

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ
(وَفَوْقَ كُلِّ ذِي عِلْمٍ عَلِيمٌ)



HLS Pharmacology | FINAL 1

Iron Deficiency Anemia



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بسم الله الرحمن الرحيم،

نرجو منكم الدعاء لزميلنا في الدفعة
عون العدوان، الذي وافته المنية.

اللهم ارحمه واغفر له، وأسكنه فسيح جناتك، وأنر قبره وأنس وحشته، واجعل قبره روضةً من رياض الجنة.

اللهم اجبر قلوب أهله وذويه، وارزقهم الصبر والسلوان، وألهمهم جميل الصبر وحسن العزاء.

رحمه الله رحمةً واسعةً وأسكنه الفردوس الأعلى من الجنة...

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.**

This typical history for micro cystic hypochromic anemia which has many causes :

Vitamin B6 deficiency

Lead poisoning

Iron deficiency ,most common

Why it's typical? Because females have regular blood loss during menstruation so they more susceptible to iron deficiency if not get enough iron from their diet

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**(that why absorption is low)

Iron

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

Normally 10% be absorbed , but in **Growing children** absorbed increased as the result of increase requirements (the teenagers have high growth spurt).

Also in **Pregnancy** (the fetus takes necessary from the mother's blood

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

Why myoglobin is lower in women?
Because of lower muscular mass than males.

~ Relative anemia

Iron~Replacement treatment

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. If we have a problem or disease absorption won't occur
- Iron absorption increases in response to **low iron stores** or **increased iron requirements**:

Iron

- A. 1-2 mg/day are absorbed in menstruating women, When females aren't on their menstrual cycle, iron level will be normal same as males.
- B. 3-4 mg/day are absorbed in pregnant women for growing fetus.
- Iron in vegetable leafy green like spinach and grains, is often tightly bound to organic compounds and is much less available for absorption.

Why it less? Because it's in ferric form need to reduced by ascorbic acid(like lemon), because our body absorbs in the ferrous form.

- Iron in red 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** Amount of ferritin in serum is proportion to the amount in storage so In blood test , we test ferritin not iron

Iron

2. Transport:

- Iron is transported in the plasma bound to transferrin (A carrier of ferric not ferrous)
- The transferrin-iron complex enters maturing erythroid cells by **transferrin receptor-mediated endocytosis**.

The way that we give it : Oral or injection
But, injection don't always have the fastest respond cause it mainly depends on the bone marrow.

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(to increase the binding to any available iron)

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
- .What detect in serum Give us an insight of what is stored (circulating ferritin is proportional to ferritin amount stored in body) .

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 **common** ,
- because of the misuse chronic NSAIDs (without prescription) occult bleeding may happen .

Iron

3. Inadequate iron absorption:

a. Gastrectomy (?) HCl, Why is HCl necessary?

Gastrectomy → ↓ Gastric acid (HCl) → ↓ Iron absorption → Iron deficiency anemia.

1. It is involved in the early stages of protein digestion.

2. It helps conversion of ferric iron (Fe^{3+}) into ferrous iron (Fe^{2+}).

Both gastric acid (HCl) and vitamin C are required to convert ferric iron, which is present in leafy vegetables, into the absorbable ferrous form.

b. Severe small bowel disease – generalized malabsorption, which results in multiple nutritional deficiencies, including iron deficiency.

اللهم آانس وحشته ونور قبره وأرحمه
و اغفر له وتجاوز عنه يارب العالمين ..

Iron

Very important slide

B. Treatment:

1. Oral Ferrous Iron Salts:

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

The treatment of iron deficiency anemia involves **iron replacement**, as dietary intake alone is insufficient. Therefore, patients are prescribed **ferrous iron salts**.

When treating iron deficiency anemia, the type of iron salt and tablet size are not the primary considerations. The most important factor is the **amount of elemental iron per tablet**.

The required iron dose is calculated based on the elemental iron content of each tablet.

Although the three iron preparations presented in the table have the same tablet size, they contain different amounts of elemental iron. Therefore, **they are not identical or interchangeable**, and the dose must be calculated according to their elemental iron content.

Iron salts are generally **not well tolerated** by patients because they can cause gastric irritation.

To reduce this irritation, patients may be advised to take iron **with meals rather than before or after meals**.

Taking iron with food reduces its contact with the gastric mucosa, thereby decreasing irritation. However, this may reduce the effectiveness of iron treatment.

Differences Between Ferrous Iron Preparations

Physicians may recommend iron preparations that cause less gastric irritation.

Ferrous gluconate:

- Contains less elemental iron.
- May cause less gastric irritation.
- Taking it with meals may further reduce irritation.

Ferrous fumarate:

- Is rarely tolerated by patients.

Clinical Implications for Dose Calculation

When calculating the required dose of ferrous iron salts, the elemental iron content must be considered.

For example, a patient may require **more ferrous gluconate tablets than ferrous sulfate tablets** to receive the same amount of elemental iron.

Although ferrous gluconate contains less elemental iron per tablet, increasing the number of tablets to achieve the required dose increases the total iron intake.

Consequently, the patient may experience gastric irritation again, despite initially choosing a preparation with a lower elemental iron content.

Key point: The choice and dosage of iron preparations should consider both the amount of elemental iron and the patient's ability to tolerate the treatment.

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.**

Remember: Approximately 10% of dietary iron is absorbed, compared with 25% of ferrous sulfate. Therefore, a tablet containing 65 mg of elemental iron provides approximately 16 mg of absorbed iron.

- 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.**

For example, a daily dose of 300 mg of elemental iron corresponds to approximately **5 ferrous sulfate tablets or 10 ferrous gluconate tablets (or slightly fewer).**

Taking multiple tablets in a single dose increases gastric irritation, which may affect treatment tolerability. Treatment should continue even after hemoglobin levels normalize, as restoring iron stores is also essential. If treatment is inadequate or poorly tolerated due to significant gastric irritation, a longer treatment duration may be required.

- These dose calculations are particularly important in clinical practice rather than exams.

Iron

Adverse effects:

1. Nausea, epigastric discomfort, abdominal pain, constipation and diarrhea.
 - These are the most common adverse effects of oral iron therapy.
 - Constipation is usually followed by diarrhea after approximately one week.
 - These effects should not be underestimated, as they are a major cause of patient noncompliance with treatment.
- 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.

- Black, tar-like stools may occur with gastrointestinal hemorrhage, particularly from the upper gastrointestinal tract, as digested hemoglobin passes through the digestive tract.
- If gastrointestinal bleeding was the underlying cause of anemia, patients receiving iron therapy may become concerned that persistent black stools indicate continued bleeding.
- This can cause unnecessary anxiety and may complicate the distinction between iron-induced stool discoloration and ongoing gastrointestinal bleeding.
- Therefore, physicians should explain this adverse effect to patients to prevent confusion and unnecessary concern.

Iron

2. Parenteral iron therapy, an alternative to oral iron therapy:

Important: Administering iron parenterally does not necessarily result in a faster or better response than oral iron therapy.

- The rate of recovery depends on the response of the **bone marrow**, rather than the route of iron administration.
- Therefore, the response to treatment depends on the ability of the bone marrow to respond.
- IV iron injections are given for specific indications, not simply to accelerate recovery.

Although IV injections are generally administered to achieve a faster response for various reasons, **this is not the case with iron therapy**. IV iron does not necessarily produce a faster response than oral iron, as the rate of recovery depends on the bone marrow's ability to respond.

- **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, such as **Regional enteritis (Crohn's disease) and Ulcerative colitis (UC)**: May cause more continuous bleeding.
 - In ulcerative colitis, abnormalities primarily affect the colon, although the disease does not necessarily involve the entire colon.
 - Regional enteritis primarily affects the small intestine, but the large intestine may also be involved.

Iron

Preparations include:

A. Iron dextran, the most important parenteral iron preparation discussed:

- 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; resulting in greenish-blue skin discoloration.

- Staining occurs when some of the injected iron leaks back through the needle track toward the skin.
- To minimize this complication, iron dextran should be administered by deep IM injection using the **Z-track technique**.

Z-track technique:

- Pull the skin laterally before inserting the needle.
- Administer the injection into the muscle.
- Withdraw the needle and release the skin, allowing it to return to its original position.

This creates a displaced needle track, preventing the injected iron from leaking back toward the skin and reducing tissue staining.

Iron

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

IV iron infusion should be administered under medical observation in a clinic or emergency setting because of the risk of severe hypersensitivity reactions, including anaphylaxis.

Acute reactions may include bronchospasm and anaphylaxis.

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

B. Other alternative parenteral iron preparations are available.

Excessive iron administration, including an overdose resulting from incorrect dose calculation, may lead to iron accumulation in organs and cause tissue damage.

- **Antidotes (For iron excess):** the chelating agents; these agents bind excess iron and facilitate its elimination from the body.
- Deferoxamine (parenteral) and Deferasirox (PO).

Additional Resources:

رسالة من الفريق العلمي:



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Corrections from previous versions:

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