HEMATOLOGY
&LYMPH SYSTEM

Pharmacology sheet

Number	5
Done BY	Ruba Hussein
Correction	Abdullah Alzibdeh
Doctor	Dr. Malik

بسم الله الرحمن الرحيم

Before we start: Dr. Malik suggested for the third immunity lecture to be a continuation for the hematology pharmacology. And he will discuss the drugs for treating leukemia and lymphoma in a different way than the last year. Now let's start the lecture:

In hematopoiesis, 200 billion RBCs are produced each day in a normal adult, but it will be affected in case of increase demand such as pregnancy, or it will decrease with effect of chemotherapy, for example.

In hematopoiesis we need nearly all minerals (Fe, Ca, Na, K, Zn, Cu…etc) and vitamins (Folic acid, vit.B12) and each one has a specific vital role.

Iron deficiency anemia:

As you already know, this anemia results from low iron concentration and storage in the blood, and this will directly affect the production of Hb, which will result in small RBCs with low Hb **(microcytic hypochromic**.)

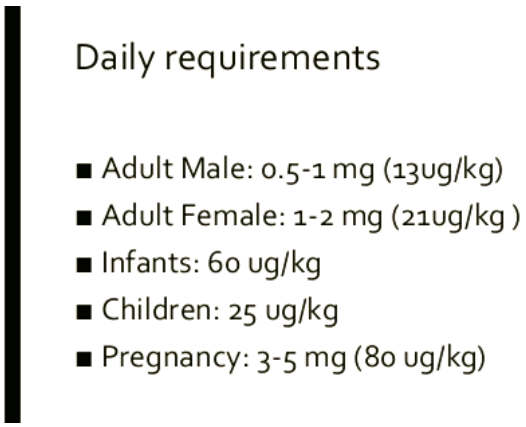
Iron deficiency is the most common cause of chronic anemia.

Iron deficiency anemia affects the cardiovascular system, causing tachycardia (abnormal cardiac rhythm, increased heart rate so that it pumps very fast in order to compensate for the low volume and low transport of blood and oxygen, respectively), hyperplasia of the cardiac muscle (to compensate also) and eventually heart failure, so at last you can't and you shouldn't let the patient stay anemic, you have to treat him to avoid all these consequences.

Total iron in the body is 3.5 g (2.5 g in Hb; the rest is either in myoglobin or bound to transferrin or stored in ferritin).

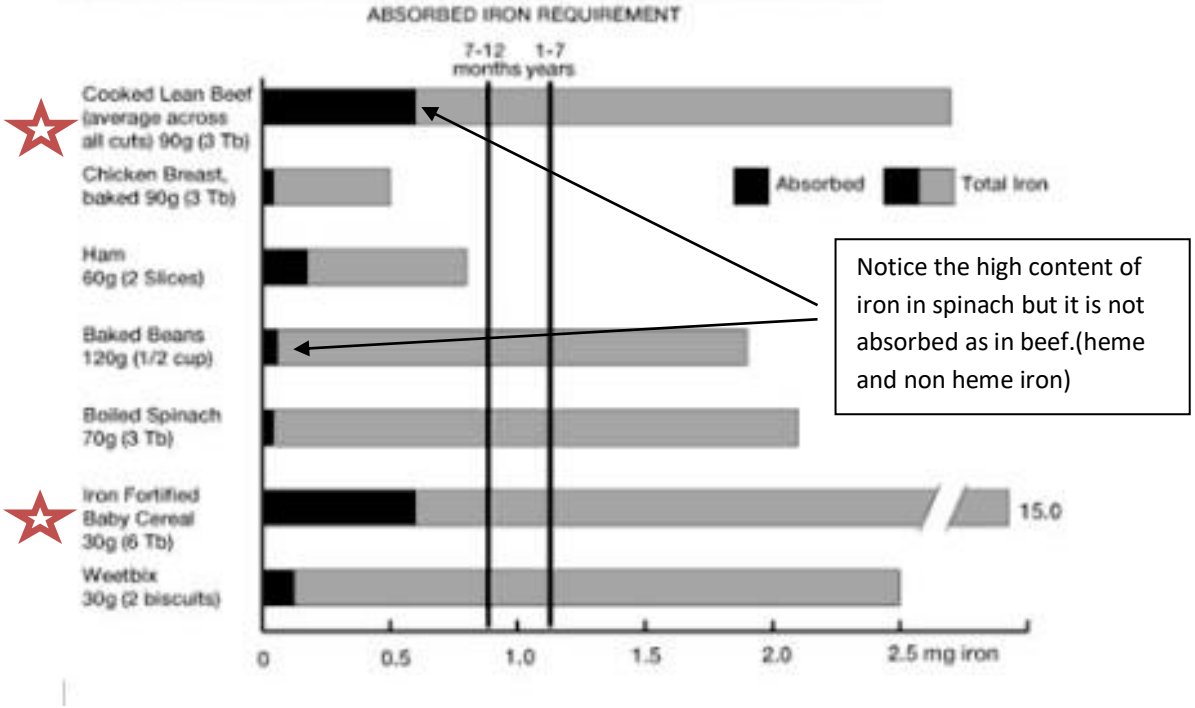
Absorbed iron is usually 10 to 25 % of ingested iron, and this percentage increases to 30 % in case of iron deficiency anemia.

Daily iron requirements:



In the diet, we have two forms of iron; it can either be bound to heme and is better absorbed (meat), or non heme iron as in vegetables and fruits, and it needs to be disintegrated from proteins in order to be absorbed: 10 min.

Figure 1 _ Iron content of common foods consumed by children



Treatment or prevention of iron deficiency anemia :

Use iron supplements in case of:

- infants
- pregnant and lactating women
- chronic kidney disease (we need strong intervention because dialysis causes loss of erythrocytes at relatively high rate and also because of kidney disease the kidneys can't produce erythropoietin so we give those patients an exogenous erythropoietin by injection (nice drug but expensive), which will increase hematopoiesis, and increase demand on iron.
- patients with problem in absorption; such patients who had gastrectomy, small bowl disease, colon cancer (bleeding), Crohn's disease, ulcerative colitis and inflammatory bowel disease and any disease that is related to the upper duodenum, all will affect iron absorption.

Oral iron supplements are on three levels:

The doctor made a mistake in the previous sheet and he corrected it in this sheet:

1. **Ferrous fumarate : 33%** highly iron content , it is the best (new) but is associated with more side effect
2. **Ferrous sulphate: 20%** the drug of choice; has lesser amount of iron than ferrous fumarate but with lesser side effects.

3. **Ferrous gluconate: 12%** very low iron with the least side effects.

The doctor said that when the iron content increases in the tablet, the side effects increase, and that's why ferrous fumarate causes a higher side effect than ferrous sulphate and glutamate.

Side effects of oral iron supplements: (important)

25 % of patients taking oral iron will suffer from side effects and mainly are related to the GI tract :

- nausea
- epigastric pain
- constipation
- abdominal cramps
- black stole , not in all patients

Iron should be taken before food but;

Because of those side effects, some patients can't tolerate them; so they either take it with food (this will decrease its absorption), or we turn to parenteral iron (IV) as a last choice, because it develops other side effects.

Drugs that decrease iron absorption:

- anti-acids
- tetracyclines

For how long we should take oral iron supplements?

>> Treatment with oral iron should be continued for 3 to 6 months in order to replenish iron store, then we measure iron levels, if normal we should maintain it with food (heme source iron, meat).

Parental iron:

IV, might be taken IM (not preferable); it causes staining to muscular tissue. 20 min.

Mostly prescribed for:

- The patients with very severe iron deficiency.
- Patients who can't tolerate or absorb oral iron.
- Patients with extensive chronic anemia (patients with kidney failure) who take erythropoietin which needs high amounts of iron.

Side effects of parental iron:

- headache

- fever
- arthralgia
- back pain

- In the past it causes: flushing, urticarial bronchospasm, anaphylaxis and death.

These side effects are very rare now because in the past they used to give iron alone then they started to give iron with dextran and that reduces the side effects and now they give it with sucrose nearly those side effects didn't appear.

The sucrose iron is much better.

Acute iron toxicity:

Common exclusively in young children who accidently ingest iron tablets because they think it is like candy and the coat of the tablet contains sugar which has a sweet taste.

As few as 10 tablets can be lethal in young children, 2 g can cause toxicity:

Toxicity causes:

- necrotizing gastroenteritis
- vomiting
- abdominal pain
- bloody diarrhea
- shock ,lethargy and dyspepsia
- maybe death

Don't wait for signs and symptoms!

Never wait for signs and symptoms for iron toxicity (Dr. by mistake said " for iron deficiency anemia")

Once the child comes to the emergency room and his mother told you that he ingested a whole iron tablet you should work fast; because we don't want the iron to be absorbed

You should do :

1. whole bowl irrigation or gastric lavage غسيل معدة
2. give Deferoxamine

Don't give him charcoal (حبوب الفحم); it doesn't absorb iron.

Chronic iron toxicity:

- Iron overload and hemochromatosis: common in patients with genetically inherited hemochromatosis.
- Patients with repetitive blood transfusion; such in thalassemia and hemophilia.

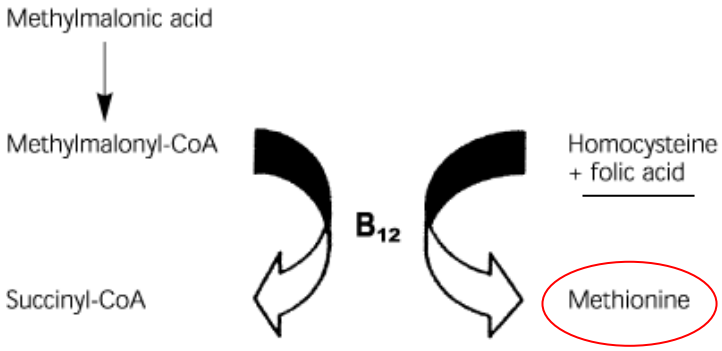
Chronic iron overload in absence of anemia is treated with blood donation; one unit of blood can be removed from the patient every week.

Megaloblastic anemia:

Can result due to:

- Folate deficiency
- Vit. B12 deficiency

Both are linked with DNA synthesis; simply because they are linked with coupling reaction (transport of methyl group to homocystiene and then production of methionine.)



When there is deficiency in vit. B12 or folic acid , this will decrease the synthesis of DNA and during the erythropoeisis the cell should increase both DNA and cytoplasm and then divide but here there is no enough DNA so the cell increases in cytoplasm with no division and when the cell progress in maturation and differentiation it will result in a big RBC , **Macrocytic**. 30 min

- The main causes of B12 deficiency is lack of the intrinsic factors that is responsible for the absorption of vitamin B12; such as in pernicious anemia.
- Folic acid deficiency caused by hemodialysis, and other causes.

Vit.B12 deficiency needs 6 to 20 years to appear because there is a reapportion system in our body

Signs and symptoms of Vitamin B12 deficiency: appear when there is severe deficiency

- Neurological symptoms ; paresthesia
- Numbness

Dr. said there is no relation between fatigue syndrome and vitamin B12 deficiency.

It is not enough to treat megaloblastic anemia with folic acid only or with vit.B12 only; you have to investigate whether this megaloblastic anemia is caused by folate or B12 deficiency.

? ? A common question asked by patient is whether to prescribe B12 to them even though they don't suffer from and deficiency or not? or whether to take B12 that is already presented in the their fridge or not ?

>> The Dr. said that our body works in a way that if there was an efficient amount of vit.B12 then the body will not absorbed an extra amount. 40 min

For how much to take B12?

>> Vit.B12 for prenatal injection is available as cyanocobalamin and hydroxocoblamin (better.)

>> Initial therapy should consist of a 100 or 1000 mcg of vit.B12

>> IM daily or every other day for one to two weeks to replenish the body stores then we give every week if the patient still had neurological symptoms and doesn't take enough B12 from diet or has pernicious anemia (lack of intrinsic factor) we give every week for six months then we give once monthly for the life .

Is oral vitamin B12 efficient?

>> Efficiency of oral is lesser than injection, but we can use it after we replenish the body stores of vitamin B12 (a maintenance therapy.)

Oral vit.B12:

- Vit.B12 with intrinsic factors if the patient is intrinsic factors deficient (pernicious anemia.)
- Vit. B12 without intrinsic factors.

Folic acid :

Folic acid is very important mainly in pregnant women because its deficiency is linked to neural tube formation defects. So, in Jordan, once the woman becomes pregnant, we put her on 5 months of folic acid.

In Jordan, bread is fortified; they add folic acid to the bread so there is no problem with folic acid but always be on the track.

The guide line says you should give folic acid for 3 months to women before they think of becoming pregnant.

We give it orally and there is no need for injection because its absorption is very good.

Megaloblastic anemia caused by folate deficiency develops within 6 months, depending on patient nutritional state.

Drugs that cause Folate deficiency:

- Methotrexate (dihydrofolate reductase inhibitor) a cancer drug
- Sulphonamides
- Trimethoprime ; might cause folate deficiency in children

The End