**Objectives**

**Overview**
1. Optimal Preoperative Hb target - Men v women
2. Why blood transfusion can be bad

**Preoperative**
1. Screening
2. Diagnosis
3. Optimization – how
4. Management - Elective versus urgent cases

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**Current WHO Definition of Anemia**

World Health Organisation

- Man < 13.0g/dl
- Woman < 12.0g/dl
- Pregnant Woman < 11.0g/dl

Ref: World Health Organization.


Serum ferritin level < 30 μg/l is the most sensitive and specific test used for the identification of absolute iron deficiency. In the presence of inflammation (CRP > 5 mg/l) and/or transferrin saturation < 20%, a serum ferritin level < 100 μg/l is indicative of iron deficiency.

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**Prevalence of Iron Deficiency in Women Undergoing Surgery**

*major non-cardiac surgical procedures*

<table>
<thead>
<tr>
<th>Ferritin &lt; 30 mcg/l</th>
<th>Tsat &lt; 20%</th>
<th>Serum iron / TIBC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb ≥ 13.0 g/dl</td>
<td>24%</td>
<td></td>
</tr>
<tr>
<td>Hb 12.0–12.9 g/dl</td>
<td>42%</td>
<td></td>
</tr>
<tr>
<td>Hb &lt; 12.0 g/dl</td>
<td>51%</td>
<td></td>
</tr>
</tbody>
</table>

Large Proportion of women are iron deficient


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**Implication for Clinical Practice**

- Women are more likely to be iron deficient than men
- Women are less likely to have the iron stores necessary to respond to acute blood loss – whether preoperative or post operative
- Screening and repletion of iron stores may help optimize preoperative Hb and accelerate post operative recovery

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**Consensus Statement**

International consensus statement on the peri-operative management of anaemia and iron deficiency


When treating anaemia pre-operatively, the target haemoglobin concentration should be ≥ 130 g in both sexes to minimise the risk of transfusion associated unfavourable outcomes.
Anemia and Surgical Outcome

1. Data from large series now suggest that anemia is an independent risk associated with poor outcome in both cardiac and non-cardiac surgery.

2. Blood transfusion does not appear to ameliorate this risk, and in fact may increase the risk of postoperative complications and hospital length of stay.


BLOOD TRANSFUSION AND SURGICAL OUTCOMES

In conclusion, we report that abnormal preoperative Hb concentrations are highly prevalent, and that anemia is associated with increased in-hospital mortality and worse outcome in patients undergoing non-cardiac and non-neurological surgery. Preoperative assessment and correction of Hb concentrations to normal values might reduce mortality and reduce the intensive care resource use in these patients.
Use of Blood and Cancer Recurrence

Multiple studies show blood transfusion is a downstream risk for cancer recurrence.

Blood Transfusions and Local Tumor Recurrence in Colorectal Cancer
Evidence of a Noncausal Relationship

838 Critical Care Patients
Hb target 7.0-9.0/dl versus 10-12g/dl

Results
30-day mortality was similar in the two groups (18.7 percent vs. 23.3 percent, P=0.11).  
1) Acute Physiology and Chronic Health Evaluation II score of ≥20 (8.7% in the restrictive strategy group and 16.3% in the liberal strategy group, P=0.03)  
2) Patients less than 55 years of age (5.7% and 13.0%, respectively; P=0.02), but not among patients with clinically significant cardiac disease (20.5% and 22.9%, respectively; P=0.69).  
The mortality rate during hospitalization was significantly lower in the restrictive strategy group (22.2% vs. 28.1%, P=0.05).  

Conclusions
A restrictive strategy of red-cell transfusion is at least as effective as and possibly superior to a liberal transfusion strategy in critically ill patients, with the possible exception of patients with acute myocardial infarction and unstable angina.

Association Between Anemia, Bleeding, and Transfusion with Long-term Mortality Following Noncardiac Surgery

• 3050 subjects who underwent orthopedic surgery  
• Preoperative anemia was present in 17.6% (537) of subjects, hemorrhage occurred in 33 (1%), and 766 (25%) received at least one red blood cell transfusion.  
• Over 9015 patient-years of follow-up, 111 deaths occurred  
• Anemia (hazard ratio [HR] 3.91; confidence interval [CI], 2.49-6.15) Hemorrhage (HR 5.28; 95% CI, 2.20-12.67) were independently associated with long-term mortality after multivariable adjustment.  
• Red blood cell transfusion during the surgical hospitalization was associated with long-term mortality (HR 5.96; 95% CI, 2.74-13.0), which was attenuated by severity of anemia (no anemia [HR 4.39], mild anemia [HR 2.77], and moderate/severe anemia [HR 0.81]; P for trend .0015).
Association between mortality and red cell transfusion in non cardiac surgery

The American Journal of Medicine 2016 129, 315-323.e2DOI: (10.1016/j.amjmed.2015.10.012)

Rationale – Why?

- Anemia increases all cause risk for patients
- Anemia increases costs and resource allocation
- Blood transfusion does not fix this – downstream risks
- Optimal Perioperative pathway screens and optimizes Hb and iron stores prior to surgery

PREOPERATIVE OPTIMIZATION OF HEMOGLOBIN

Anemia of Chronic Disease

- Chronic disease can cause a state of functional iron deficiency leading to anemia.
- The key iron regulatory protein hepcidin is activated in response to inflammation and inhibits absorption of iron from the gastrointestinal tract and reduces bioavailability of iron stores for red cell production in the marrow.
- Although iron stores (predominantly ferritin) may be normal, the transport of iron either from the gastrointestinal tract or iron stores to the bone marrow is inhibited, leading to a state of ‘functional’ iron deficiency and subsequent anemia.
- Since absorption from the gastrointestinal tract is blocked, increasing oral iron intake is ineffective

Anemia of Chronic Disease - Why Oral Iron May Not Work

PREOPERATIVE OPTIMIZATION OF HEMOGLOBIN

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PREOPERATIVE OPTIMIZATION OF HEMOGLOBIN
Intravenous Iron

- Replenishes iron stores and increases Hb in anemia due to iron deficiency with or without inflammation
- Dosing may be calculated from the baseline and target Hb and patient’s body weight, adding 500 mg for iron stores
- Low incidence of reactions
- 1000–1500 mg is sufficient in most surgical patients
- Given by slow infusion over less than 1 h in one sitting or in two–three divided doses over 2-3 weeks
- Most patients feel better in 3 days with a rapid Hb response (50% at 5 days, 75% at 10–14 days, maximal at 3 weeks)


Intravenous Iron Preparations – Absolute rates of life-threatening ADEs


The absolute rates of life-threatening ADEs were:

- 0.6 per million for Venofer
- 0.9 per million for Ferrlecit
- 3.3 per million for InFed
- 11.3 per million for Dexferum

Acute reactions are due to nanoparticles – rate dependent, give antihistamines and steroids

Relative Risks – Acute Reactions

<table>
<thead>
<tr>
<th>Condition</th>
<th>Blood Transfusion</th>
<th>Iron Infusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allergic reaction</td>
<td>1 in 333</td>
<td>1-11 in 1,000,000</td>
</tr>
<tr>
<td>DHTR</td>
<td>1 in 5,400</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td></td>
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</table>

Cost Benefit of IV Iron versus Oral Iron

- Colorectal Surgery - Direct and indirect costs for acquisition and administration of iron product and RBC concentrates as well as hospitalization costs, were included in the cost model.
- Ferric carboxymaltose reduced hospital stay by 2.3 days
- Iron sucrose reduced hospital stay by 2.6 days (compared with oral iron)
- Cost savings of £ 437 (485€, $532) and £ 245 (274€, $300) per patient, respectively.


Erythropoeitin

- Studied extensively in anemia
- Effective in chronic kidney disease
- Concern in cancer patients – tumor growth

Hb below which organ dysfunction occurs

CRITICAL HEMATOCRIT
Objective: To discover the effects of the lowest hematocrit during cardiopulmonary bypass on end-organ function and mortality in patients who did not receive red blood cell transfusion and to identify predictors of nadir hematocrit.

Methods: From November 1, 2004, to October 1, 2009, 7973 patients underwent cardiac surgery supported by cardiopulmonary bypass and were not transfused. The relationship between nadir hematocrit and mortality, markers of end-organ function, and survival was studied using generalized propensity score analysis. Factors associated with nadir hematocrit were identified by linear regression.

Balance between tolerable anemia and interventions to correct anemia

What level of Hb is Threshold for Transfusion?

- Tolerate Hb 7.0 to 9.0 g/dl (ASA Guidelines)
- Individualized: Cardiac and Respiratory Patients – higher target
- Elderly should have higher target
- Rate of change of Hb – ie bleeding also a significant factor in giving blood
- Evidence support maintaining HCT >30%
Nadir / Critical Hematocrit

Which preoperative Hb target?

- Work out blood volume on ideal body weight
- Work out red cell volume
- Work out predicted blood loss
- Work out likely nadir hematocrit for patient to get complications
- Elective or urgent?

Anemia Clinic - Practical Tips

- Screening - not just rely on ferritin
- Fe; TIBC; TSAT all needed
- Need to exclude cause – cancer until proved otherwise
- Hematological and internal medicine ‘buy in’
- Referral process for difficult diagnosis

Anemia Clinic - Practical Tips

- Infusion clinic – set up powerplan for IV Iron
- Ideally 1 infusion but may need 2 or 3
- Need to measure efficacy – CBC
- Close liaison with surgeon for urgent cases or where blood loss is ongoing
- Need to have a means of logging patients for iron therapy – virtual clinic
- Funding – Medicare v Insured
Transfusion Trigger

- Individualize
- Know likely nadir hematocrit
- Depends on the co-existing organ dysfunction
- Know Average Blood Loss for the procedure
- Estimate blood volume for patient (I use ideal body weight)
- Estimate starting Hb necessary to avoid Nadir Hematocrit

Summary

- Preoperative anemia is one of the most important modifiable elements to effect perioperative outcomes
- A pre-operative anemia clinic is warranted to change surgical outcomes
- Intravenous iron is safe and can be used for anemia of chronic disease or when iron stores are low
- Individualized plans to avoid nadir Hematocrit may be beneficial

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