Pre-Operative Anemia:
Common, Consequential and Correctable

Kathrine Frey, MD   Fairview Southdale Hospital, Sept 2014
Credentials and Conflicts of Interest

- Pathologist (AP/CP/Tx. Med) and Director of Patient Blood Management and Pre-OP Anemia Services, Fairview Southdale Hospital
- AABB Standards Committee: Patient Blood Management
- AABB/SABM PBM liaison committee

- Medtronic Speakers Bureau for “Rethinking Blood Conservation”
- Chief Medical Officer, Patient Readiness Institute.
Fairview Southdale Hospital

- 350 Beds
- 1700 total joint procedures/year
- 350 CV surgery procedures/year
- Patient Blood Management: 2008
  - Sustained > 35% reduction all blood components,
    2750 fewer red cells/year
- Pre-Operative Anemia Management: 2011
“Patients deserve all the care they need……none they don’t, efficiently, effectively and at least cost.”  

Don Berwick, MD
Objectives

• Recognize prevalence of pre-operative anemia
• Learn impact of pre-operative anemia on post-operative outcomes
• Review causes and diagnosis of anemia
• Become familiar with the medical treatments for anemia and their safety/risks
• Suggest components and some details of a pre-operative anemia management program
Anemia

• WHO definition- Hgb < 12g/dL (f, pre-menopausal), < 13 g/dL (m)
• 20% of world population, iron deficiency most common cause
• Present in 5-75% of Pre-Surgical Patients, varies by surgery type
Incidence of Anemia Increases With Age

N = 65,788
1980–2000
WHO anemia definition

Patients (%)

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>20-30</td>
<td></td>
<td></td>
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<tr>
<td>31-40</td>
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<td>81-90</td>
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<td></td>
</tr>
<tr>
<td>&gt; 90</td>
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</tbody>
</table>


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Pre-Operative Anemia Scope

- 5-75% of surgical patients
- 25-30% Elective Joint replacement
- 20-30% CABG
- > 50% Valve replacement
- Greatest Predictor of transfusion
- **Overall a real, but modifiable, problem**
- Significant results - Ex. Patient Blood Management Program with pre-operative anemia avoidance component has 5% transfusion rate for elective joint replacements rather than @ 40% in unmanaged programs

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Anemia in High Blood Loss Surgery Patients:
overall 40 +%, CABG @ 20-30%, Valve replacement 50-65%

• Numbers are even higher if using > 12 g/dL for females (STS < 13 for M and F)
• Women disadvantaged by lower Hgb cutoff in addition to lower body mass, red cell mass and blood volume
Meet Your Patient, Mitzi

• 75 year old spry female
• Lives independently alone
• Primary Hip surgery in 3 weeks
• 135 Lbs
• Hgb 11.6 gm/dl
• What is her likelihood of transfusion?
Anemia and Risk of Perioperative Transfusion

Fig. 2. Probability of allogeneic transfusion only in knee and hip replacements unilateral, non-revision, no erythropoietin. (x) Men; (□) women.

Development and validation of Transfusion Risk Understanding Scoring Tool (TRUST) to stratify cardiac surgery patients according to their blood transfusion needs

Abdullah A. Alghamdi, Aileen Davis, Stephanie Brister, Paul Corey, and Alexander Logan

**TABLE 4. Statistical details of the final model (Model B)**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>df</th>
<th>Regression coefficient</th>
<th>SE</th>
<th>Odds ratio</th>
<th>95% LCL</th>
<th>95% UCL</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb</td>
<td>1</td>
<td>1.15</td>
<td>0.06</td>
<td>3.15</td>
<td>2.81</td>
<td>3.53</td>
<td>&lt;0.0001</td>
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<td>Female sex</td>
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<td>Redo surgery</td>
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<td>0.64</td>
<td>0.11</td>
<td>2.32</td>
<td>1.53</td>
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<td>&lt;0.0001</td>
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<td>Creatinine level</td>
<td>1</td>
<td>0.63</td>
<td>0.09</td>
<td>1.88</td>
<td>1.58</td>
<td>2.24</td>
<td>&lt;0.0001</td>
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<tr>
<td>Nonelective surgery</td>
<td>1</td>
<td>0.64</td>
<td>0.06</td>
<td>1.90</td>
<td>1.70</td>
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<tr>
<td>Age</td>
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<td>0.06</td>
<td>2.14</td>
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<tr>
<td>Body weight</td>
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<tr>
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<td>0.52</td>
<td>0.07</td>
<td>1.67</td>
<td>1.46</td>
<td>1.92</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

df = degrees of freedom; LCL = lower confidence limit; UCL = upper confidence limit.

**TRANSFUSION RISK:**
Score 3: 50%
Score 4: 80%
Your Patient, Mitzi

• 75 year old female, P-THA in 3 weeks
• Hgb 11.6 gm/dl
• Transfusion likelihood > 40%
• Does Mitzi have other peri-operative risks than transfusion?
Effect of Preoperative Anemia

- Pre-Surgical anemia alone is associated with increased morbidity and mortality
- Pre-Surgical anemia is the strongest predictor of need for blood transfusion
- Blood Transfusion is also associated with increased morbidity and mortality in a dose dependent manner
Risk Associated with Preoperative Anemia in Cardiac Surgery: A Multicenter Cohort Study

Keyvan Karkouti, et al; Circulation, Jan 2, 2008

Preoperative anemia independently associated with adverse outcomes (n=3500, Hgb < 12.5, 7 hosp, 500 pts each, retrospective)

- Association independent of transfusions

- Propensity matched:
  - Death = 51% increase
  - Stroke = 60% increase
  - Acute kidney injury = 80% increase
  - Second most predictive variable after CPB time.

1 > 100% increase in Creatinine above normal or dialysis

3286 patients

Kathrine Frey, MD   Fairview Southdale Hospital, Sept 2014
Impact of Preoperative Anemia on Outcome in Patients Undergoing Coronary Artery Bypass Graft Surgery

Alexander Kulier, MD; Jack Levin, MD; Rita Moser, MD; Gudrun Rumpold-Seitlinger, MD; Iulia Cristina Tudor, PhD; Stephanie A. Snyder-Ramos, MD; Patrick Moehnle, MD; Dennis T. Mangano, PhD, MD; for the Investigators of the Multicenter Study of Perioperative Ischemia Research Group and the Ischemia Research and Education Foundation

4804 patients

Hgb < 12 with non-cardiac adverse events (renal, cerebral)

Hgb < 11 with cardiac component

Patients with comorbidities did worse (Euroscore > 4)

Even mild preoperative anemia is independently associated with an increased risk of 30-day morbidity and mortality in patients undergoing major non-cardiac surgery.

Your Patient, Mitzi

- 75 year old female
- Primary Hip surgery in 3 weeks
- 135 Lbs
- Hgb 11.6 gm/dl
- Transfusion likelihood > 40%
- Is blood safe?

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Dose-Response for Transfusion & Infection in Cardiac Surgery

Effect of **blood transfusion** on long term survival after CV surgery

- Retrospective study; primary CABG (N=1915)
- Patients transfused and not transfused in hospital matched by propensity score
- 5-year mortality: 2x higher in transfused group
- 5-year mortality (comorbidity correction): remained 70% higher in transfused group (p<.001)

Blood Transfusion: Avoid when Possible

- Evidence if compelling that blood transfusion is associated with increased morbidity (surgical site infection, increase ventilator time, renal complications, other lung injury, increased LOS) and mortality

- Serious Hazards of Transfusion, SHOT

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Your Patient, Mitzi

- 75 year old female, P-THA in 3 weeks
- Hgb 11.6 gm/dl
- Transfusion likelihood > 40%
- Anemia and transfusion are undesirable
- Why could her Hgb be low?
Causes of Anemia

- **Decreased Production of RBCs or Hgb**
  - Heme: Iron deficiency (absolute, inflammatory, functional)
  - Globin chains: Vitamin B 12, folate, Thal/Hgb-opathy
  - Medications: H2 Blockers, PPI’s, some CV meds, anticoagulants
  - Inflammation: Affects Iron and Erythropoietin negatively
  - Marrow Failure: MDS, tumor

- **Increased Red Cell Destruction or Loss**
  - Blood loss (GI, GU, GYN)
  - Hemolysis (intra and extravascular)
Anemia in Elective Pre-Surgical Population

• Iron deficiency (30%)- poor diet, blood loss, impaired absorption
• Anemia of Chronic Disease (inflammatory iron deficiency) (25%)
• Chronic Kidney Disease (15-20%)
• B12 deficiency (3%)
• Folate deficiency (5%)
• Medication related (inhibited erythropoiesis and/or anticoagulant-associated bleeding)
• Blood loss- Recent Invasive Procedure (ex. Angiogram can have 1-2 gm Hgb loss into soft tissues)
• Unexplained Anemia of the elderly (UAE)

MULTIFACTORIAL
(ex. CKD + IDA + Medication components)
Iron Restricted Erythropoiesis

Figure 1. Iron deficiency syndromes. The relationships between absolute iron deficiency, iron sequestration, and functional iron deficiency are illustrated. Patients can have ≥1 combinations that all result in iron-restricted erythropoiesis. Adapted from Goodnough LT.61

Absolute Iron deficiency-Lack of stored iron

- Chronic blood loss-can’t absorb enough Fe to keep up with losses
- Diminished intestinal absorption- Celiac Disease, post surgical (bariatric)
- Diminished intake- Vegetarian
- Medications- Antacids (H2 blockers, Proton Pump Inhibitors, Tums (Ca2+))
Anemia of Inflammation: Iron Sequestration
(decreased iron absorption and bioavailability, Fe present but not accessible)

- Interleukin 6, increases hepcidin production
- Impaired enteric absorption
- Impaired release of storage iron
- Decreased transferrin, increased ferritin
- Patients-Chronic inflammatory disease (DM, CHF), autoimmune disease, infections
- Happens postoperatively too
Functional Iron deficiency

• Patient receiving erythropoietin therapy or with increased endogenous erythropoietin may have iron on board but the speed of red cell production drive outpaces body’s ability to release stored iron.

• Transferrin saturation decreases within one week of initiation of ESA therapy
Iron Restricted Erythropoiesis

Figure 1. Iron deficiency syndromes. The relationships between absolute iron deficiency, iron sequestration, and functional iron deficiency are illustrated. Patients can have ≥1 combinations that all result in iron-restricted erythropoiesis. Adapted from Goodnough LT.61

Table 3. Potential Role of Iron Therapy in Management of Anemia

<table>
<thead>
<tr>
<th>Condition</th>
<th>Expected hepcidin levels</th>
<th>Iron parameters</th>
<th>Iron therapy strategies</th>
<th>Potential hepcidin therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Absolute iron deficiency anemia (IDA)</td>
<td>Low</td>
<td>Low Tsat and ferritin</td>
<td>Orally or IV if poorly tolerated or malabsorbed</td>
<td>No</td>
</tr>
<tr>
<td>Functional iron deficiency (ESA therapy, CKD)</td>
<td>Variable, depending on ± CKD</td>
<td>Low Tsat, variable ferritin</td>
<td>IV</td>
<td>Antagonist (if hepcidin levels not low)</td>
</tr>
<tr>
<td>Iron sequestration (anemia of inflammation[AI], mixed anemia [AI/IDA, or Al/functional iron deficiency anemia])</td>
<td>High</td>
<td>Low Tsat, normal-to-elevated ferritin</td>
<td>IV</td>
<td>Antagonist</td>
</tr>
<tr>
<td></td>
<td>Variable</td>
<td>Low Tsat, low-to-normal ferritin</td>
<td>IV²</td>
<td>Antagonist (if hepcidin levels not low)</td>
</tr>
</tbody>
</table>

Tsat = transferrin saturation; CKD = chronic kidney disease; ESA = erythropoiesis-stimulating agent.

²Mixed anemia is a diagnosis of exclusion without a therapeutic trial of iron.

Adapted from Goodnough LT.61
Your Patient, Mitzi

• 75 year old female, P-THA in 3 weeks, Hgb 11.6 gm/dl

• Transfusion likelihood > 40%

• Anemia and transfusion are undesirable

• What additional lab tests are needed?
Lab Testing

Initial Panel
- CBC (need more than just Hgb)
- Reticulocyte count
- Creatinine with GFR
- Serum Iron, % saturation TIBC
- Ferritin

Add on tests as needed
- CRP (i)
- Red cell folate
- Serum B12
- Soluble transferrin receptor
- Reticulocyte Hgb
- LDH
- Haptoglobin
- DAT
- Differential
- blood morphology
- Type and Screen
- Hepcidin (future)
Anemias

• Absolute Iron deficiency- normocytic or microcytic, \textit{\% saturation < 20\% Ferritin < 100}, increased RDW, increased plts (sometimes)

• Inflammatory Iron Sequestration- normocytic, \textit{\% sat < 20 \%, Ferritin > 100}, CRP (i) increased, medical history chronic disease/inflammation

• Renal failure associated, normocytic, \textbf{Cr > 1.2, GFR 59 or <}

• Thalassemia-microcytic, erythrocytosis, nl iron studies or increased iron
Iron Deficiency- Anemia is Late Stage, Microcytosis is Even Later

• Iron depletion: near absent storage iron, no anemia, asymptomatic, **treat with oral iron with Vitamin C**

• Iron deficiency without anemia-stored and blood borne iron below normal, can be asymptomatic or symptomatic (fatigue), **treat with oral iron with Vitamin C**

• Iron deficiency anemia- initially normocytic, as severity increased, microcytic...
Your Patient, Mitzi

• 75 y/o female, P-THA 3 weeks
• Transfusion likelihood > 40%
• Anemia and transfusion are undesirable
• Hgb 11.6, retic 1.1%, Cr 1.2, GFR 46, % saturation 32, Ferritin 90
Mitzi-
Hgb 11.6, retic 1.1%
% sat 23, Ferritin 90
Cr 1.2, GFR 46
Your Patient, Mitzi

- 75 y/o female, 135 lbs, P-THA 3 weeks
- Hgb 11.6, retic 1.1%, Cr 1.2, GFR 46, % saturation 23, Ferritin 90
- Diagnosis: Mild anemia w/o regeneration, CKD Stage 3, with low iron stores
- What does treatment include and what is timeframe for improvement?
- Is treatment safe?
Anemia Treatment
Safely increase Hgb 0.5-1 gm/week

• Treatment Options: IV iron, enteric iron, Erythropoietin stimulating agents (ESA’s), Vitamin B-12, folate, treat co-morbidities, delay and defer

• IV iron, effect at 1 week, max effect at 2 weeks, several doses needed (1 gram divided dose common)

• ESA action onset 4-6 days, max at 10 days, must give with iron to avoid functional iron deficiency

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Conditions treated and agents:

• IDA (absolute iron deficiency)- IV iron effect at 1 week, Iron effect, max at 2 weeks, several doses needed (1 gram divided dose common)

• Anemia of chronic disease/inflammation- IV iron (despite high ferritin @ 500-700) and sub Q erythropoietin, EPO action onset 4-6 days, max at 10 days

• Renal failure associated- Sub Q Epo and IV iron, correct iron stores prior to starting ESA
IRON - the heavy lifter of anemia management

**Enteric** - lower cost, slow response, 30-40% of patients have GI intolerance, poor absorption in tolerant patients (antacids, gastritis, other malabsorption, inflammatory conditions), short timeframe to surgery. **Give with Vitamin C.**

**Parenteral** - few adverse drug events. Overall 3/1M doses, life threatening 0.6/1M doses, common reactions are urticarial, flushing and hypotension.
IV iron dosing

- 150-200 mg Iron for each gm/dl hgb deficit

- Plus 500-800 mg to replace true iron stores if
  - tsat < 10 (regardless of ferritin)
    OR
  - tsat < 20 AND ferritin < 100 ng/dl

- Normal hgb + decreased Ferritin
  - [100 – ferritin] x 10

- Acute blood loss – mg per cc
### Table 4. Currently Available IV Iron Preparations

<table>
<thead>
<tr>
<th>Trade name</th>
<th>DexFerrum</th>
<th>INFeD</th>
<th>Ferrlecit</th>
<th>Venofer</th>
<th>Feraheme</th>
<th>Ferinject&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Monofer&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Manufacturer</td>
<td>American</td>
<td>Pharmacosmos</td>
<td>Sanofi Aventis</td>
<td>Vifor</td>
<td>AMAG</td>
<td>Vifor</td>
<td>Pharmacosmos</td>
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<tr>
<td>Carbohydrate</td>
<td>High-molecular-weight dextran</td>
<td>Low molecular weight dextran</td>
<td>Gluconate</td>
<td>Sucrose</td>
<td>Carboxymethyl dextran</td>
<td>Carboxymaltose</td>
<td>Isomaltoside 1000</td>
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<td>Molecular weight measured by manufacturer (Da)</td>
<td>265,000</td>
<td>165,000</td>
<td>289,000–440,000</td>
<td>34,000–60,000</td>
<td>750,000</td>
<td>150,000</td>
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<td>Total-dose or &gt;500-mg infusion</td>
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<td>No</td>
<td>No</td>
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<td>Premedication</td>
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<td>No</td>
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<td>Test does required</td>
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<td>Yes</td>
<td>No</td>
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<td>Iron concentration (mg/mL)</td>
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<td>12.5</td>
<td>20</td>
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<td>100</td>
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<td>Vial volume (mL)</td>
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<td>2 or 10</td>
<td>1, 2, 5 or 10</td>
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<td>Preservative</td>
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<td>None</td>
<td>Benzyl alcohol</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
</tbody>
</table>

Ferric gluconate and iron sucrose are also referred to as iron salts.

TDI = total-dose infusion.

<sup>a</sup>Not approved in the United States.

Adapted from Auerbach.⁶⁹
Erythropoietin

• 165 amino acid glycoprotein hormone synthesized primarily in the kidneys (adult 9:1 kidney:liver). Recombinant forms for patient care.
• Primary role involves the programmed cell death of red cell precursors.
• It induces red cell production by promoting production and differentiation of red cells from their progenitor cells.
• EPO also exerts a protective role against tissue ischemia by activating biochemical mechanisms that provide anti-apoptotic anti-oxidative and anti-inflammatory response to hypoxia.
Effective for Pre-Operative anemia

• Check CMS guidelines -
  – Elective Hip and Knee surgery HCTS < 39
  – **Not on label for CV or vascular surgery**
  – CKD Stage 3 and > and HCTS < 30 or symptomatic with ending Hcts 36
  – Patient can’t be Iron deficient at start of treatment
- Give iron with ESA

Goodenough Transfusion 34:66-71, 1994
*J Thorac Cardiovasc Surg* 2001;122:741-745
Sowade Blood 1997 89: 411-418

Kathrine Frey, MD  Fairview Southdale Hospital, Sept 2014
European Epoetin Alfa Surgery Trial

• Orthopedics: Multicenter trial EPO v routine (6 countries- 700 pts)

• **Anemic pts** – hgb 10-13 g/dl

• EPO 40 lu/ kg/wk x 3 + DOS + iron both groups (oral treatment/iv or oral control)

• Results:
  – higher hgb levels throughout
  – 12% v. 46% transfusion
  – No effect post op recovery (time ambulation, d/c, infection rate
  – Time to ambulation, d/c longer in transfused v. non-transfused
  – Side Effects comparable

EPO and Thrombosis

- RCT 680 spine pts 600 u/kg x 4 doses (1 per week x 4 weeks) vs. standard of care

- Rate all DVT by doppler on POD 4 only
  - Greater in EPO than control (4.7 v 2.1)

- Rate of symptomatic DVT same for both groups

- Post-hoc analysis of combined PE + DVT same for both groups

- Only mechanical DVT prophylaxis post op (joint replacement patients use anticoagulants as well)

- Basis for thromboprophylaxis

Spine 2009; 34:2479-85

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Basis for the FDA exclusion of ESA for use in CV surgery

- 182 patients randomized to 150 or 300 IU/Kg of EPO or placebo Pre-Op day 5, DOS and POD 2 after CABG (8 doses)
- Trend toward increased mortality in treatment groups (p=.06)
- 4/5 deaths “possibly drug related” due to thrombotic or vascular events
- 2/4 deaths were > 3 months post op
- No deaths in the placebo group
- No difference in non-fatal complications in the treated and placebo groups

- Study not applicable for pre-operative anemia, transfusion reduction was measurement (not beneficial)
- Mean baseline Hgb 14.0 +/- 1 gm/dl in 3 groups
- 89% male, 94% CABG
- Attempt to exclude iron deficiency but parameters were Ferritin < 20, % Sat 16
- 91% “hematologically normal”
- **Basis for the FDA exclusion of ESA for use in CV surgery**
Preoperative very short-term, high-dose erythropoietin administration diminishes blood transfusion rate in off-pump coronary artery bypass: A randomized blind controlled study

- Prospective European Study, 320 consecutive CAB only pts, 158 got ESA, 162 controls
- EPO 14,000 IU Pre OP Days 2 and 1; 8,000 IU DOS and 8,000 IU POD 1 and 2 (5 doses)
- Given to patients unless Hgb >14.5 or Cr > 2
- **Endpoint transfusion**
- POD 4 Hgb 15.5% higher in treatment group, less blood needed/Tx
- No adverse events related to ESA use but short follow up, no differences in 45 day mortality
- **Patients with most benefit noted to be those with anemia**

Weltert, L. J Thorac Cardiovasc Surg 2010;139:621-7

Kathrine Frey, MD  Fairview Southdale Hospital, Sept 2014
Effects of Preoperative Intravenous Erythropoietin Plus Iron on Outcome in Anemic Patients After Cardiac Valve Replacement (Spain)

• 75 consecutive patients- EPO + IV iron x 5 doses
• 59 observational cohort

• Post op morbidity \( \text{OR} \ 0.13 \quad p = 0.008 \)
• In hospital mortality \( \text{OR} \ 0.16 \quad p = 0.04 \)
• Decreased postop renal failure \( \text{OR} \ 0.23 \quad p = 0.03 \)
• Transfusion rate \( 67 \  v \ 93\% \quad p=0.01 \)
• LOS (median) \( 10 \  v \ 15 \quad p = 0.01 \)

• Adjusted for Operative Risk Score, type of intervention, time of CPB, year of surgery

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Cladellas M, Am J Cardiol 2012;110:1021-26
Role of ESA Therapy in Cardiac Surgery


• Unresolved Question
• Valuable tool for patients with special requirements such as Jehovah’s Witness.
• In selected populations such as off pump CABG. short-term, high dose ESA has been shown to diminish blood transfusion rates.
• Until additional safety data are forthcoming, the off label use of ESA in patients undergoing cardiac or vascular surgery in the US cannot be recommended.

Kathrine Frey, MD Fairview Southdale Hospital, Sept 2014
On “warnings”, Patient signs Informed Consent for ESA Rx.

• ESA- black box
  o Increased mortality,
  o Serious cardiovascular and thrombo-embolic events
  o Increased mortality and/or
  o Increased risk of tumor progression or recurrence

• If there were a “black box” for red cell transfusion
  o Increased mortality,
  o Lung injury
  o Circulatory overload
  o Tumor progression recurrence
  o Infection
  o Thrombo-embolic events
  o Hemolysis
  o Renal failure and
  o Allergic reactions.

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ESA Dosing

• Only one ESA approved for pre-surgical use, joint replacement and Jehovah’s Witness
• 300-600 u/kg/week for 4 weeks
Presurgical EPO - summary

- Use with caution CKD, malignancy, h/o VTE
- Use Lowest dose (with IV iron!)
- Consider Thromboprophylaxis – high risk pts
Your Patient, Mitzi

• 75 y/o female, P-THA 3 weeks
• Hgb 11.6, retic 1.1%, Cr 1.2, GFR 46, % saturation 23, Ferritin 90
• Diagnosis: Mild anemia w/o regeneration, CKD Stage 3, borderline low iron stores, having joint replacement (ESA on label)
• Treatment: ESA x 2 with IV iron 600 mg in divided 300 mg doses, gave iron before starting ESA
• How did she do?
75 y/o female, P-THA 3 weeks, Mild anemia w/o regeneration, CKD Stage 3, borderline low iron stores

Treatment: ESA x 2 with IV iron 600 mg in divided 300 mg doses, gave iron before starting ESA

• Initial Labs: Hgb 11.6, retic 1.1%, Cr 1.2, GFR 46, % saturation 23, Ferritin 90
• Day of Surgery Labs: Hgb 13.5, retic 3.4%
• Not transfused, lowest Hgb in hospital 10.2, LOS 3 days

Kathrine Frey, MD  Fairview Southdale Hospital, Sept 2014
Pre-Operative Anemia Evaluation

- **Current process- None**
  - Patient to PCD* when convenient or directed
  - PCD likely doesn’t see anemia as problem
  - Transfusion might be needed (blood is safe)
  - Surgery already scheduled

- **Better process-**
  - Anemia evaluation start when surgery need identified
  - Patient to PCD for early pre op including anemia eval with Hgb target
  - Patient to Anemia program that does this and hands patient into PCD/Hospital with best red cell mass

*PCD=Primary Care Doctor
Role and Responsibilities of a Pre-Surgical Anemia Management Program

• To provide best surgical outcome for patients
• Reliably identify and distinguish treatable and triage-worthy anemic patients (PCD, Heme, GI)
• Provide effective and reimbursable treatment recommendations and treatment
• Reliably communicate findings (to Surgeon, PCD, Patient)
Pre-Operative Anemia Programs-

• DON’T serve as chronic anemia management services.
• DON’T eliminate need for hematologist services at times.
• DON’T provide for care other than for anemia.
Patient Enrollment Options

• Directed by Primary Care Providers

• Directed by Surgeons

• Sub component of Pre-Operative Clinic program, for certain procedures

• Directed from surgery schedule, cases 3+ weeks out, certain DRGs

• Enrollment options - ad hoc consult or pre-surgical requirement
Personnel Needed

- Medical Director, generally part time in conjunction with primary specialty (Pathologist, Anesthesiologist, Hospitalist, Hematologist, Other)
- Nurse(s)
- Administrative Assistant
- IT support
Anemia Screening and Diagnosis

• Medical history and current medications

• Surgical procedure and timeframe
Lab Testing: Use an Algorithm
Draw enough blood initially for follow on tests

Algorithm for Managing Preoperative Anemia

Kathrine Frey, MD  Fairview Southdale Hospital, Sept 2014
Anemia Treatment

• Use standardized order sets, including coding for pharmacy approval and reimbursement

• IV iron is the most commonly used agent

• ESA use: Non CV or vascular surgery, anemia's with inflammatory or renal components, no autologous blood donation, check state CMS rules

• Patients getting ESA need concomitant iron and DVT prophylaxis in hospital
Sample Order Set for Pre-Operative Anemia Management

**PHYSICIAN’S PLANS (ORDERS)**

<table>
<thead>
<tr>
<th>DATE</th>
<th>TIME</th>
<th>ANOTHER MEDICATION SIMILAR IN FORM AND ACTION MAY BE DISPENSED PER MEDICAL STAFF POLICY UNLESS CHECKED.</th>
<th>Read Back</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Anemia Management Order Set</td>
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<tr>
<td></td>
<td></td>
<td>Call Blood Conservation Office at 932-6183 or the Blood Conservation Coordinator at 440-8131 for assistance.</td>
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<td>To be used in conjunction with Anemia Prevention Protocol</td>
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<tr>
<td></td>
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<td>1. Determine etiology of anemia</td>
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<td>2. Please draw the following labs:</td>
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<td>[ ] Draw today and once weekly: CBC</td>
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<td></td>
<td></td>
<td>[ ] Draw today: iron transferrin and ferritin</td>
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<tr>
<td></td>
<td></td>
<td>[ ] 72 hours after initiation of erythropoietin: draw reticulocyte count</td>
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<td></td>
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<td>[ ] Draw transferrin receptor [soluble transferring receptor (STFR)] if ferritin greater than 600</td>
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<td>** IMPORTANT NOTES:** PHARMACY WILL HOLD A COPY OF THIS ORDER AND SEND MEDS AS APPROPRIATE WHEN LAB RESULTS ARE AVAILABLE**</td>
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<tr>
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<td></td>
<td>3. Iron store replacement:</td>
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<td></td>
<td>If ferritin &lt; 100 or TSAT &lt; 20%, or if STFR is above the upper limit of normal, replace iron stores as follows:</td>
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<td></td>
<td>[ ] Venofer (iron sucrose) 300 mg over 1-2 hours once weekly</td>
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<td></td>
<td></td>
<td>[ ] Folic acid 1 mg PO daily if NPO, give 1 mg daily in IV fluid or subcutaneously</td>
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<tr>
<td></td>
<td></td>
<td>[ ] Multivitamin 1 tablet PO daily if NPO, give 10 mL in IV fluid daily</td>
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<td></td>
<td></td>
<td>[ ] Consult dietician regarding foods rich in iron</td>
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<td></td>
<td></td>
<td>DO NOT GIVE iron if TSAT &gt; 45% OR FERRITIN &gt; 600 UNLESS STFR ELEVATED</td>
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</tr>
</tbody>
</table>

**Affix patient label to ALL pages (including carbon copies)**

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**PHYSICIAN’S PLANS (ORDERS)**

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</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Anemia Management Order Set (cont.)</td>
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<tr>
<td></td>
<td></td>
<td>4. Erythropoietin therapy:</td>
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<td></td>
<td>The following criteria must be met before erythropoietin is initiated:</td>
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<td></td>
<td>[ ] Hb &lt; 10 or Hct &lt; 30</td>
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<td></td>
<td></td>
<td>[ ] Iron stores checked and replaced as needed</td>
<td></td>
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<td></td>
<td></td>
<td>[ ] If patient meets above criteria, initiate treatment:</td>
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<td></td>
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<td>[ ] Erythropoietin 40,000 units subcutaneous weekly (may IV push, but subcutaneous preferred)</td>
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<td></td>
<td></td>
<td>[ ] Continue iron replacement as directed above throughout erythropoietin therapy</td>
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<tr>
<td></td>
<td></td>
<td>Discontinue erythropoietin and iron therapy when Hb 12 or Hct 36 (May restart erythropoietin if levels fall again)</td>
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<td>5. Red Blood Cell Transfusion</td>
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<td></td>
<td></td>
<td>Refer to “Red Blood Cell Transfusion Order Set” for indication and instructions</td>
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</tr>
</tbody>
</table>

**Physician’s signature**

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Rules, Regulations, and Logistics

- Labs- CMS doesn't reimburse for labs >30 days from surgery, evaluate patient with known anemia ASAP as anemic patient rather than pre-surgical.

- Medications-strict rules for use of iron with lab test evidence and proper coding. Same for Erythropoietin and also black box warnings and patient informed consent needed.

  ESA- Black Box, increased mortality, serious cardiovascular and thrombo-embolic events, and/or increased risk of tumor progression or recurrence

  “Black Box” for red cell transfusion - increased mortality, lung injury, circulatory overload, tumor progression or recurrence, infection, thrombo-embolic events, hemolysis, renal failure and allergic reactions.

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Costs

• Every red cell unit NOT TRANSFUSED saves the hospital 700-1100 $ (component not transfused and no procedure costs)
• Iron therapy safe and reimbursed
• ESA therapy on label safe and reimbursed
PBM 6: Pre-Operative Anemia

• “Formal protocols for preoperative testing of Hgb for potential high-blood loss elective surgeries would be used to identify and intervene for optimal management of blood resources.
• Early recognition of anemia offers patients an opportunity to receive the most appropriate transfusion-sparing strategy and avoid the risk of a potential transfusion.”
• Use in elective surgical patients for whom blood transfusion is a probability (defined as any procedure for which a preoperative blood type and crossmatch is requested).
• Test a minimum of 30 days before the scheduled procedure”
Pre-Operative Anemia: Summary

• Prevalence: 25% Ortho, 25% CABG, 50% valve surgery
• Consequences: Increased M&M even if mild anemia (hgb 10-12) and if no transfusion
• Transfusion Consequences: Increased M&M, dose dependent
• Anemia Causes: Iron restricted hematopoiesis (absolute, inflammatory, functional), renal disease, medications, multifactorial
• Anemia Diagnosis: Standard lab panel with add on tests and an algorithm
• Anemia Treatment: On label IV iron (most common tx.) and ESA safe and effective, use order sets, consider thrombo-prophylaxis for ESA, when using ESA iron replacement is also needed
• Who evaluate: All elective patients needing T & C on SBOS, Expected blood loss > 300 ml with 3 or > weeks to surgery
• Communication imperative, especially with PCD with any anemic patient

Kathrine Frey, MD   Fairview Southdale Hospital, Sept 2014
References