;82:13-20)  
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- Series of studies by cardiac surgery team Cleveland Clinic Foundation, transfusion & adverse outcomes
  - Observational cohort, data collected prospectively
1. In-hospital mortality & morbidity in CABG (n= 11,963)
  2. Long-term (up to 10 years) survival in CABG (n=10,289)
  3. Postoperative (6 to 12 mths) functional recovery in CABG, VR, CABG + VR (n=7,321)

Crit Care Med 2006; 34:1608–1616

### 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

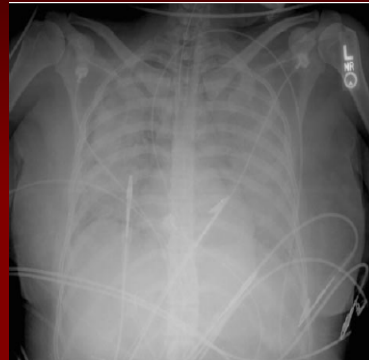
1. **In-hospital mortality & morbidity in CABG (n= 11,963)**
  - **48.6% transfused**
  - **Adjusted for variables known to contribute to sicker patient profile**
  - **Mortality:**
    - **Dose-dependent relationship between each RBC unit txd and adjusted odds for postop mortality**
    - **Receiving 1 unit RBC had a 77% increased adjusted odds for postop mortality, escalated rapidly after 5 units**
  - **Morbidity:**
    - **RBC txn associated with risk-adjusted increased risk for every postoperative morbid event (renal failure, prolonged ventilatory support, serious infection, cardiac complications, neurologic events)**

## Transfusion- Related Acute Lung Injury (TRALI)



### TRALI is the leading cause of transfusion related mortality!

- Unexplained acute lung injury within 6 hours of a transfusion<sup>1</sup>
  - SOB, dyspnea, hypoxemia
- HLA antibody reaction or as a result of a “2 Hit” phenomena
- Incidence 1:1000- 1:5000 transfusions
  - FFP high risk
  - Estimated 300-500 U.S. deaths/ year
    - › Likely underestimated
- Treatment – supportive (O2 and vent)



<sup>1</sup> Toy- CritCareMed 2005;33(4)

## Transfusion Related Immunomodulation (TRIM)<sup>1</sup>



### Allogeneic transfusions cause dose- dependent alterations in immune system function

- Immune system “overload” leads to adverse effects (downregulation)
- Statistical increase in the incidence of infection rates have been shown in the following patient populations:
  - Critical Care – VAP<sup>3</sup> and line sepsis<sup>3</sup>
  - Cardiac/Ortho Surgery - postop infections
  - Oncology - increased cancer recurrence in some studies

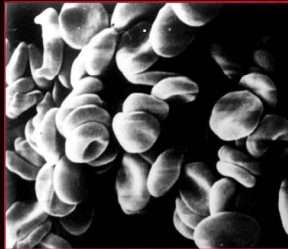


<sup>1</sup> Blumberg- Transfusion 2005;45(S)

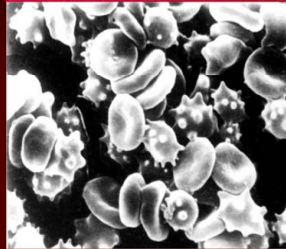
<sup>2</sup> Trulzi- Transfusion 1992;32

<sup>3</sup> Shorr-CritCareMed 2004;32(3)

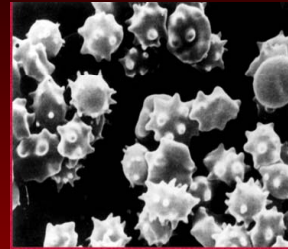
## Stored allogeneic blood is an imperfect substitute for endogenous hemoglobin!



Day 1



Day 21

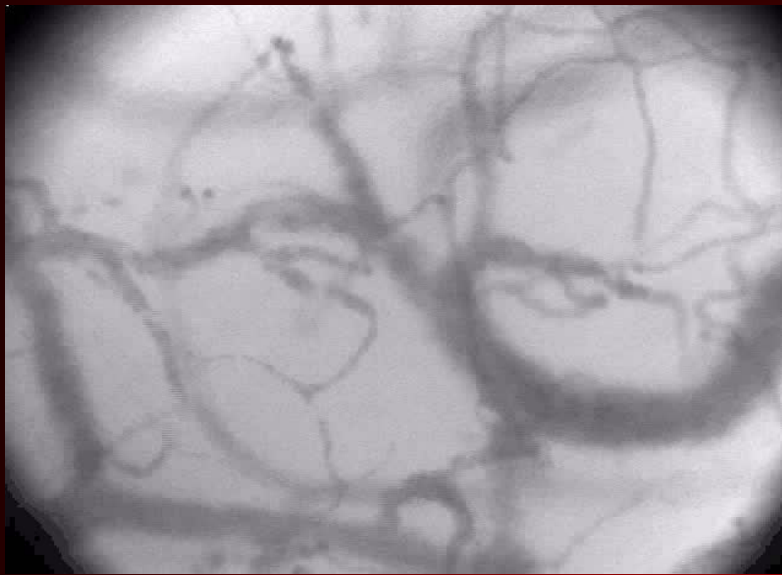


Day 35

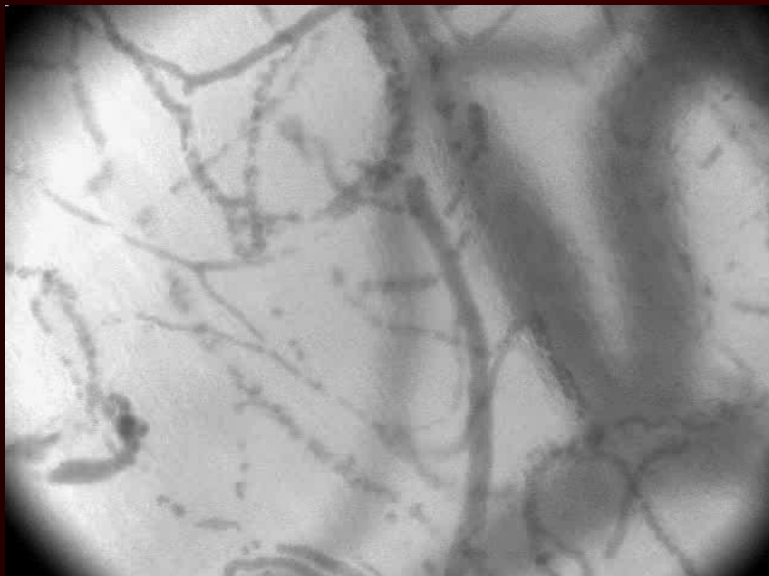
- Scanning electron micrographs of RBCs isolated from stored blood on Day 1, Day 21 and Day 35
- During storage, the shape of RBCs changed gradually from normal discoid to echinocytes (dented or shriveled red cells)

Reproduced with permission from Hovav et al. Transfusion, 1999;39:277-281.

## Pre-transfusion Cytoscan



# Post-Transfusion Cytoscan



"C'mon, c'mon—it's either one or the other."

*Spiess, CritCareMed 2005;33(8)*



## Do Transfusions Improve Outcomes in Anemic Patients?

*"You can't solve a problem with the same mind that created it."*  
Albert Einstein

### A multicenter, randomized controlled clinical trial of transfusion requirements in critical care<sup>1</sup>



- Prospective, randomized multicenter Canadian study with 838 critically ill ICU patients
- Liberal transfusion strategy (Hb 10.0 g/dL) vs restrictive strategy (Hb 7.0 g/dL)
  - Restrictive transfusion group had a mean Hgb of 8.5 and received 2.6 +/- 4.1 units
  - Liberal transfusion group mean Hgb 10.7 and received 5.6 +/- 5.3 units



<sup>1</sup> Hébert et al- NEJM 1999;340(6)

## A multicenter, randomized controlled clinical trial of transfusion requirements in critical care<sup>1</sup>



- Overall, the adjusted multi-organ dysfunction score and in-hospital mortality were significantly higher in the *liberal* transfusion group than in the restrictive transfusion group
- No sub-group of these critically ill patients demonstrated an added benefit of higher Hgb levels, and most patients in the liberal transfusion group had worse outcomes.

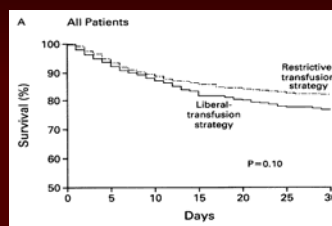
	<u>Restrictive (%)</u>	<u>Liberal (%)</u>	<u>p</u>
MI	0.7	2.9	0.02*
Pulm edema	5.3	10.7	<0.01*
ARDS	7.7	11.4	0.06
Angina	1.2	2.1	0.28
Infections	10.0	11.4	0.38

<sup>1</sup> Hébert et al- NEJM 1999;340(6)

## A multicenter, randomized controlled clinical trial of transfusion requirements in critical care<sup>1</sup>



### Mortality



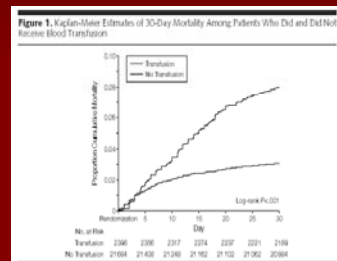
	<u>Restrictive (%)</u>	<u>Liberal (%)</u>	<u>p</u>
All patients	18.7	23.3	0.10
Death (in hospital)	22.2	28.1	0.05*
APACHE ≤20	8.7	16.1	0.03*
<55yo	5.7	13.0	0.02*
Cardiac Dx	20.5	22.9	0.69
Severe inf/ sepsis	22.8	29.7	0.36

<sup>1</sup> Hébert et al- NEJM 1999;340(6)

## Relationship of blood transfusion and clinical outcomes in pts with ACS<sup>1</sup>



- Retrospective review of 24,112 patients with acute coronary syndromes (ACS)
- Multivariate analysis and propensity scoring was used to adjust for confounding factors
- Adjusted probability of mortality with transfusion as an independent predictor for patients with ACS was - OR 3.94
- Landmark analysis showed predicted probability of 30 day mortality increased with transfusion above HCT 25%



<sup>1</sup> Rao et al- JAMA 2004;292(13)

## Relationship of blood transfusion and clinical outcomes in pts with ACS<sup>1</sup>



*“Blood transfusion in the setting of acute coronary syndromes is associated with higher mortality, and this association persists after adjustment for other predictive factors and timing of events.”*

*“We suggest caution regarding the routine use of blood transfusion to maintain arbitrary hematocrit levels in stable patients with ischemic heart disease.”*



<sup>1</sup> Rao et al- JAMA 2004;292(13)

# Transfusion and the Heart



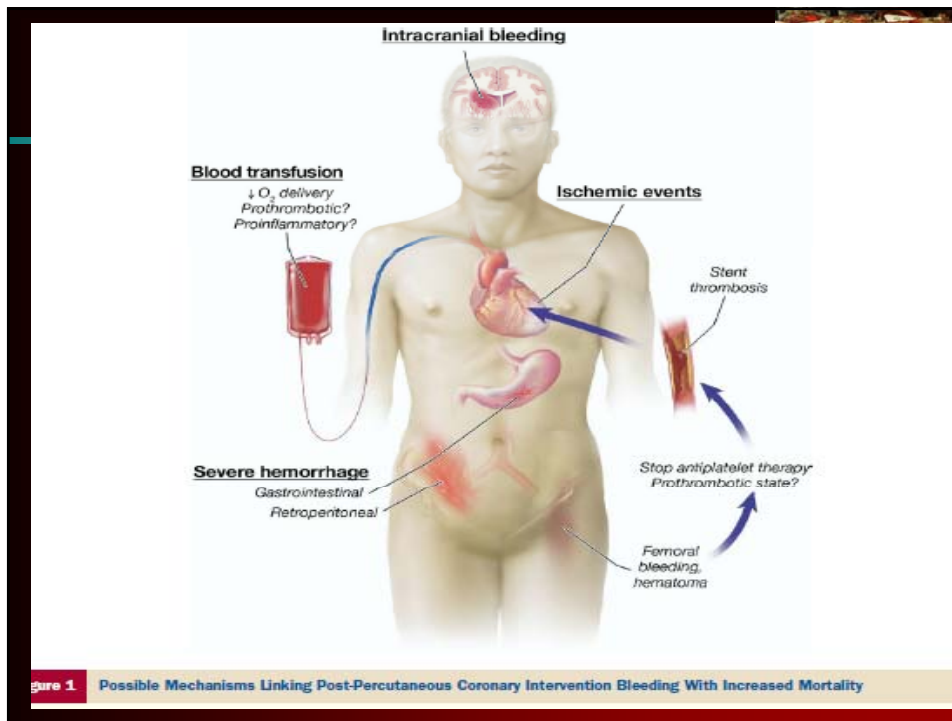
## Bleeding, Blood Transfusion, and Increased Mortality After Percutaneous Coronary Intervention

### Implications for Contemporary Practice

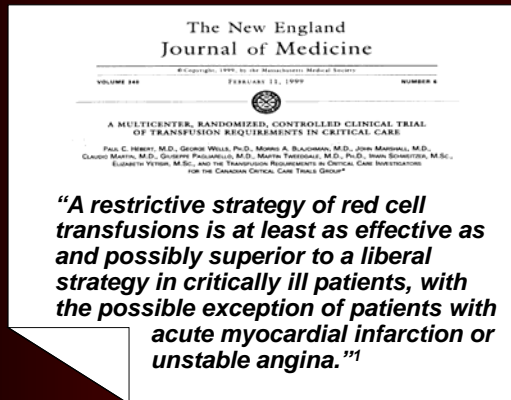
Brendan J. Doyle, MB, BCh,\* Charanjit S. Rihal, MD, MBA,\* Dennis A. Gastineau, MD,†  
David R. Holmes, JR, MD†

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Advances in percutaneous coronary intervention (PCI) during the past decade have led to more widespread use of these procedures in older and sicker patients. Refinement of periprocedural antithrombotic therapy has played a particularly important role in reducing ischemic complications to very low levels in routine practice. Although the use of more powerful antiplatelet agents has been associated with increased risk of bleeding (especially among the elderly and patients with serious comorbidities), such complications have traditionally been viewed as benign in nature. Recent studies, however, have identified major bleeding after PCI as an important predictor of increased mortality. Whether this relationship between bleeding and risk of death is cause-and-effect, or merely an association based on shared risk factors, remains unclear. In this review, we examine the basis for a possible causal link between post-PCI bleeding and subsequent mortality. Possible mechanisms underpinning such a link are discussed, including a potential adverse role for blood transfusion in this setting. A framework for further clinical evaluation of this issue is presented. (J Am Coll Cardiol 2009;53:2019-27)  
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## A multicenter, randomized controlled clinical trial of transfusion requirements in critical care<sup>1</sup>



Ranked as the #1 landmark study that has changed the practice of transfusion medicine<sup>2</sup> but how many physicians are familiar with it?

<sup>1</sup> Hébert et al- NEJM 1999;340(6)

<sup>2</sup> Blajchman- Transfusion 2005;45



## Blood Management in Cardiac Patients

## Blood Management Best Practices



- Following evidence based transfusion guidelines
  - Transfusion triggers
  - Dosing (less is more)
- Anemia management
  - Erythropoiesis stimulating agents
  - Iron management
- Blood conservation strategies in cardiac surgery
- Reduce iatrogenic blood loss from lab draws

## Recommendations for RBC Transfusion in the Critically Ill Patient



1. RBC transfusion is indicated for patients with evidence of hemorrhagic shock (1)
2. RBC transfusion may be indicated for patients with evidence of acute hemorrhage and hemodynamic instability or inadequate oxygen delivery (1)
- 3. 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 (1)**
- 5. In the absence of acute hemorrhage, RBC transfusion should be given as single units (2)**

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## Recommendations for RBC Transfusion in the Critically Ill Patient



8. Consider transfusion if Hb 7 g/dL in critically ill patients with stable cardiac disease. There is no benefit of a “liberal” transfusion strategy (transfusion when Hb 10 g/dL) in critically ill patients with stable cardiac disease (2)

10. RBC transfusion may be beneficial in patients with acute coronary syndromes (ACS) who are anemic (Hb 8 g/dL) on hospital admission (3)

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## Transfusion Requirements After Cardiac Surgery

### The TRACS Randomized Controlled Trial



- Single center study (Sao Paulo, Brazil)
- Prospective, randomized, controlled trial; N = 502 (2/09-2/10)
- Patients randomly assigned to restrictive transfusion strategy (Hct <24%) or liberal strategy (Hct <30%)
  
- No significant difference in the outcome criteria between the 2 randomized groups
- Overall, patients that received transfusion had:
  - Longer hospital LOS, respiratory, cardiac, renal, and infectious complications
  - 30 day mortality in transfused patients – OR 1.2

JAMA. 2010;304(14):1559-1567

## Anemia Management - ESAs



- Erythropoiesis Stimulating Agents (epoetin alfa, darbepoetin alfa)
  - Very effective in the treatment of anemia
  - Some concerns have been expressed with using ESAs in cardiac patients (increased thrombotic activity)
    - Especially when targeting Hb >12 g/dl
  - Beneficial in cardiac patients with CKD
    - Treat if Hb. level < 10 g/dl
    - Maintain Hb level 10-12 g/dl
    - Goal is to maintain Hb. at 11 g/dl

## Anemia Management – Iron Management



- Oral Iron
  - Remains first line therapy; however, poorly tolerated
- Intravenous Iron
  - Newer, safer preparations are available
  - Very effective in the rapid improvement of iron deficiency anemia
  - Benefits demonstrated in cardiac patients with CHF (cardio-renal syndrome)
    - Treat if Hb. level < 10 g/dl
    - Maintain Hb 10-12 g/dl?

## Blood Transfusion and Blood Conservation in Cardiac Surgery<sup>1</sup>



### THE ANNALS OF THORACIC SURGERY



REPORT FROM THE STS WORKFORCE ON EVIDENCE BASED SURGERY

***“A multimodality approach involving multiple stakeholders, institutional support, enforceable transfusion algorithms supplemented with point-of-care testing, and all of the already mentioned efficacious blood conservation interventions will limit blood transfusion and provide optimal blood conservation for cardiac operations”***

***(Class I, Level of evidence A)***

<sup>1</sup> Ferraris, AnnThoracSurg 2007;83:S27-86

## Cardiac Blood management – Bleeding and Platelet Function



- A growing number of preoperative patients are placed on anticoagulants or platelet inhibitors
- Many inhibit platelet function for the life of the platelet
  - FDA guidelines state that patients should have anti-platelet discontinued for at least 5 days prior to non-emergent surgery
- The ability to provide platelet function can provide an objective measurement for the surgical team to make an educated decision about proceeding with surgery

## Cardiac Blood management – Surgical Techniques and Technologies



### Minimize Hemodilution

- Minimize pre-op volume
- Circuit Size
- Hemoconcentration

### Minimize Inflammation/Platelet Activation

- Coated Circuits (level IIb)



### Minimize Coagulopathy

- Heparin / Protamine Management
- › Consumptive coagulopathy
- Point of Care Testing

## Minimize Iatrogenic Blood Loss



- Reduce lab draws/iatrogenic blood loss (level IIa)
- Iatrogenic blood loss is a leading cause of anemia in high acuity patients
- Phlebotomy loss averaged 40-70 ml/day in the ICU
  - Accounted for 30% of blood transfused
- Strategies
  - Smaller volume tubes
  - Judicious use of point of care
  - Eliminate / minimize standing orders for labs
  - Reinfusion device to eliminate discard (VAMP system)
    - › Central line, arterial line

## Summary



- Transfusions still save lives but the benefit/risk ratio is under fire
- We have grossly overestimated the benefits of transfusion and grossly underestimated the risks
- The main issues with transfusion in Cardiac patients are immunomodulation, systemic inflammation, microcirculatory disruption and the storage lesion
- A more restrictive transfusion strategy is as effective, and possibly superior to a liberal transfusion strategy



## Questions?

*"I believe in the old and sound rule that an ounce of sweat can save a gallon of blood."*

General George Patton



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