



HLS

MODIFIED NO5

PHARMACOLOGY

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Hematopoiesis

Color code

■	Slides
■	Doctor
■	Additional info
■	Important

- **200 billion new blood cells per day**
- **The hematopoietic machinery requires a constant supply iron, vitamin B₁₂, and folic acid.**
- **Hematopoietic growth factors, proteins that regulate the proliferation and differentiation of hematopoietic cells.**
- **Inadequate supplies of either the essential nutrients or the growth factors result in deficiency of functional blood cells called Anemia.**
- **A deficiency in oxygen-carrying erythrocytes, is the most common and several forms are easily treated**

Iron Deficiency Anemia

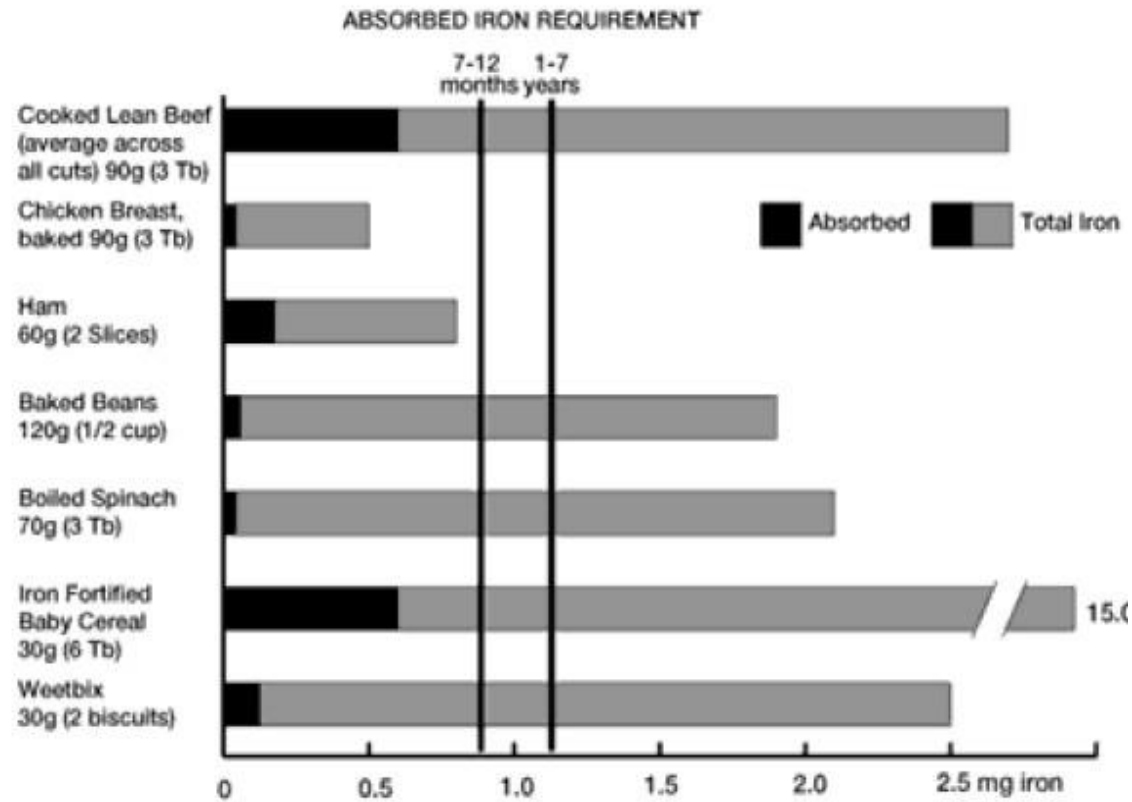
The most common type of anemia that affected nearly half of the population, especially in females because of menstruation and pregnancy .

- Iron forms the nucleus of the iron-porphyrin heme ring, which together with globin chains forms hemoglobin.
- In the absence of adequate iron, small erythrocytes with insufficient hemoglobin are formed, giving rise to microcytic hypochromic anemia.
- Iron deficiency is the most common cause of chronic anemia.
- The cardiovascular adaptations to chronic anemia causing tachycardia, increased cardiac output, vasodilation, this compensation can worsen the condition and cause heart failure.

We need to treat this condition due to iron loss and the reduction of red blood cells (RBCs), which are essential for transporting oxygen to tissues. This deficiency can lead to cardiovascular adaptations

Iron Deficiency Anemia

- Body has ~ 3.5 g total iron; 2.5 g is in hgb.
 - Humans are poor at absorption, usually only 5-10% of intake is absorbed, this is increased to 20-30% in deficiency as an adaptive response.
 - Requirement:
 - Adult males 13 ug/kg.
 - Female 21 ug/kg,
 - pregnant women and infants 80 ug/kg.
 - dietary iron in form of heme (meat) can be absorbed intact
 - Non-heme iron from vegetables, grains, therapeutic iron must be broken down to elemental iron for absorption
- Heme iron which is sourced from meat, is absorbed more efficiently by the body than non-heme iron, which is present in plant-based foods.



www.ironpanel.org.au/AIS/AISpics/IronGraph.gif

This figure shows the amount of iron absorbed from various foods.

It's clear that iron absorption is significantly higher from cooked lean beef than iron-fortified baby cereal.

Indications for the Use of Iron

- **Treatment or prevention of iron deficiency anemia.**
- **Iron deficiency is commonly seen in populations with increased iron requirements.**
 - ✓ **infants, especially premature infants; children during rapid growth periods;**
 - ✓ **pregnant and lactating women;**
 - ✓ **chronic kidney disease who lose erythrocytes at a relatively high rate during hemodialysis**
and also form them at a high rate as a result of treatment with the erythrocyte growth factor erythropoietin.

Indications for the Use of Iron

- **Inadequate iron absorption can also cause iron deficiency.**
 - **This is seen frequently after gastrectomy**
 - **severe small bowel disease that results in generalized malabsorption.**

Let's summarize the indication for the use of iron :

1- populations with increased iron requirements: infants, pregnant and lactating women, chronic kidney disease

2- inadequate iron absorption due to gastrectomy and severe small bowel disease

Oral Iron

- Preparations:
 - **ferrous fumarate 33% elemental iron.**
 - **ferrous gluconate 12% iron.**
 - **ferrous sulfate 20%.**

These percentages show the levels of iron in each drug, making **ferrous fumarate the most effective option among them.**

Oral Iron

Adverse Effects: 20-25% have GI problems: nausea, epigastric pain, constipation, abdominal. Cramps. Especially in female

- **Food decreases absorption by 30 - 50%.**

Food affects iron absorption, which is why it is often recommended to take iron supplements on an empty stomach. However, doing so can sometimes lead to gastrointestinal issues, particularly in females. Therefore, it is advised to take iron with a small amount of food to mitigate these problems.

- **– Drug interactions: tetracycline and antacids decrease iron absorption.**

Tetracycline chelates iron, while antacids reduce acidity, resulting in decreased iron absorption due to the oxidation of iron.

Oral Iron

- Treatment with oral iron should be continued for 3–6 months in order to replenishes iron stores **in the liver mainly**
- Patients taking oral iron develop black stools and **epigastric distress cramps**.

Parenteral Iron (Depot iron therapy)

- should be reserved for

(1) patients with documented iron deficiency

(2) patients who are unable to tolerate or absorb oral iron

(3) Patients with extensive chronic anemia who can't be maintained with oral iron alone, as :

a. patients with advanced chronic renal disease requiring hemodialysis and treatment with erythropoietin to stimulate hematopoiesis.

b. inflammatory bowel disease involving the proximal small bowel, and malabsorption syndromes.

Iron is commonly administered orally, but when patients are unable to tolerate nausea, vomiting, or pain in the upper abdomen, parenteral iron can be administered as an alternative. It is usually given via IV injections, as intramuscular injections can lead to irritation, skin discoloration, and discomfort around the injection area.

Parenteral Iron

It can be given by deep intramuscular injection or by intravenous infusion, although the intravenous route is used most commonly.

Intravenous administration eliminates the local pain and tissue staining that often occur with the intramuscular route and allows delivery of the entire dose of iron necessary to correct the iron deficiency at one time.

- Adverse effects of intravenous iron dextran therapy include
 1. headache, light-headedness, (the most common effect)
 2. fever, arthralgias, back pain,
 3. flushing, urticaria, bronchospasm, and, rarely, anaphylaxis and death.

*Parenteral iron does not cause black stools because it is administered intravenously rather than orally.

Parenteral iron has the potential to cause allergic responses, and in uncommon cases, this reaction can progress to anaphylaxis.

Acute iron toxicity

Might be fatal

- Exclusively in young children who accidentally ingest iron tablets because it seems candies.
- as few as 10 tablets can be lethal in young children.
- Children who are poisoned with oral iron experience necrotizing gastroenteritis, with vomiting, abdominal pain, and bloody diarrhea followed by shock, lethargy, and dyspnea.

What is the approach in this case?

- Whole bowel irrigation should be performed to flush out unabsorbed pills.
- Deferoxamine, a potent iron-chelating compound, can be given systemically to bind iron that has already been absorbed and to promote its excretion in urine and feces.

Deferoxamine is an antidote for iron and is used in cases of iron toxicity.

Antidote is a substance that can counteract a form of poisoning

Chronic iron toxicity (iron overload) hemochromatosis

- **excess iron is deposited in the heart, liver, pancreas, and other organs. It can lead to organ failure and death.**
- **It most commonly occurs in patients with inherited hemochromatosis, a disorder characterized by excessive iron absorption.**
- **and in patients who receive many red cell transfusions over a long period of time (eg, patients with thalassemia major).**
- **Chronic iron overload in the absence of anemia is most efficiently treated by intermittent phlebotomy. (One unit of blood can be removed every week)**

Megaloblastic Anemias (macrocytic)

Marrow disorder caused by defective DNA synthesis.

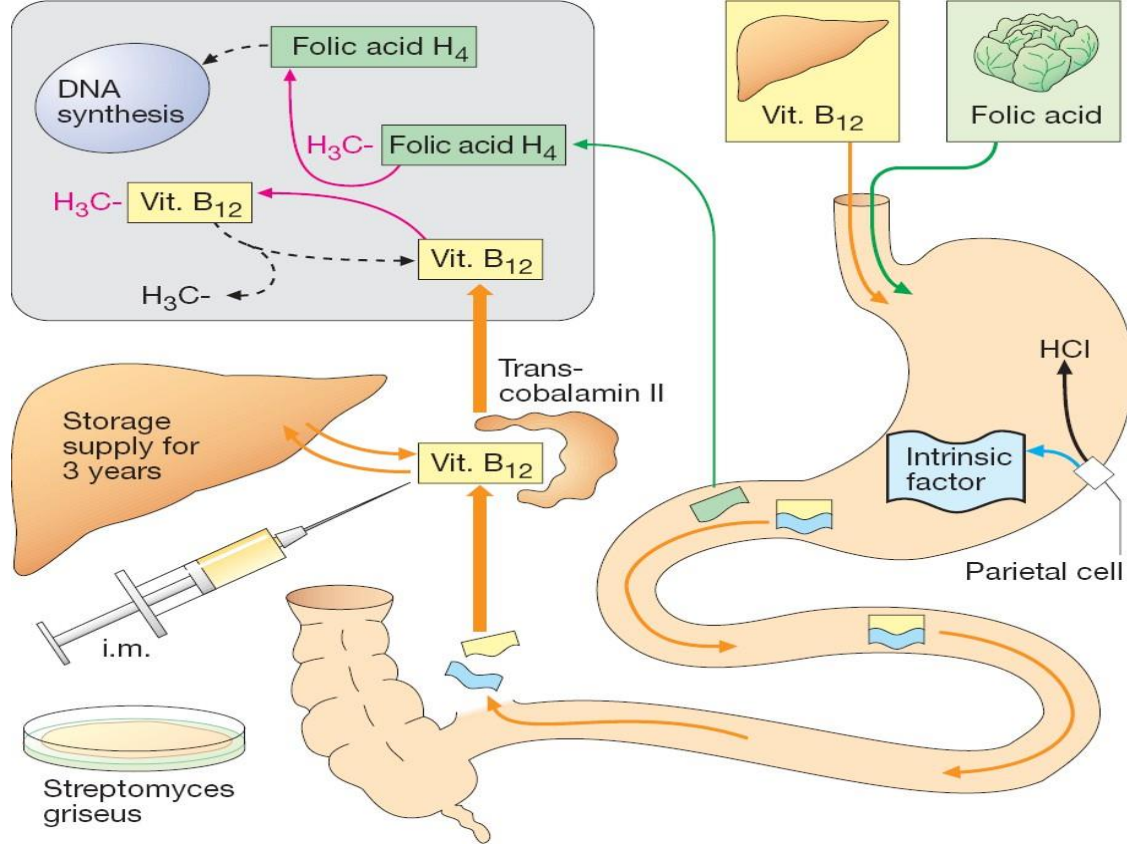
Caused by:

- 1) Vit. B12 Deficiency → more common and cause neurological symptoms.**
- 2) Folic Acid Deficiency → without neurological symptoms.**

- **Anemia may result from (1) deficiency (strict vegetarians, Vit. B12 primarily found in animal products like meat) or impaired absorption (Pernicious anemia) from decreased intrinsic factor (protein secreted by stomach), gastrectomy, malnutrition, RA, thyroid conditions.**

Vitamin B12 is used to treat or prevent deficiency.

Vit B12 deficiency distinguished from other anemias by its Neurological Syndrome Delirium, numbness, tingling of hand and feet, loss of fine learned B12 movements, difficulty in walking, bladder and bowel dysfunction.



Folic acid (Vit B6) and Vit B12 are used to synthesize CH₃ which is important in DNA synthesis, so DNA synthesis is stimulated with higher level of those vitamins.

In patient with vit B12 deficiency, impaired DNA synthesis can be masked by folate supplement while neurological symptoms can't.

- Vitamin B₁₂ is used to treat or prevent deficiency.
- There is oral form of Vit B12 but injectable only benefit if deficiency
 - Neurologic symptoms (paresthesias occur first, then balance) in severe deficiency may be irreversible after several months
 - May need lifelong injections if malabsorption **as in pernicious anemia** ; can not absorb B12/intrinsic factor complex

Note:

1. Folic acid alleviates anemic syndrome but the neurological disorder progresses.
2. Antagonism of Vit B12 by nitrous oxide (inactivates Vit B₁₂ dependent enzymes) leads to megaloblastic response, neuropathies.

Vitamin B₁₂

- Vitamin B₁₂ for parenteral injection is available as cyanocobalamin or hydroxocobalamin. Hydroxocobalamin is preferred because it is more highly protein-bound and therefore remains longer in the circulation.
- Initial therapy should consist of 100–1000 mcg of vitamin B₁₂ intramuscularly daily or every other day for 1–2 weeks to replenish body stores.
- 1000 mcg dose is administered in a high level of vitamin B₁₂ deficiency.
- Maintenance therapy consists of 100–1000 mcg intramuscularly once a month for life.
- If neurologic abnormalities are present, maintenance therapy injections should be given every 1–2 weeks for 6 months before switching to monthly injections.
- Oral vitamin B₁₂-intrinsic factor mixtures and liver extracts should not be used to treat vitamin B₁₂ deficiency; however, oral doses of 1000 mcg of vitamin B₁₂ daily are usually sufficient to treat patients with pernicious anemia who refuse or cannot tolerate the injections.

Megaloblastic Anemia- continued

- **Folic Acid (folate, Vitamin B9) found in fresh green veggies, yeast, animal proteins but easily destroyed.**
- **Anemia may be indistinguishable from B12 deficiency but occurs rapidly and Vit B12 causes neurological symptoms.**
- **Must evaluate fully before treatment- folate therapy will correct hematological abnormalities but not neurological problems**
- **deficiency; B12 deficiency may be masked by folate supplementation**

- because body stores of folates are relatively low and daily requirements high, folic acid deficiency and megaloblastic anemia can develop within 1–6 months after the intake of folic acid stops, depending on the patient's nutritional status and the rate of folate utilization.
- Patients with alcohol dependence and patients with liver disease can develop folic acid deficiency because of poor diet and diminished hepatic storage of folates.
- Patients who require renal dialysis develop folic acid deficiency because folates are removed from the plasma during the dialysis procedure.

FOLIC ACID

- Drug interactions:

In large doses may counteract the effects of anticonvulsants potentially leading to seizures.

- Adverse reactions:

Erythema, itching, and rash.

سُورَةُ التَّوْبَةِ

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قُلِ الْحَمْدُ لِلَّهِ وَسَلَامٌ عَلَىٰ عِبَادِهِ الَّذِينَ اصْطَفَىٰ ۗ اللَّهُ
خَيْرٌ أَمَّا يُشْرِكُونَ ﴿٥٩﴾

VERSIONS	SLIDE #	BEFORE CORRECTION	AFTER CORRECTION
V1→V2			
V2→V3			



امسح الرمز و شاركنا بأفكارك لتحسين أدائنا !!