

Anemia

Objectives :

- Hemoglobin & Hb structure.
- Hematopoiesis and Erythropoiesis
- Normal ranges of blood contents.
- Anemia and its clinical features and classifications.
- iron deficiency and its causes, development, signs and symptoms investigation, treatment and prevention
- Iron absorption and studies.
- Anemia of chronic disease and its treatment, cause and prevention.

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- Impotent
- Notes
- Doctor's slides

Hemoglobin

▪ Each hemoglobin contains:

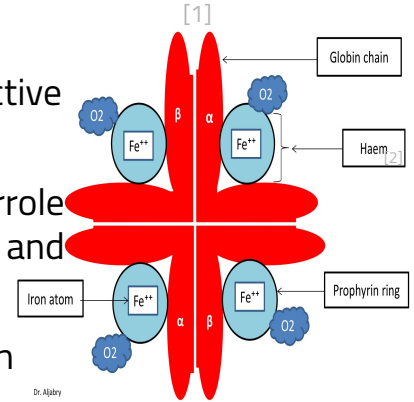
➤ 4 globin chain: polypeptide chain composed of large number of different amino acids.

➤ 4 haem molecules: specialized structure consist of central (Fe^{+2}) surrounded by prophyrin ring.

➤ 4 iron atoms: located within the haem molecule in the active reduced form.

➤ 4 prophyrin rings: organic compounds containing four pyrrole rings functioning as a metal-binding cofactor in hemoglobin and certain enzymes.

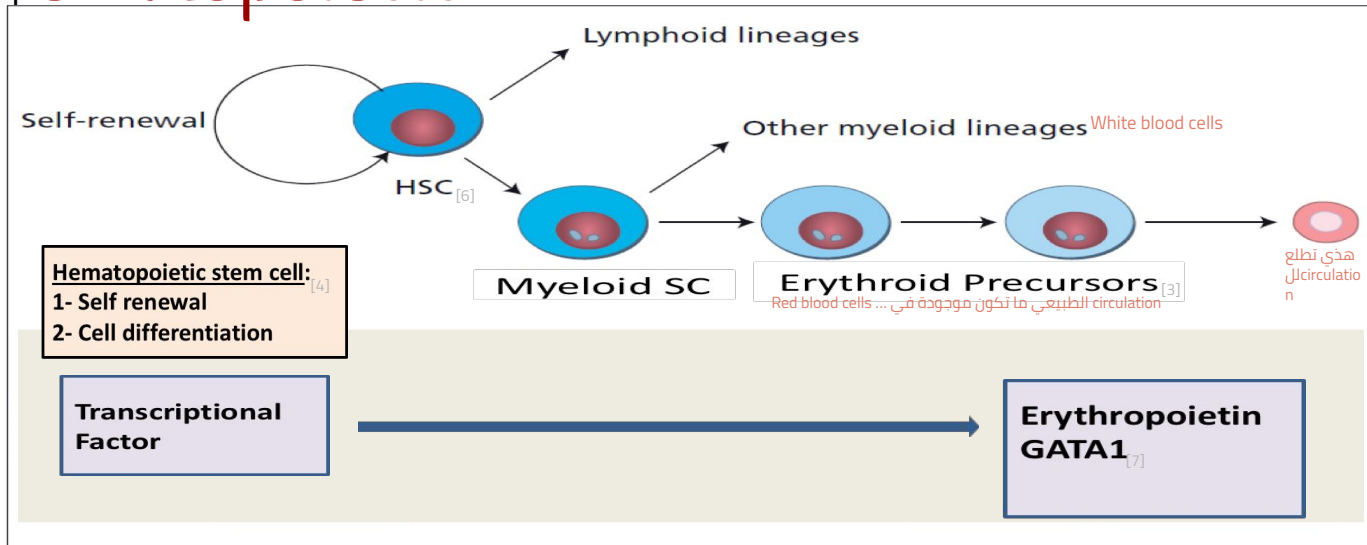
➤ 4 oxygen molecules :the maximum capacity per hemoglobin molecule.



-Hemoglobin is the protein molecule in RBC **that carries O2 from the lungs to the body's tissues and returns carbon CO2 from the tissues back to the lungs.**

- Hemoglobin maintains the shape of RBC also.

Hematopoiesis^[5]



[1] Any defect in any part of this structure can cause anemia.. and each part has specific type of anemia, and Iron the most common cause.

[2] Haem = Iron + oxygen.

[3] If there is any defect in these will cause early stage of malignancy or disease.

[4] تطع منها كل خلايا الدم مو بس الحمراء

[5] Formation of blood cells.

[6] HSC من تبي mesenchymal Hemangioblast.

-Hemoglobins has a buffering effect , buffering is increases the amount of acid or alkali necessary to produce a unit change in pH

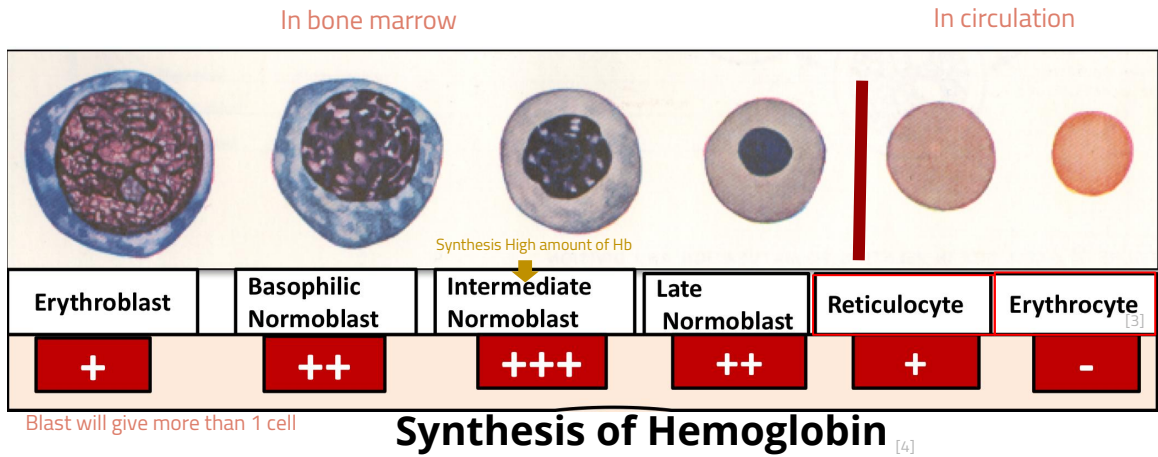
[7]

- 2 hormones control hematopoietic.
- Erythropoietin the most important one.
- Erythropoietin secreted mainly by renal , so any problem in renal system can cause defect.
- 90% by renal and 10% by liver.

Erythropoiesis^[1]

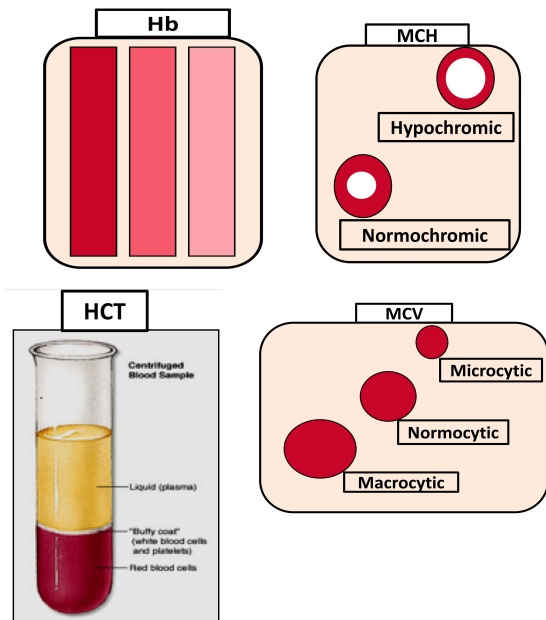
The "Bone Marrow" is the major site with the need of:

Folic acid - Iron "Ferrous" - Vit B12 - Erythropoietin^[2] - Amino acids minerals - other regulatory factors



Normal Ranges^[5] Important

Indices	Male	Female
Hemoglobin(g/dL)	13.5-17.5	11.5-15.5
Hematocrit (PCV) (%)	40-52	36-48
Red Cell Count ($\times 10^{12}$)	4.5-6.5	3.9-5.6
Mean Cell Volume (MCV) (fL)	80-95	
Mean Cell Hemoglobin (MCH) (pg)	30-35	



ANEMIA

-An (without) -aemia (blood)

-Reduction of Hb concentration below the normal range for the age and gender

-Leading to decreased O₂ carrying capacity of blood and thus O₂ availability to tissues (hypoxia)

[1] Formation of **red blood cells**.

[2] أي نقص في هذي المكونات تسبب أنيميا

[3] **Mature red blood cells**.

[4] Erythrocyte إشارة + توضح ان في كل المراحل يكون فيه تكوين للهيموقلوبين الا في اخر شيء لما يكون عندي

[5] Table for adult .. neonates are different

-Classification of anemia depends on: Hb, MCH and MCV.

Clinical Features

Presence or absence of clinical feature depends on:

1-Speed of onset :

Rapidly progressive anemia causes more symptoms than slow onset anemia due to **lack of compensatory mechanisms:**

(cardiovascular system, BM^[1] & O₂ dissociation curve

2-Severity:

- Mild anemia :no symptoms usually
- Symptoms appear if Hb **less than 9g/dL** ^[2]

3- Age:

- Elderly tolerate anemia less than young patients

General features of anemia	Specific features
<p>Weakness</p> <ul style="list-style-type: none"> • Headache • Pallor • Lethargy • Dizziness • Palpitation (tachycardia) • Angina • Cardiac failure <p>Related to anemia</p> <p>Related to compensatory Mechanism</p>	<p>Specific signs are associated with particular types of anemia :</p> <ul style="list-style-type: none"> v <u>Spoon nail</u> with iron deficiency, v <u>Leg ulcers</u> with sickle cell anemia v <u>Jaundice</u> with hemolytic anemia v <u>bone deformities</u> in thalassemia <p>مهم مره تفرقون كل ساين مع اي نوع</p>

Classification of Anemia [هذا الجدول مهم](#)

Hypochromic Microcytic Anemia	Macrocytic Anemia	Normocytic Normochromic Anemia
<ul style="list-style-type: none"> • site= Hb • Structure affected: <ol style="list-style-type: none"> 1. porphyrin: Sideroblastic anemia 2. Iron : iron deficiency anemia 3. Globin Chain: Thalassemia 	<ul style="list-style-type: none"> • site= DNA synthesis. • Megaloblastic anemia due to : <ol style="list-style-type: none"> 1. Vit B12 deficiency. 2. Folate deficiency. 3. Myelodysplastic syndrome(MDS). 	<ul style="list-style-type: none"> • RBC Count due to ^[3] <ol style="list-style-type: none"> 1. Blood loss: acute bleeding. 2. hemolysis: (autoimmune, enzymopathy, membranopathy, mechanical , sickle cell anemia). 3. RBC production (Bone marrow failure) : <ul style="list-style-type: none"> ✓ chemotherapy. ✓ malignancy . ✓ Aplastic anemia. ✓ anemia of chronic disease.

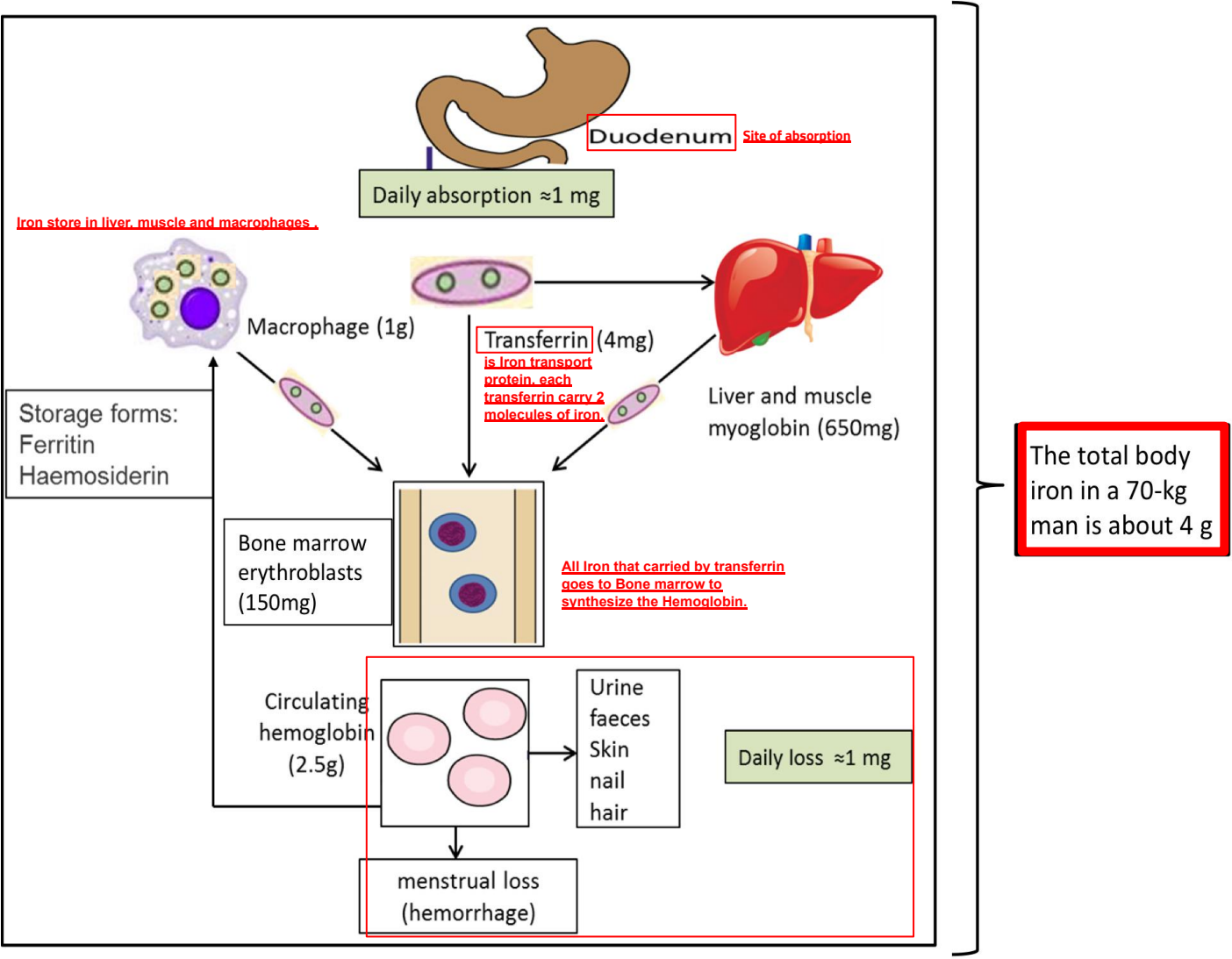
[1] BM=bone marrow .. cellularity of bone marrow will increased.

[2] ممكن يجون اشخاص يكون أكثر من 9 لكن الأعراض واضحة عليهم

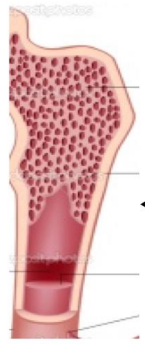
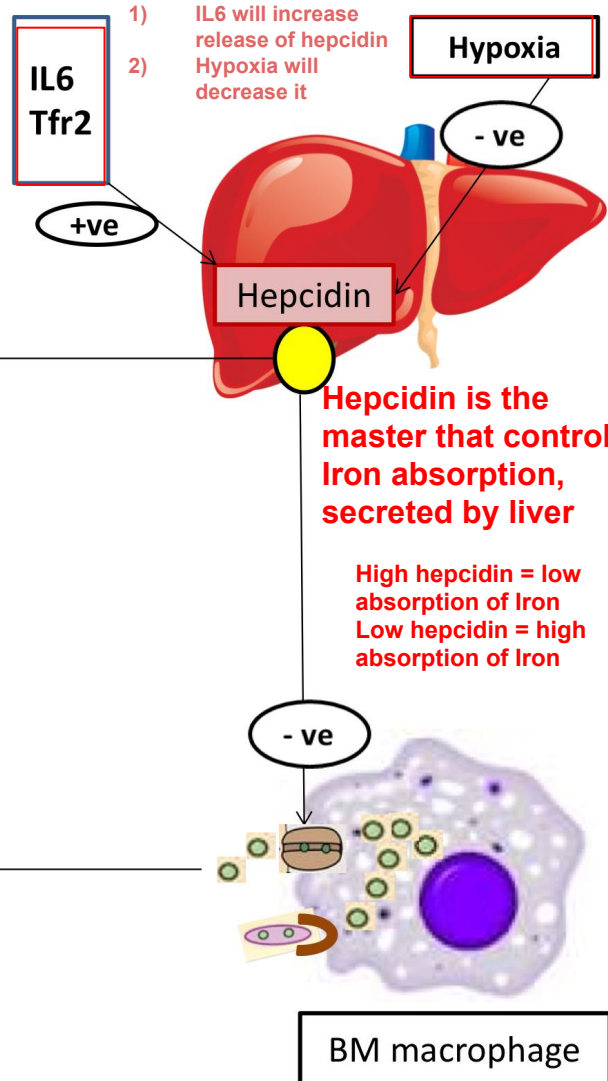
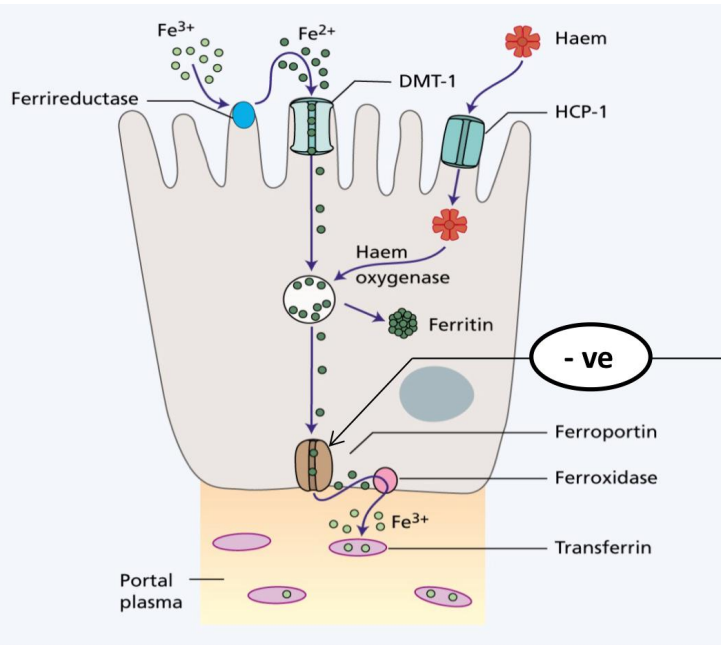
[3] يكون الخلل في الدم نفسه هو الهيموقلوبين

Iron Deficiency Anemia

- Iron is among the abundant minerals on earth (6%).
- **Iron deficiency is the most common disorder**(24%).
- Limited absorption ability :
 - 1-Only 5-10% of taken iron will be absorbed
 - 2- Inorganic iron can not be absorbed easily.
- Excess loss due to hemorrhage



This process (iron absorption) take place in duodenum.



Iron for erythropoiesis

In organic (non-heme) Iron needs to one additional step to absorb which is converted the Fe³⁺ form (Ferric iron) which is non-absorbable form to the Fe²⁺ form (Ferrous Iron) which is absorbable form , by 2 enzymes

- 1) Ferrireductase.
- 2) DMT-1

At the end all Iron that absorbed will export to the plasma through Ferroportin where we control the Iron absorption indirectly by Hepcidin in the liver that control Ferroportin by negative feedback control.

During the iron passage through Ferroportin it converted again to inactive form (Fe³⁺) which is the Irons storage form and then it took by transferrin

Iron Absorption

Factors favoring absorption	Factor reducing absorption
Haem iron ^[1]	Inorganic iron ^[3]
Ferrous Iron (Fe ⁺⁺)	Ferric iron Fe ⁺⁺⁺
Acid	Alkalines
Iron def	Iron overload
Pregnancy	Tea ^[4]
Hemochromatosis ^[2]	Increased hepcidin
Solubilizing agent (Sugar)	Precipitating agent(phenol)

1-Body Iron status:

- Increased demands (iron def.,pregnancy..) —> Low iron stores —> **high absorption.**
- Iron overload —> Full iron stores —> **Low absorption.**

2- Content and form of dietary iron

- More Iron ,Haem Iron and Ferrous Iron—> More absorption.

3- Balance between dietary enhancers and Inhibitory factors:

- Enhancers: Meat (haem iron) , fruit (**Vit-C**), sugar (solubilizing agent),and acids.
- Inhibitory: Dairy foods (calcium), high fiber foods (phytate), coffee and tea (polyphenols), and anti-acids .

[1] Or meat or organic iron.

[2] Disorder of iron , the hepcidin will decrease.

[3]In vegetable .

[4] Also! coffee and green tea شربه بعد ساعه ونص يفضل شربه , and if you eat a lot of iron the tea won't cause anemia

Causes of iron Deficiency Anemia

1-Chronic blood loss:

- GIT Bleeding: peptic ulcer, esophageal varices , hookworm & cancer.
- Uterine bleeding.
- Hematuria.

2- Increased demands:

- Immaturity.
- Growth.
- Pregnancy.
- EPO therapy

3-Malabsorption: *problem in duodenum because it is a site of absorption.*

- Enteropathy.
- Gastrectomy

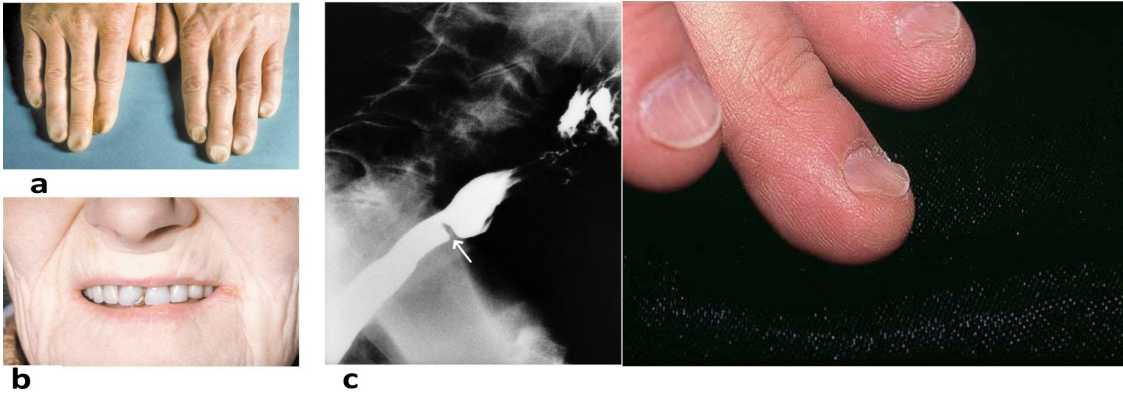
4-Poor diet: Rare as the only cause (rule out other causes)

Development of iron Deficiency Anemia

	1 Normal	2 Pre-latent <small>عشان يلاحظونه بسوون BM study</small>	3 Latent	4 Iron def. anemia
Stores	Normal	Low	Low	Low
MCV/MCH	Normal	Normal	Low	Low
Hemoglobin	Normal	Normal	Normal	Low

Signs of anemia

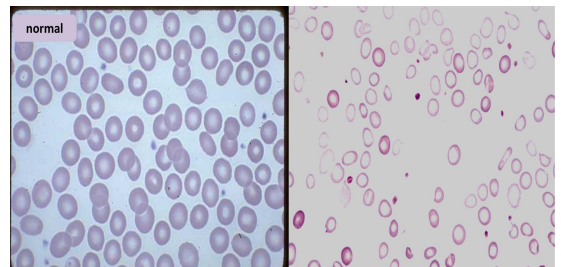
Signs and symptoms of IDA



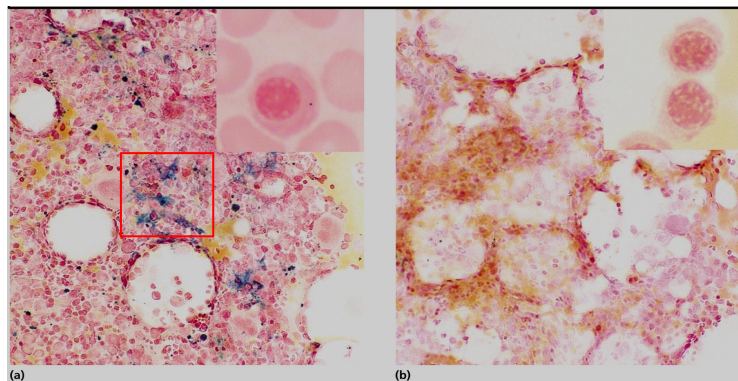
- Beside symptoms and signs of anaemia +/- bleeding patients present with:
 - (a): **Koilonychia** (spoon-shaped nails).
 - (b): **Angular stomatitis and/or glossitis**.
 - (c): **Dysphagia** due to pharyngeal web (Plummer-Vinson syndrome).

Investigation

- Microcytic hypochromic anemia with:
 - **Anisocytosis** (variation in size). In CBC
 - **Pokilocytosis** (variation in shape)



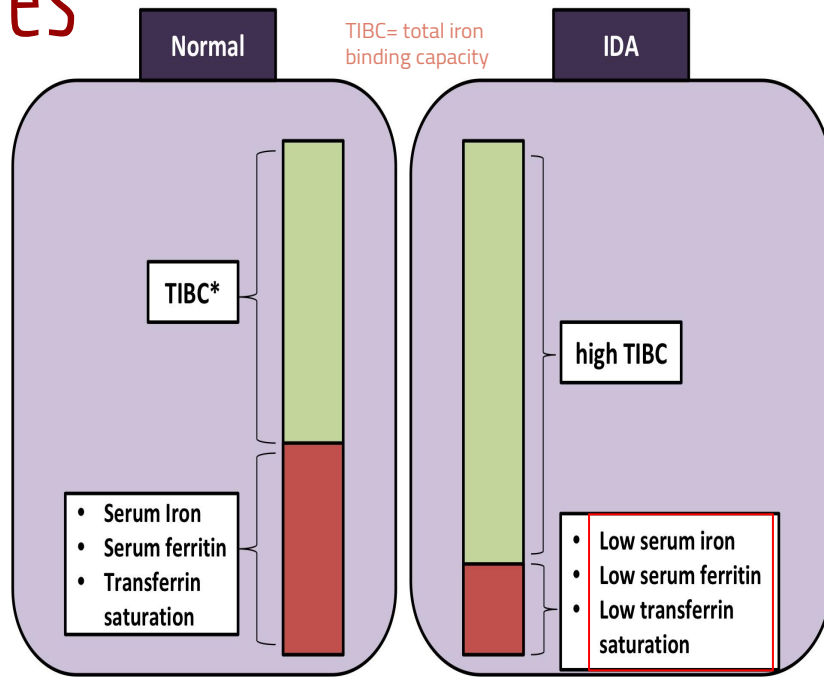
- BM Iron stain (**Perl's stain**):
The gold standard but invasive procedure



Normal

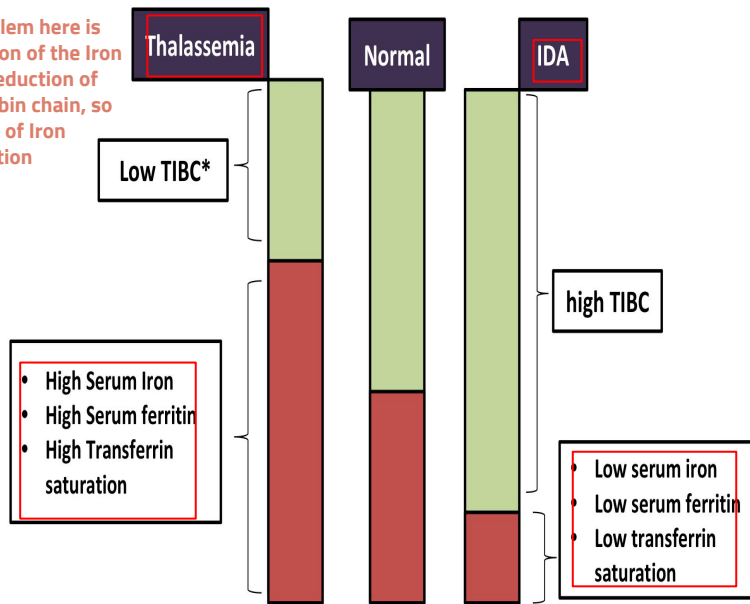
IDA: reduced or absent iron stores (hemosiderin)

Iron Studies



There is a lot of Free transferrin which is iron transport protein because of less amount of Iron.

Because the problem here is not in the reduction of the Iron but, because of reduction of production of globin chain, so there will be a lot of Iron without any function



Treatment of IDA

- Treat the underlying cause.
- Iron replacement therapy:
 - *Oral :(Ferrous Sulphate OD for 6 months).
 - *Intravenous:(Ferric sucrose OD for 6 months).

البدايه تكون اورال اذا ما استجاب نعطيه انترافينيس

-Hb should rise 2g/dL every 3 weeks

good response يدل على ان فيه

PREVENTION OF IDA

- Dietary modification : Meat is better source than vegetables.
- Food fortification (with ferrous sulphate)
 - GIT disturbances ,staining of teeth & metallic taste.
- Iron supplementation: For high risk groups.

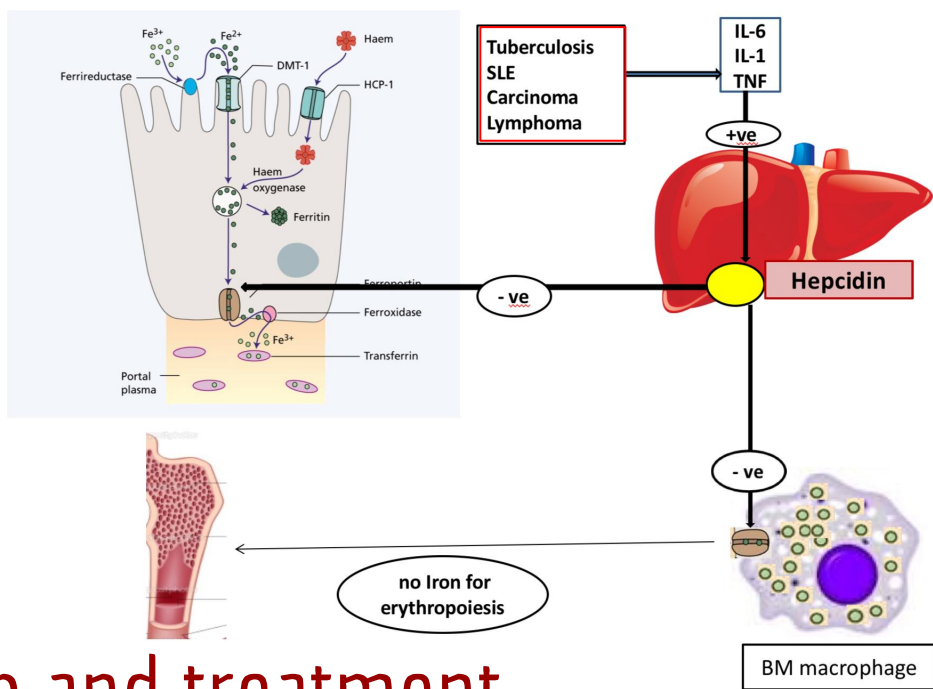
نعرف مكان المشكله اللي ما تخلى في امتصاص للحديد ونحاول نحلها , لو مثلا فيه GIT disturbances we should give the patient iron by IV

Anemia of chronic disease

• **Normochromic normocytic** (usually) anemia **caused by decreased release of iron** from iron stores and reduction of iron absorption due to raised serum Hepcidin .

- Associated with
 - Chronic infection including HIV, malaria
 - Chronic inflammations
 - Tissue necrosis
 - Malignancy

These diseases release cytokines which cause increased synthesis of hepcidin. When hepcidin increase release of the iron from Macrophages will decrease

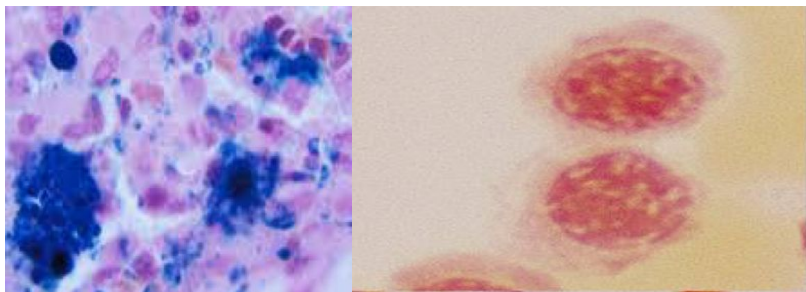


Work-up and treatment

- Normocytic normochromic or mildly microcytic anaemia.
- Low serum iron and TIBC.
- Normal or high serum ferritin (acute phase reactant).
- High haemosiderin in macrophages but low in normoblasts

Management:

- Treat the underlying cause.
- Iron replacement +/- EPO



Summary

Important notes!

- **normal range** : You should to know the difference between male and female ... for example, if they ask you about 12g/dL of Hemoglobin.. it will be **normal** in female but **abnormal** in male.
- Erythropoietin → control **hematopoietic** , Erythropoietin secreted mainly by **renal**.
- Hepcidin is the master that control **Iron absorption**, secreted by liver.
- Hematopoiesis is formation of all blood cell.
- Erythropoiesis is formation red blood cells only.
- **Erythrocyte** is the mature red blood cell and in this stage there is no synthesis of hemoglobin.
- Symptoms of anemia appear if Hb **less than 9g/dL**.
- The **specific features and classification** of anemia very important.
- The absorption of Iron in **duodenum** .
- The Iron store in bone marrow **macrophages** , liver and muscle.
- **transferrin** is Iron transport protein. each transferrin carry 2 molecules of iron.
- When we eat the food Iron needs to one additional step to absorb which is converted the **Fe³⁺ form (Ferric iron) which is non-absorbable form to the Fe²⁺ form (Ferrous Iron) which is absorbable form** , by 2 enzymes Ferrereductase and DMT-1.
- **(Perl's stain): The gold standard.**
- Treatment of IDA : **Hb should rise 2g/dL every 3 weeks.**
- Anemia of chronic disease **caused by decreased release of iron.**
- decrease hemoglobin cause **anemia** .. increase cause **polycythemia**
- women have **anemia** more than **polycythemia**
- The erythoblast wil give 4 basophilic normoblast .. and the number of cell will increase till reticulocyte.
- erythropoietin will push the myeloid stem cells to differentiate into red blood cells
- Tea affect 10-15% of the absorption of iron so if you eat a lot of iron you won't have anemia
- Hemoglobin has a buffering effect