

Hematology – Biochemistry

(Numbering is according the 7th set of slides on the websites)

ONLY EXTRA NOTES

*** The lecture does not contain a lot of extra information; actually the slides are almost enough, but they need careful reading.**

Slide 1

- Last snippet words are examples of heme-proteins (Guanylate cyclase, nitric oxide synthase, cytochromes).

Slide 2

- Transferrin belongs to beta 1 globulins family.
- It has 2 non-cooperative iron-binding sites, meaning that 2 irons bind independently without one affecting the affinity for the other.
- You just have to know that transferrin is partially saturated, with average of about 33%.
- Unsaturated transferrin has a very high affinity for iron, so it deprives the offending microorganism of the essential iron.
- Apotransferrin means a transferrin without iron.
- Transferrin receptor is heterodimer (2 different subunits); it only binds transferrin with 2 irons.

Slide 3

- Lactoferrin binds iron with high affinity. It has some antimicrobial effects as well as anti-inflammatory ones, so it is sometimes taken as a supplement.
- H and L stand for heavy and light, respectively. They form a shell together to enclose about 4300 iron atoms per molecule.
- We absorb the iron as ferrous, but ferritin stores iron as ferric. H-chain has a ferroxidase activity that oxidizes ferrous into ferric to be able to bind apoferritin, so the latter becomes ferritin (with stored iron).
- Plasma levels of ferritin are very sensitive for measurement; they're frequently used to test plasma iron in young ladies.
- When excess iron accumulates, some alterations occur in the protein portion of ferritin. As a result, a less soluble and less mobilized structure is formed for the storage of excess iron (named hemosiderin)

Slide 5

- Spinach is a poor source of absorbable iron because that iron is tightly bound to some compounds like phytate (inositol hexaphosphate) and other absorption inhibitors.
- The cooking process, stomach acidity as well as ascorbic acid favor the dissociation of iron and then reduction of ferric into ferrous because we can only absorb ferrous in cases of dietary iron (not heme iron because heme is easily absorbed).

- Notice the diagram below: if we have iron deficiency, the iron enters the mucosal cells from the intestinal lumen, and then it is sent to the plasma (capillary) for delivery to the various tissues in need. But if there are high iron levels, then the iron after entering the mucosal cells is taken up by ferritin (made in the mucosal cells) for storage and does not pass to the capillaries. This stored iron remains there until the mucosal cells "slough" after 5-6 days and release their ferritin content back into the intestinal lumen again.

Slide 7

- This is the process of receptor-mediated endocytosis. After the iron enters along with the receptor and transferrin, they form the endosome. A drop of pH causes the endosome to dissociate the iron inside of it (like the acids in the GIT that favor the dissociation of dietary iron). This iron (inside the enlarged endosome) is ferric; it needs to be reduced into ferrous in order to be transported into the cytoplasm, and this transport is favored by DMT-1 enzyme. The iron (ferrous) now is in the cytoplasm; it needs to be oxidized again into ferric to be able to bind apoferritin and form ferritin for storage. The remnants of the endosome (receptors and apotransferrin) are expelled out to undergo recycling.

Slide 8

- In iron deficiency, the active IRE-BP binds to the 3' end of transferrin receptor mRNA to protect it from endonucleases and binds to the 5' end of Apoferritin mRNA to stop translation. As a result, in iron deficiency there are low apoferritin levels as well as large transferrin receptor amounts. In iron excess, high apoferritin levels (bind the excess iron then and become ferritin that is then sloughed out into the GI lumen) are detected.

Slide 9

- Growth: infants need relatively larger amounts of iron for development of their blood circulation.

Slide 10

- Thalassemia patients already have iron overload (because of transfusions); they cannot be supplied with iron.

Slide 11

- In second stage, the body still produces transferrin without available iron to be bound, so transferrin levels are increased.

- 3rd stage is serious.

Slide 12

- Hemochromatosis is generally more common in males.

- In secondary hemochromatosis, alcohol increases the absorption of iron so it worsens the case.