Hematology

BIOCHEMISTRY

☑ Sheet ☐ Slide ☐ Handout

Number: **7**

Subject: **Iron regulation**

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Price:

**** This sheet was written according to the recording that belongs to section 2.**

-Last lecture we talked about transport of iron, transferrin, ferritin, and compartment of the iron.

*Metabolism of iron:

-"Iron is a one way metabolite"

- Iron is obtained either from plant origin or animal origin.
-Iron in heme is easily absorbed 15%.
-Iron in plants is not easily absorbed 5%, it needs cooking, and need gastric acidity low pH; in order to free iron and then help in its reduction (Vit C and glutathione help in reduction from ferric to ferrous, that's why especially females who take iron it's preferred to take it with Vit C in order to be absorbed).

There are products that reduce iron absorption like:

- Tannin (tannic acid In dark tea)
- Oxalate
- Phytates
- Inorganic phosphate
- Antiacids

These are not recommended to take with iron.

Iron has to be in the ferrous state In order to be absorbed by mucosal cells, duodenum is the major site of absorption, and some of the upper jejunum.

- Once the ferrous has been absorbed, it will undergo oxidation then it will link to Apoferritin (only links ferric) in mucosal cells.

- If the body needs iron it will undergo reduction to ferrous by ferroreductase in ferritin in order to cross and reach the plasma.

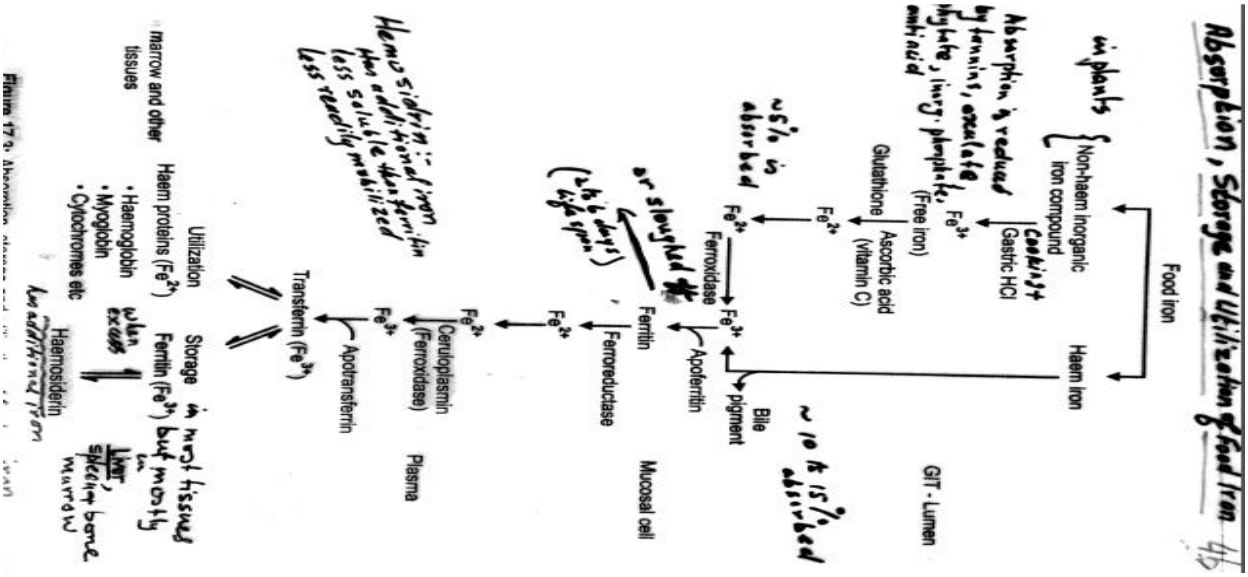
- If the iron is not needed the iron bound on ferritin is being sloughed (life span from 2 to 6 days) which will be destroyed and emptied in the lumen and it will be excreted.

So here occurs the real regulation of iron; between mucosal cells and blood. (If it's needed it will continue, if not it will be removed.)

- In the plasma, ferrous will be oxidized to ferric by ceruloplasmin which has ferroxidase activity.

- Then ferric binds to the transferrin to be distributed to most tissues, either for utilization (to make HB, MB, Cytochromes…), or enter the tissues for storage (mainly liver, spleen, bone marrow).

- If the iron was in excess in ferritin it will become Haemosiderin.



Some few points from slides:

- Ferrous is only absorbed by mucosal cells.
- Majority of dietary iron is ferric in complex with organic compound.
- Spinach is a poor source of available iron though it's rich with it (because iron binds to phytates "inositol hexaphosphate" which reduces its absorption).
- Cooking of food, low pH, ascorbic acid these help in dissociation and reduction of iron.
- Heme is more easily absorbed.
- Absorption is regulated at the level of mucosal-capillary interface.
- Large portion of iron is not absorbed (about 5% is absorbed)

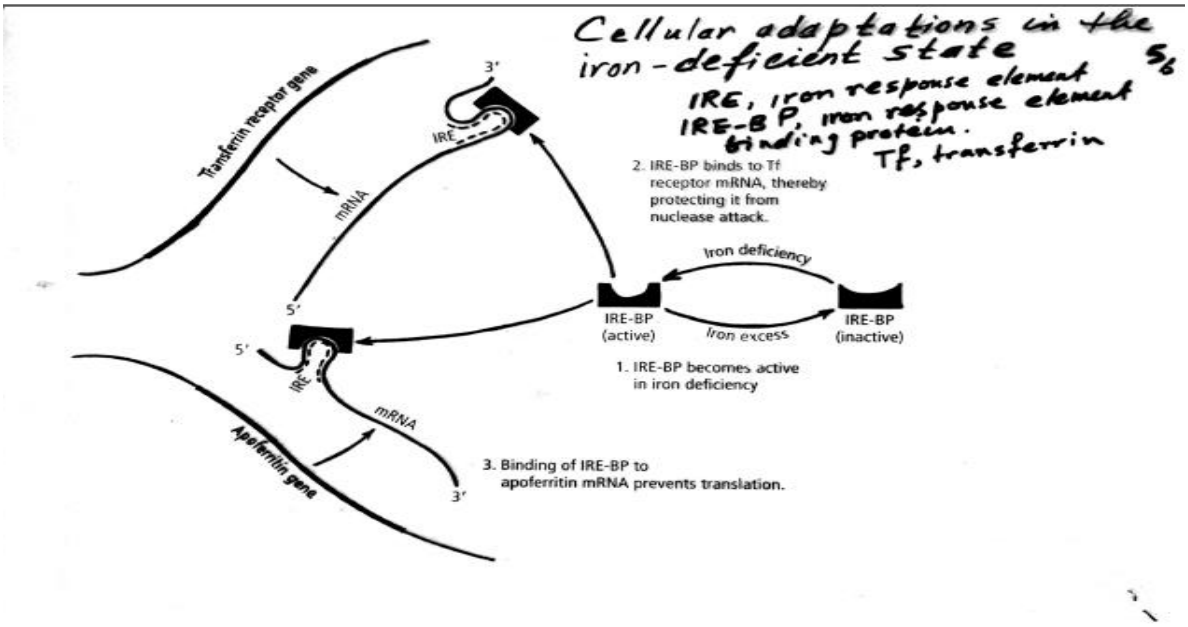
*Utilization of transferrin-bound iron by receptor mediated endocytosis:

We said that transferrin binds to iron and distribute it to tissues, this transferrin binds up to two irons and binds to its receptor, it will be taken in forming endosomes that become acidified (low pH) to dissociate iron and reduce it, then iron is released from the endosome and transported by DMT-1 (Divalent Metal (ion) Transporter-1) and it will be bound by Apoferritin after its oxidation and will be stored. Receptors and transferrin will now be excluded and returned back to the plasma.

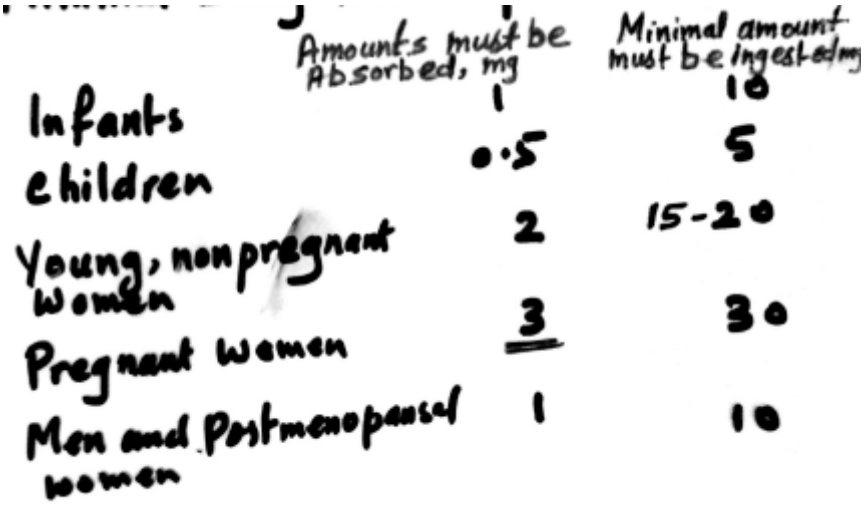
- ***Iron regulation:**

If there's an iron deficiency and there's a need for it transferrin and its receptor increase in number, if there's excess iron ferritin increase to store this excess. So how does this happen?

- There's a protein called Iron Response Element- Binding Protein (IRE-BP), which binds to IRE on mRNA of Transferrin receptor gene or Apoferritin gene;
- When there's deficiency this binding protein becomes active and binds to the 3 prime site of Transferrin receptor gene (thereby protecting it from nuclease attack and stabilize it to give the chance to make more of these receptors) and to the 5 prime site of Apoferritin gene (block translation and ferritin will not be made).
- When there's excess of iron this protein becomes less active and don't bind to neither sites, so transferrin receptor will be degraded and more ferritin will be synthesized to receive the excess iron.



- **<u>* Iron daily requirements:</u>**



	Amounts must be Absorbed, mg	Minimal amount must be Ingested mg
Infants	1	10
children	0.5	5
Young, nonpregnant women	2	15-20
Pregnant women	3	30
Men and Postmenopausal women	1	10

These numbers give idea about the iron loss.

- 1 Liter of blood contains 500-550 mg iron
- In each menstrual period 20-40 ml blood loss
- Which equals 11-22 mg iron per menstrual cycle is lost
- Which means 0.35 to 0.9 mg iron lost per day

- During delivery of fetus: 80-400 mg iron lost
- During pregnancy: 250-300 mg
- During lactation: 100-180 mg

These justify how much pregnant women need iron.

- *** Hemochromatosis:**

Refers to iron over load, which can reach about 100 gr (normal 5 mg), 20 and more => hemochromatosis.

There is no effective way to excrete iron except the way we said (sloughed with ferritin) one way.

We lose a total of 1mg of iron a day (small amount) through the sweat, bile, urine and mucosal cells.

Initial storage of iron in ferritin, when it's in excess it becomes hemosiderin.

Initially asymptomatic but excessive accumulation means iron is a destructive element because it will accelerate forming free radicals (ROS).

Males suffer more from excessive iron than females, because women lose iron in pregnancy and menstrual cycle…

***Hemochromatosis can be of two causes:

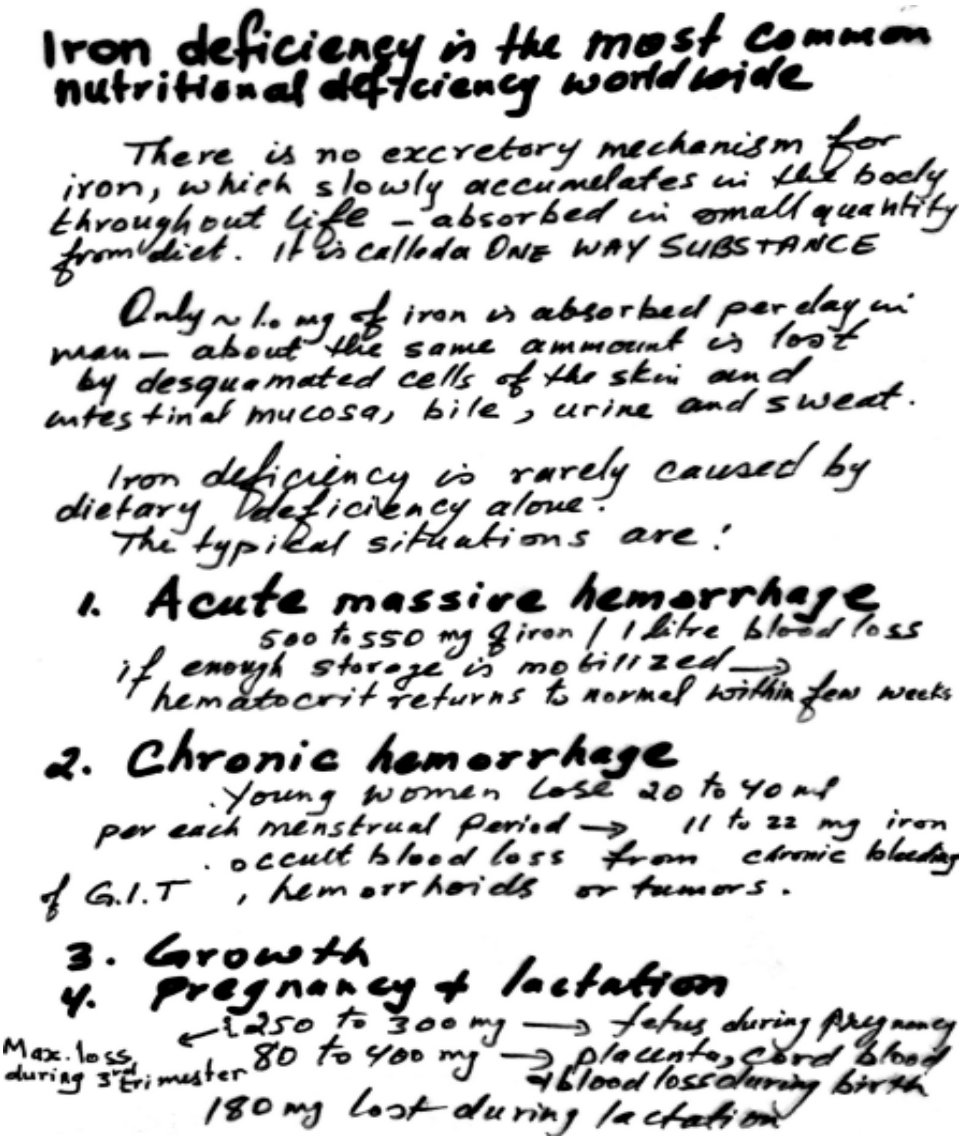
1- Primary (genetic) → increase absorption of iron, this gene is more found among the white population (1 of every 400 is homozygous, 10% is heterozygous), they absorb iron about 4 mg/daily instead of 1mg/daily and accumulate in heart, liver, pancreas and joints.
   --We treat with blood withdrawal.

2- Secondary (acquired) →in absence of predisposing gene, from iron rich diet especially from alcohol and cooked food.

Patients with hemolytic anemia or thalassemia or pyruvate kinase deficiency they require blood every now and then, so we have to watch out for their iron, those we can give them iron chelators.

*<u>Iron deficiency:</u>

The doctor read this slide:



* Iron deficiency anemia:

We have to make sure that it's not thalassemia (we must not give thalassemia patients iron),

- Treated with ferrous sulphate and ascorbic acid.

- Most prevalent in growing children, menstruating females and pregnant women.

- Most prevalent nutritional deficiency,

2-10% in developed countries

10-50% in developing countries

- Common cause: excessive menstrual flow, multiple birth, G.I bleeding.

** Initial stage of iron deficiency: (<u>important</u>)

- Depletion of the store, ferritin in plasma is decreased, the most accurate test to iron deficiency is to measure ferritin, ferritin is very accurate measurement
- Level of saturation and plasma transferrin is normal.

**Second stage:

- HB level begins to fall
- Morphological changes
- Fall in serum iron
- Rise in transferrin level
- Decrease In transferrin saturation

**Third stage:
-Pronounced effect, because not only iron decrease, but also iron containing enzymes are effected, pronounced metabolic defects.

AGAIN: FERRITIN IS A VERY SENSITIVE INDICATOR FOR IRON DEFICIENCY.

Wish you all best luck **:D**