Oral Iron
Safe, Effective, and Misunderstood
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• I have no relevant disclosures.

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Outline

• Definitions
• Does Iron Deficiency Still Matter?
• Diagnosis
• Etiology
• Oral Treatment
• Inadequate Response
• Take home points
What is anemia?

• U.S Preventive Services Task Force
  – Hemoglobin level below the normal range for the population

• Centers for Disease Control and Prevention
  – Hb <12 g/dl for menstruating women
  – Hb <13 g/dl for males after puberty
  – Hb <11 g/dl in pregnancy
  – Hb <10 g/dl- Severe iron deficiency anemia (WHO)
Big Four Microcytic Anemias

- Iron Deficiency Anemia
- Thalassemias
- Hb C and Hb E
- Anemia of Inflammation
Does Iron Deficiency Matter?

- Most common cause of anemia worldwide
- In the U.S.
  - 10% of woman 20 to 49 years of age
  - Frequent after bariatric surgery (11 to 51%)
- Multiple adverse associations
  - Cognitive impairment and ADHD
  - Restless legs syndrome
  - Ischemic stroke (10x increased risk with IDA)
  - Anemia (increased mortality in older adults)

Patel KV et al., *Br. J HAem* 2009;145(4)
Diagnosis

- Gold standard remains BM aspirate
  - Requires stromal particles for interpretation
- Ferritin
  - If low, specific for iron deficiency
- Transferrin saturation <20%
- Soluble transferrin receptor/ferritin ratio
- Low reticulocyte hemoglobin <28 pg

## Diagnosis of Microcytic Anemia

<table>
<thead>
<tr>
<th>Test</th>
<th>Fe Def.</th>
<th>Inflammation</th>
<th>Combined</th>
<th>Thalassemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>MCV</td>
<td>↓</td>
<td>↓ or nl</td>
<td>↓</td>
<td>↓</td>
</tr>
<tr>
<td>RDW</td>
<td>↑</td>
<td>nl</td>
<td>↑</td>
<td>normal</td>
</tr>
<tr>
<td>Ferritin</td>
<td>↓</td>
<td>nl or ↑</td>
<td>nl or ↑</td>
<td>nl or ↑</td>
</tr>
<tr>
<td>Transferrin</td>
<td>↑</td>
<td>↓ or nl</td>
<td>↓ or nl</td>
<td>nl</td>
</tr>
<tr>
<td>Transferrin Sat</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
<td>nl or ↑</td>
</tr>
<tr>
<td>sTfR-Ferritin index</td>
<td>&gt;2</td>
<td>&lt;1</td>
<td>&gt;2</td>
<td>&lt;2</td>
</tr>
<tr>
<td>Reticulocyte Hb</td>
<td>&lt;28 pg</td>
<td>≥ 28 pg</td>
<td>&lt;28 pg</td>
<td>&lt;28 pg</td>
</tr>
<tr>
<td>Hepcidin</td>
<td>↓</td>
<td>↑</td>
<td>↑</td>
<td>nl</td>
</tr>
</tbody>
</table>

sTFR indicates soluble transferrin receptor

Smann AA et al. Int J Lab Hematol 2012;34;605-613
Etiology

• Inadequate absorption
  – Decreased dietary intake
  – Decreased absorption
• Increased iron losses
• Increased demand
Inadequate Absorption

• Limited iron or calories in diet
  – Too much alcohol, some vegetarian diets
  – No red meat, fortified or iron rich foods
  – No iron in TPN
Inadequate Absorption

• Decreased absorption
  – Atropic or autoimmune gastritis
  – Chronic treatment to reduce gastric acid
  – Gastric or duodenal surgery
  – Celiac Disease
  – Inflammation
    • Cancer
    • Chronic infection, e.g. *Heliobacter pylori* chronic gastritis
    • Inflammatory bowel disease or rheumatologic disorders
Increased Losses

• Gastrointestinal bleeding
  – Ulceration, gastritis, or varices
  – Polyps, AV malformations, or GI malignancy
  – Diverticulosis or hemorrhoids
  – Inflammatory bowel disease

• Menorrhagia

• Epistaxis

• Surgery

• Frequent blood donation
Increased Demand

• Pregnancy and breast feeding
  – Requires ~1000 mg of iron
• Rapid increase in lean body mass

http://irondeficiency.com/sites/default/files/IDA_content_hub_thumbnail_948x627_290316_0015_ANIMATIONS_pregnancy.jpg
http://store.bbcomcdn.com/deploy/images/brands/top150/Arnold_Ironmass_04.jpg
How should we give oral iron?

• Ferrous sulfate 325 mg once daily
  – Twice daily dosing decreases total absorption
  – Iron absorption ↑3X as dose ↑6X (40 → 240 mg)

• Rapid response
  – Reticulocytosis at 4 days, maximal by 7-10
  – Hemoglobin should increase >1 g/dl/week
  – Continue 2-3 months after resolution

• Other preparations
  – Less iron, more tolerable
  – Polysaccharide iron complex (Niferex)

Oral Treatment: Special Cases

• Decreased gastric acidity
  – Give with Vitamin C and check response
  – Low threshold for IV iron

• End Stage Renal Disease
  – Ferric citrate-median daily dose 8 gm (1680 mg Fe)
  – ↑ Tfsat, ferritin
  – ↓ IV iron and ESA use, GI and hepatobiliary SAEs
  – Approved by FDA as phosphate binder

Umanath K et al J Am Soc Nephrol 2015;26:2578-2587
Causes of Poor Response

• Poor adherence
• Administered with food
• Incorrect diagnosis
• Occult blood loss
• Decreased absorption
Evaluation of Poor Response

• Exclude other potential contributors
  – Evaluate iron stores, inflammation, losses

• Oral iron absorption test
  – Hold iron supplements for 24 hours
  – Administer ferrous sulfate elixir (5 mg/kg = 1mg/kg elemental iron) after overnight fast
  – Measure serum iron before, 1 and 2 hours
  – Serum iron should ↑ >100 ng/ml
  – Gastroenterology referral if ↓ absorption
Treatment Options

• Decreased absorption
  – Treat underlying process
  – Increased oral dose with Vitamin C
  – Intravenous iron +/- erythropoietin

• Increased losses
  – Treat coagulopathy, anatomical lesions
  – Intravenous iron if required
Expensive IV Preparations-AWP

- LMW Iron dextran (INFeD, $0.30/mg)
- Ferric gluconate (Ferrlecit, $0.51/mg)
- Iron sucrose (Venofer, $0.60/mg)
- Ferumoxytol 510 mg (Feraheme $1.72/mg)
- Ferric carboxymaltose (Injectafer, $1.56/mg)
- Oral
  - Ferric Citrate-$6/gm-typically $48/day
  - Ferrous sulfate $0.03 for 325 mg, $1-2/month

UptoDate Drug Information Accessed 4/10/17
Take Home Points

• Iron deficiency remains common
• Evaluation for etiology essential
• Oral iron effective for many
  – Inexpensive
  – Well tolerated at lower doses
  – Need to optimize absorption