Iron Deficiency Anemia

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- An 19 years old female started to complain of tiredness, dizziness, and tachypnea. She has been found to be pale, and having tachycardia. A lab test have shown a hemoglobin of 8 g/dl, and microcytic hypochromic RBCs.

Iron

- **Iron deficiency is the most common cause of chronic anemia – microcytic hypochromic anemia**
- **Most of the iron used to support hematopoiesis is derived from damaged RBCs.**
- **Normally small amounts are lost each day and thus, daily requirements are small.**

Iron

- **Daily requirements may increase and iron deficiency may develop in certain circumstances (growing children, pregnancy, menstruation, …etc).**

Iron

- **Iron content in the body in normal adults:**

	Iron content (mg)	
	Men	Women
Hemoglobin	3050	1700
Myoglobin	430	300
Enzymes	10	8
Transport (transferrin)	8	6
Storage (ferritin)	750	300
Total	4248	2314

Iron

Pharmacokinetics:

1. Absorption:

- The average diet contains 10-15 mg of elemental iron daily.
- Normally, 5-10% of which (0.5-1 mg) is absorbed, in the duodenum and proximal jejunum.
- Iron absorption increases in response to low iron stores or increased iron requirements:

Iron

A. 1-2 mg/day are absorbed in menstruating women.
B. 3-4 mg/day are absorbed in pregnant women.

- Iron in vegetables and grains, is often tightly bound to organic compounds and is much less available for absorption.
- Iron in meat protein is efficiently absorbed, because heme iron can be absorbed intact.

Iron

- **Nonheme iron in food and iron in inorganic iron salts must be reduced to ferrous iron (Fe^{2+}) to be absorbed from intestinal mucosal cells.**
- **Ferrous iron is transported efficiently across the luminal membrane of intestinal enterocytes by the divalent metal transporter (DMT1).**
- **Excess iron can be stored in mucosal cells as ferritin**

Iron

2. Transport:

- **Iron is transported in the plasma bound to transferrin.**
- **The transferrin-iron complex enters maturing erythroid cells by transferrin receptor-mediated endocytosis.**

Iron

- **The iron released in endosomes is used for hemoglobin synthesis, whereas the transferrin-transferrin receptor complex is recycled to the plasma membrane, where the transferrin dissociates and returns to plasma.**
- **Increased erythropoiesis is associated with increased number of transferrin receptors.**
- **Iron store depletion and iron deficiency are associated with increased serum transferrin.**

Iron

3. Storage:

- **Iron is stored as ferritin in macrophages in the liver, spleen, bone, and in parenchymal liver cells.**
- **Ferritin is proportionately detected in serum.**

Iron

4. Elimination:

- **No mechanism for iron excretion.**
- **Small amounts are lost by exfoliation of intestinal mucosal cells.**
- **Thus, regulation of iron balance is achieved by changing absorption and storage.**

Iron

Clinical Pharmacology:

A. Indications:

- **The only indication is treatment or prevention of iron deficiency anemia.**
- **It is seen in populations with:**

1. Increased iron requirements:

a. Infants, especially premature.

b. Children during rapid growth episodes.

c. Pregnant and lactating women.

Iron

2. **Increased iron loss:**

   a. Chronic kidney disease – loss of RBCs during hemodialysis

   b. Blood loss – most common in adults

   - Menstruation (~ 30mg/cycle)

   - Upper gastrointestinal bleeding

Iron

3. **Inadequate iron absorption:**

   a. Gastrectomy (?)

   b. Severe small bowel disease – generalized malabsorption.

Iron

B. Treatment:

1. Oral Ferrous Iron Salts:

Prepararion	Tablet size (mg)	Elemental iron per tablet
Ferrous sulfate hydrated	325	65
Ferrous gluconate	325	36
Ferrous fumarate	325	106

Iron

- In an iron-deficient individual, ~ 50-100 mg of iron can be incorporated into hemoglobin daily, and about 25% of iron given as ferrous sulfate can be absorbed.
- Therefore, 200- 400 mg of elemental iron should be given daily for 3-6 months after correction of the cause of the iron deficiency anemia, to correct the anemia and replenish iron stores.

Iron

Adverse effects:

1. **Nausea, epigastric discomfort, abdominal pain, constipation and diarrhea.**

- **These effects are dose-related and can be reduced by lowering the dose or giving it with meals or immediately after meals.**

2. **Black stools are common and may obscure the diagnosis of continued gastrointestinal blood loss.**

Iron

2. **Parenteral iron therapy:**

- **Should be reserved for patients:**

1) **Unable to tolerate oral iron.**
2) **Unable to absorb oral iron. Malabsorption syndromes, small bowel resection.**
3) **With extensive chronic blood loss.**

Iron

Preparations include:

A. Iron dextran:

- **It is a stable complex of ferric hydroxide and low-molecular-weight dextran containing 50 mg elemental iron/mL of solution.**

  It can be given by deep IM injection or IV infusion.

Adverse Effects:

1. After IM: local pain and tissue staining.

Iron

2. **After IV: headache, fever, arthralgia, nausea & vomiting, back pain, flushing, bronchospasm, anaphylaxis and death.**

- **The hypersensitivity reactions may be delayed 48-72 hours after administration.**

B. **Other alternative parenteral iron reparations are available.**

- **Antidotes (For iron excess): the chelating agents Deferoxamine (parenteral) and Deferasirox (PO).**