Iron Deficiency, GI Bleeding and Anemia

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Outline

• Why should I care?
• When should I think about this and what do I look for?
• How should I be evaluated?
• How are they treated?
What is anemia?

• When there is a decrease in the number of red blood cells or hemoglobin in the blood, we call it anemia.

• Normal RBC count is 4-5.2 x 10^{12} cells/L

• Normal hemoglobin count:
  – Men: 13.5-17.5 g/dL (135-175 g/L)
  – Women: 12-16 g/dL (120-160 g/L)

Anemia

Anemia is a manifestation of an underlying condition, not a final diagnosis.

What are the different reasons for anemia?

- Blood loss
- Decreased production
- Increased destruction
What are the different reasons for anemia?

Blood loss

Decreased production

Increased destruction

- Menstrual bleeding
- Intestinal bleeding
- Nose bleeds

Nutritional
- Deficiency of iron, B12, folate acid

Comorbid disease
- Anemia of chronic disease or inflammation

Medication
- Chemotherapy, immune suppressants

Decreased erythropoietin or EPO

Bone marrow disorders
- Myelodysplasia, aplastic anemia, etc.

Chronic kidney disease
- Decreased erythropoietin or EPO

Inherited RBC disorders
- Sickle cell anemia, Thalassemia, Spherocytosis

Immune hemolytic disorders
- Related to infections, connective tissue disorders, idiopathic

Non-immune hemolytic disorders
- ETO, defective heart valves, PIH

Hemolytic disorders
- Related to infections, connective tissue disorders, idiopathic

Inherited RBC disorders
- Sickle cell anemia, Thalassemia, Spherocytosis
What are the manifestations of anemia?

Response to decreased blood supply
- Fast heartbeat (palpitations)

Response to blood loss (hypovolemia)
- Decreased blood pressure (hypotension)
- Decreased blood circulation to important organs (shock)
- Fainting (syncope)

Response to decreased oxygen supply (hypoxia)
- Weakness and fatigue
- Headaches
- Shortness of breath with exertion
- Decreased exercise tolerance

Iron

Why do we need iron?

- Production of hemoglobin and myoglobin
- Component of protein and enzymes
- Energy metabolism and immunity
How much iron and where is all this iron?

<table>
<thead>
<tr>
<th>Component</th>
<th>Iron Content</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin</td>
<td>2.5 grams</td>
</tr>
<tr>
<td>Storage iron</td>
<td>1 gram</td>
</tr>
<tr>
<td>Myoglobin, enzymes</td>
<td>400 mg</td>
</tr>
</tbody>
</table>

Women of child-bearing age have less stored iron.

How much iron do we need?

- Iron is not made in the human body
- Iron intake = Iron loss
- Daily iron absorption is 1-2 mg
- Recommended daily dietary iron intake is 8-18 mg of elemental iron (the amount of iron available for absorption by the body)

Special situations:
- Young women = 2 mg/day
- Adolescent age = ↑
- Pregnancy/childbirth/nursing = 1 gram

What are the sources of iron?

- **Heme Iron**
  - Red meats
  - Liver
  - Egg yolk
  - Fish (Salmon, Tuna)
  - Oysters

- **Non-heme Iron**
  - Vegetables
  - Fruits
  - Grains

Average diet consists of 1-2 mg of heme iron and 10-15 mg of non-heme iron.
What are the sources of iron?

10-20 mg of iron in diet

Absorb 1.2 mg

1.2 mg lost daily

What are the clinical features of iron deficiency?

- Brittle nails
- ‘Cravings’ (Pica)
- Restless leg syndrome

- Decreased ability to concentrate
- Poor memory
- Difficulty with sports

- Spooning of nails (Koilonychia)
- Smooth, shiny, painful tongue (Glossitis)
- Sores at the corners of the mouth (Angular Cheilitis)

What are the stages of iron deficiency?

Iron Deficiency

Iron Deficiency without Anemia

Iron Deficiency Anemia

Deficiency develops gradually over time

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How do we diagnose iron deficiency +/- anemia?

- Clinical suspicion is key
- Lab tests:
  - Complete blood count
  - Blood smear
  - Ferritin +/- iron panel

Ferritin below 15 is iron deficiency until proven otherwise. A normal ferritin does not rule out iron deficiency.

Gastrointestinal (GI) bleeding

- 25-30% of people with HHT develop symptomatic bleeding.
- Most common after age 40 years.
- Telangiectasia are most common in the stomach and small bowel. They are less common in the colon and almost never in the esophagus.
- Bleeding telangiectasia are most common in the stomach and proximal small bowel.

How common is GI bleeding in HHT?
GI Bleeding, Anemia & Iron Deficiency

How common is GI bleeding in HHT?

- Acute or Overt: uncommon
  - Black or maroon stool
  - Bright red or dark (coffee ground) emesis
  - Rapid drop in blood count
  - Can cause drop in blood pressure

- Chronic or Occult: more common
  - Anemia (low blood count), fatigue
  - Stool may or may not change color
  - Slow drop in blood count
  - Need for iron and blood transfusions

- Acute on Chronic:
  - Features of both acute and chronic

How do we evaluate for GI bleeding?

- Careful history
- Blood counts
- Gold standard: endoscopy
  - establish gastrointestinal involvement from HHT
  - diagnose and treat gastrointestinal bleeding

Confounding factors while assessing for GI bleeding

- Many patients have nosebleeds
  - swallowed blood can cause black stools

- Nosebleeds and gastrointestinal bleeding can both lower blood counts

- Black stools can indicate digested blood, but also iron pills

- SMAD4 mutations can be associated with polyps that can also bleed

- Non-HHT reasons for gastrointestinal bleeding (especially when bleeding is acute)
GI Bleeding, Anemia & Iron Deficiency

**Edoscopic evaluation for GI bleeding**

- Upper endoscopy
- Small bowel enteroscopy
  - Push enteroscopy
  - Capsule endoscopy
  - Single or double balloon enteroscopy
- Colonoscopy

**Capsule endoscopy**
GI Bleeding, Anemia & Iron Deficiency

**Treatment of iron deficiency anemia**

- **not discussing other causes of anemia today**

**How do we treat iron deficiency anemia?**

- First line treatment is oral iron

<table>
<thead>
<tr>
<th>Iron Sources</th>
<th>Amount of elemental iron</th>
<th>Lower amount of elemental iron</th>
<th>Better tolerated</th>
<th>Proferrin ES</th>
<th>Significance side effects nausea, bloating, reflux, constipation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ferrous sulfate, Ferrous gluconate, Ferrous fumarate</td>
<td>Higher amounts of elemental iron</td>
<td>Yes – a healthy diet that is rich in iron containing foods is important</td>
<td>No – eating red meats, liver, oysters and spinach three times a day is unlikely to make a big difference!</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Polysaccharide iron complex (Niferex, Ferrex, Nu-Iron, Poly-Iron)</td>
<td>Lower amount of elemental iron</td>
<td>Yes – a healthy diet that is rich in iron containing foods is important</td>
<td>No – eating red meats, liver, oysters and spinach three times a day is unlikely to make a big difference!</td>
<td></td>
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**Factors that affect dietary iron absorption!**

- Amount of heme iron versus non-heme iron in diet – heme iron is absorbed better
- Factors affecting iron absorption:
  - Calcium content in diet (don’t take iron with milk)
  - Phytates (oats, bran)
  - Polyphenols (tea)
- Vitamin C (ascorbic acid) improves iron absorption
Reasons for lack of response to oral iron treatment

- Not taking it daily (non-adherence)
- Co-existing B12/folate deficiency, other causes
- Poor absorption of oral iron
  - Use of coated iron pills
  - Rapid intestinal transit (bowel resection, bypass surgery)
  - Malabsorption (Sprue, gastritis)
  - Interference with absorption by other medications (antacids, calcium)
- Ongoing blood loss

When should we consider intravenous iron?

- Consider with intolerance to oral iron or ongoing blood loss
- Advantages:
  - Larger amounts of iron replaced at a time
  - Reliable and not impacted by dietary issues
  - Overcomes GI side effects of oral agents
- Disadvantages:
  - Time, cost
  - Side effects: weakness, body aches, headaches in first 2 days
  - Risk for serious reaction (anaphylaxis)

Intravenous iron preparations

<table>
<thead>
<tr>
<th>Generic names</th>
<th>Product names</th>
<th>Amount of elemental iron per dose</th>
<th>Duration of dose administration [all preparations require test dose]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ferric gluconate</td>
<td>Ferrlecit</td>
<td>125mg</td>
<td>2 hours</td>
</tr>
<tr>
<td>Iron sucrose</td>
<td>Venofer</td>
<td>200mg</td>
<td>15 minutes</td>
</tr>
<tr>
<td>Ferumoxytol</td>
<td>FeraHeme</td>
<td>510mg</td>
<td>15 minutes</td>
</tr>
<tr>
<td>Ferric carboxymaltose</td>
<td>Ferinject/Injectafer</td>
<td>750mg</td>
<td>15 minutes</td>
</tr>
<tr>
<td>Iron dextran [low molecular weight dextran]</td>
<td>INFeD [low molecular weight dextran]</td>
<td>50mg/mL – used to replace total iron stores in single infusion</td>
<td>4 hours</td>
</tr>
</tbody>
</table>
My approach to treatment of iron deficiency anemia

Confirm diagnosis (CBC, smear, iron panel)

- Oral iron
- Niferex
- Proferrin
- Alternate oral preparation
- No response

Aggressive treatment of bleeding (epistaxis, GI)

Counseling on dos and donts while taking iron

Intravenous iron

What type of follow-up is needed after treatment?

- CBC and ferritin monthly if bleeding is an ongoing issue
- One month after initiating iron replacement — include reticulocyte count to assess response to treatment
- If hemoglobin has not increased by at least 1 gram 1 month after oral iron, consider intravenous iron
- Continue regular oral iron to maintain iron stores (if oral iron is tolerated and you respond to it)
- In patients requiring intravenous iron, be proactive to stay ahead of ongoing blood loss

Thank you

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