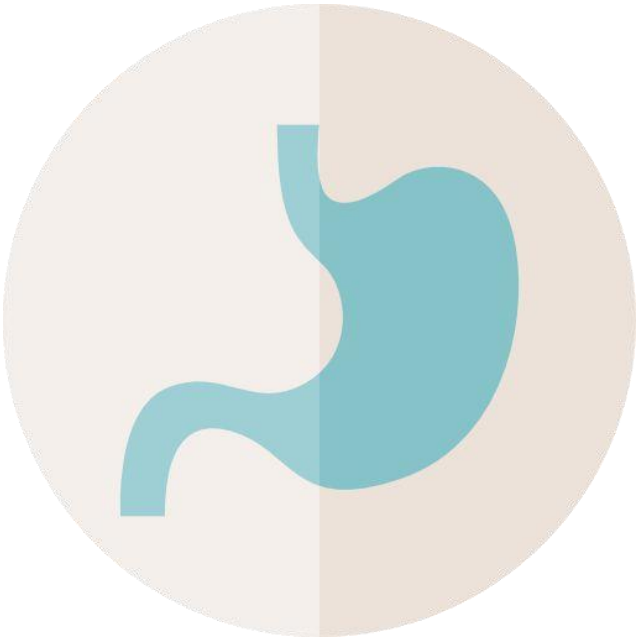
HAEMATOLOGY 436

MEDICINE
KING SAUD UNIVERSITY

تمت المراجعة
شوق الأحمري & عبدالعزيز العتري



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.

Color index
Important
Extra
Doctors' notes

References:

436 girls & boys' slides
435 teamwork slides

Editing file

Do you have any suggestions? Huuuu Please contact us!

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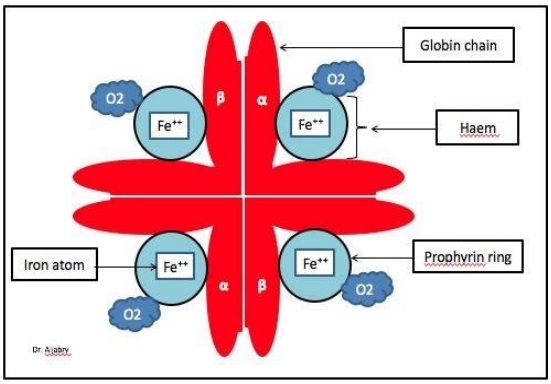
or simply use this form

Hemoglobin

Male: Hemoglobin= Heme (iron) + globin chain (alpha , beta , delta.etc)

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. Male: Max. Capacity of hemoglobin to carry o2 Is 4 molecules of oxygen per 1 hemoglobin

Hemoglobin maintains the shape of RBC also.



Hemoglobin structure

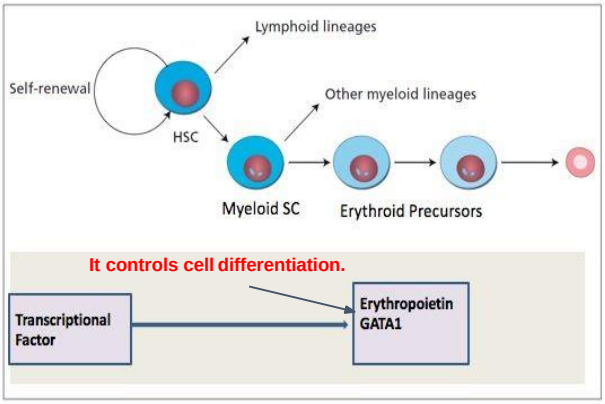
Hematopoiesis: is the production of all of the cellular components of blood and blood plasma.

Hematopoietic stem cell: Male: Will give me all types of blood cells (RBCs,WBCs,Platelets etc.)

1 Self renewal Male: when there is problems in self renewal there will be deficiency of Hematopoietic stem cells will lead to aplastic anemia (will not have RBCs, Neutrophils, platelets. Etc.)

2 Cell differentiation Male: It make other types of blood cells like (myeloid sc ,etc.). Which are functional Types

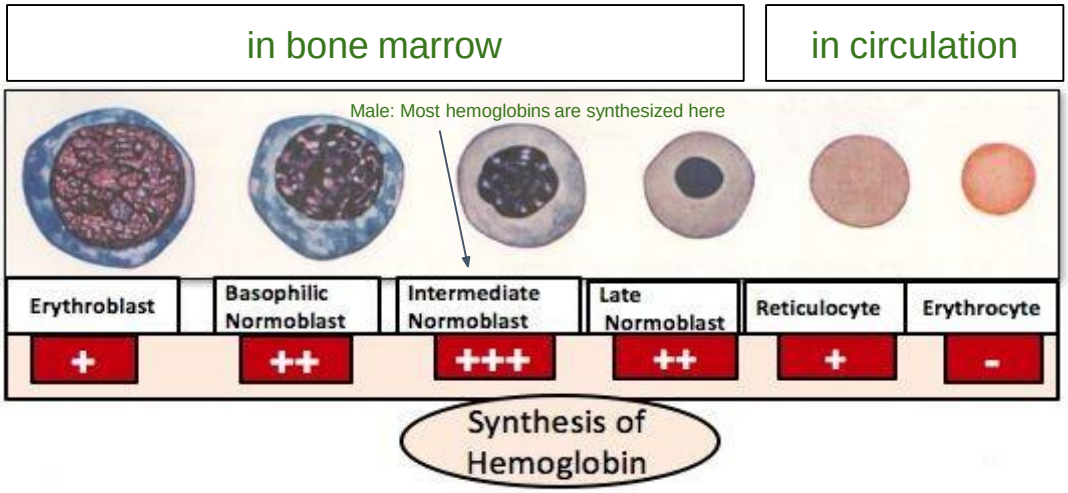
Erythropoietin= secreted from kidneys



Erythropoietin: It is like the cable that pull Hematopoietic stem cell toward the RBCs production so deficiency of it especially in renal diseases (because it produces in kidneys) will lead to deficiency of RBCs also.

Erythropoiesis: Production of RBCs

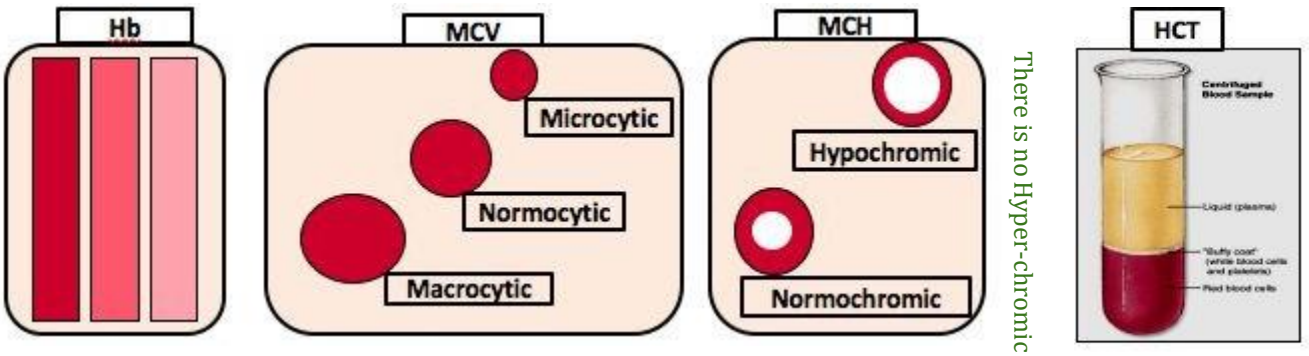
The "Bone Marrow" is the major site of erythropoiesis with the need of: Folic acid – Iron "Ferrous" – Vit B12 – Erythropoietin - Amino acids, minerals - other regulatory factors



Normal Ranges

it is very important to know the age and the sex

Indices	Female	Male
Hemoglobin(g/dL)	**11.5-15.5**	**13.5-17.5**
Hematocrit (PCV) (%) also called HCT : percentage of RBCs in the tube of whole blood	**36-48**	**40-52**
Red Cell Count ($\times 10^{12}$)	**3.9-5.6**	**4.5-6.5**
Mean Cell Volume (MCV) (fL) Average size of average RBC,if MCV<80 the it is microcell anemia ,if MCV>95 then it is macrocytic anemia .	**80-95**	
Mean Cell Hemoglobin (MCH) (pg) Hemoglobin inside each RBCs	**30-35**	



Anemia

An (without) -emia (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)

Male notes: Our body detect the anemia to start compensatory mechanisms not by calculating the Hemoglobin concentration. It detect it by detect the hypoxia, then it will send messages by the erythropoietin signals that generate from kidney to bone marrow to synthesis more RBCs & Hemoglobin.

Presence or absence of clinical feature depends on:

1Speed of onset: Rapidly progressive anemia causes more symptoms than slow onset anemia due to lack of compensatory mechanisms: (cardiovascular system Can lead to congestive heart failure , BM &O2 dissociation curve)

2Severity: Mild anemia > no symptoms usually

Symptoms appear if Hb less than 9g/dL

3 Age: Elderly tolerate anemia less than young patients. less compensation than young.

Clinical Features:

1-General features of anemia:

- Weakness -Headache -Pallor -Lethargy -Dizziness

related to anemia

- Palpitation (tachycardia) -Angina -Cardiac failure

Related to compensatory mechanism.

2-Specific features: *important

Specific signs are associated with particular types of anemia:

Spoon nail = iron deficiency
Leg ulcers = sickle cell anemia
Jaundice = hemolytic anemia
Bone deformities = thalassemia major

Classification of Anemia

Hypochromic Microcytic Anemia

Any deficiency of the contents lead to this type of anemia.

site= Hb

Structure affected:
1.porphyrin: Sideroblastic anemia
2. Iron : iron deficiency anemia
3. Globin Chain: Thalassemia

Thalassemia: Reduction of production of normal globin chain

Macrocytic Anemia

site= DNA synthesis

Megaloblastic anemia due to :
1.Vit B12 deficiency.
2. Folate deficiency.

Which have major role in DNA synthesis & repairing.

3. Myelodysplastic syndrome(MDS)

Normocytic Normochromic Anemia

1. **Blood loss:** acute bleeding.
2. **hemolysis** Destruction of RBCs inside the vessels **:** (autoimmune, enzymopathy, membranopathy, mechanical , sickle cell anemia).
3. **RBC production (Bone marrow failure) :**
   - chemotherapy.
   - malignancy .
   - Aplastic anemia. Hematopoietic stem cell Deficiency and here we have bone marrow shut down
   - anemia of chronic disease.

the most popular types of anemia are the iron deficiency anemia and the megaloblastic anemia

Iron Deficiency Anemia:

- Iron is among the abundant minerals on earth (6%).
- Iron deficiency is the most common disorder(24%).
- Limited absorption ability :

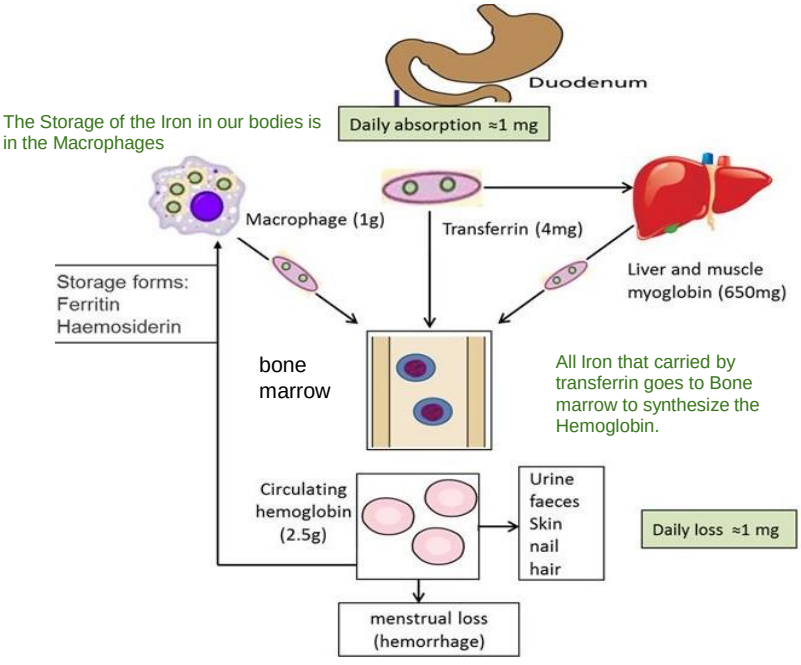
  1-Only 5-10% of taken iron will be absorbed.

  2- Inorganic iron can not be absorbed easily.
- Excess loss due to hemorrhage

Male: Why ? Because the Iron itself is very toxic for the body, and its accumulation due to increased Iron absorption for example may lead to Hemochromatosis which may lead to deficiency of many glands and leads to diseases like diabetes.

عشان كذا ينصحون الكبار في السن يتبرعون بالدم عشان ينقصون الحديد اللي عندهم وبنفس الوقت إذا زاد التبرع أو الحجامة عن حدهم الطبيعي ممكن يسببون iron deficiency anemia

Iron Absorption: *Important to understand read the notes carefully.



The Storage of the Iron in our bodies is in the Macrophages

All Iron that carried by transferrin goes to Bone marrow to synthesize the Hemoglobin.

Transferrin: is Iron transport protein. each transferrin carry 2 molecules of iron.

The total body iron in a 70-kg man is about 4 g

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 enzyme called Ferrireductase.

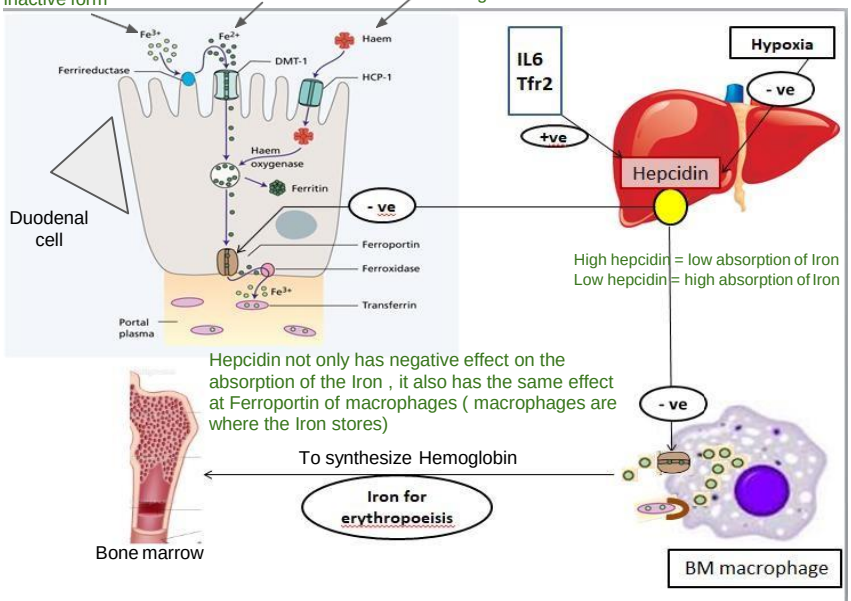
At the end all Iron that absorbed will export to the plasma through Ferroportin where we control the Iron absorption indirectly by Hepcidin in the liver that control Ferroportin by negative feedback control.

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.

Non-absorbable inactive form

Absorbable active form

Haem iron is directly absorbed without need of any enzymes through HCP-1



Hepcidin is the master that control Iron absorption

Iron Absorption

Factors favoring absorption	Factor reducing absorption
Haem iron (meat iron)	Inorganic iron
Ferrous Iron (Fe++)	Ferric iron Fe+++
Acid	Alkalines
Iron def	Iron overload only in Female slides
Pregnancy (the fetus needs iron)	Infection only in Male slides
Hemochromatosis described in previous slide.	Tea Also coffee
Solubilizing agent (Sugar)	Increased hepcidin
-	Precipitating agent (phenol) High fiber diet

Factors Affecting iron absorption only in Female slides (same as the table):

1- Iron body status:

●Increased demands (iron def., pregnancy) →low iron stores (increase release)→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- GIT mucosa:

● Disruption of GIT mucosa → cannot absorb iron.

4- Balance between dietary enhancers and Inhibitory factors:

●Enhancers: Meat (haem iron), fruit (Vit-C), sugar (solubilizing agent),and acids.

●You can combine orange juice with meat to enhance iron absorption.

●Inhibitory: Dairy foods (calcium), high fiber foods (phytate), coffee and tea (polyphenols), and anti-acids (Alkalines).

Causes of iron Deficiency Anemia:

1-Chronic blood loss:

Male: Major cause

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

2- Increased demands:

- Immaturity
- Growth
- Pregnancy
- EPO therapy

3-Malabsorption:

- Enteropathy (GIT problems)
- Gastrectomy

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

Development of IDA:

If the patient not supplemented with Iron →

	1 Normal	2 Pre-latent	3 Latent	4 Iron def. anemia (signs of anemia)
Stores	**Normal**	**Low**	**Low**	**Low**
MCV/MCH	**Normal**	**Normal**	**Low**	**Low**
Hemoglobin	**Normal**	**Normal**	**Normal**	**Low**

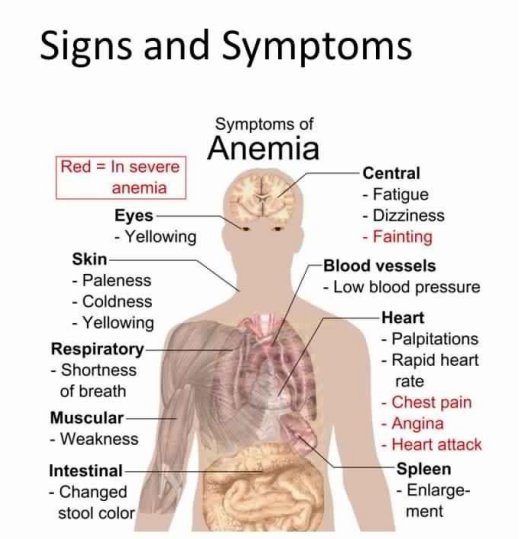
Signs and symptoms of IDA:

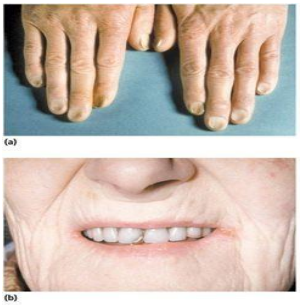
Beside symptoms and signs of anaemia +/- bleeding patients present with:

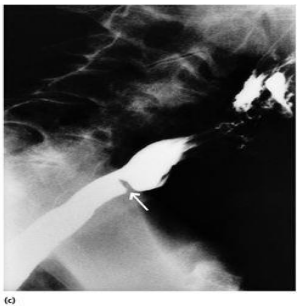
(a): Koilonychia (spoon-shaped nails)

(b): Angular stomatitis and/or glossitis

(c): Dysphagia due to pharyngeal web (Plummer-Vinson syndrome)



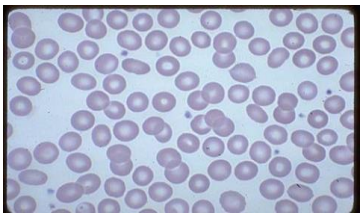


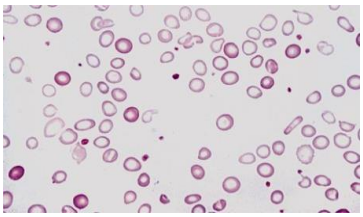


Investigations:

1.Microcytic hypochromic anemia with:

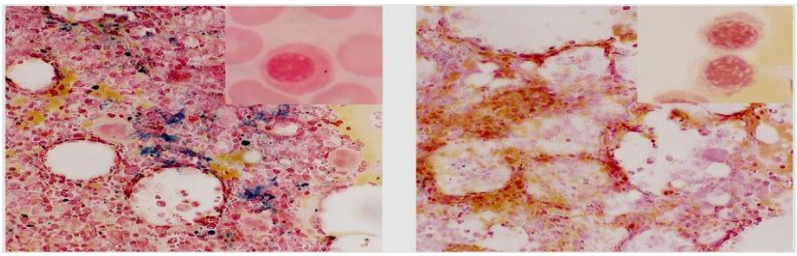
•Anisocytosis (variation in size)
•Poikilocytosis (variation in shape).





normal

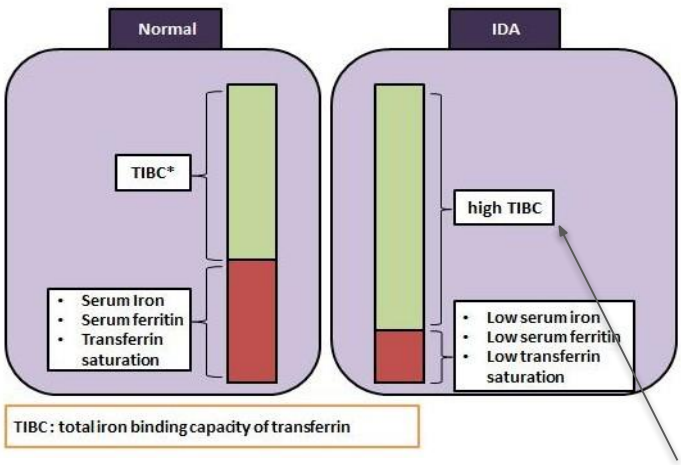
2.Bone marrow Iron stain (Perl's stain):
The gold standard but invasive procedure.



Normal

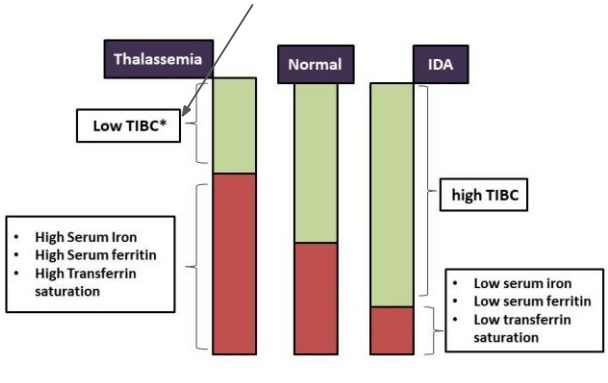
IDA: reduced or absent iron stores (hemosiderin)

Iron Studies: important



Serum ferritin= iron store

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 (cannot bind to globin chain and form hemoglobin.)



There is a lot of Free transferrin which is iron transport protein because of less amount of Iron.
مثل الطيارة اللي اغلب مقاعدها فاضية لأن ما فيه ركاب.
(Iron = الركاب)

Treatment of IDA

-Treat the underlying cause

-Iron replacement therapy: Oral (Ferrous Sulphate OD for 6 months)

-Intravenous (Ferric sucrose OD for 6 months)

-Hb should rise 2g/dL every 3 weeks.

Prevention Of IDA:

-Dietary modification Meat is better source than vegetables.

-Food fortification (with ferrous sulphate)

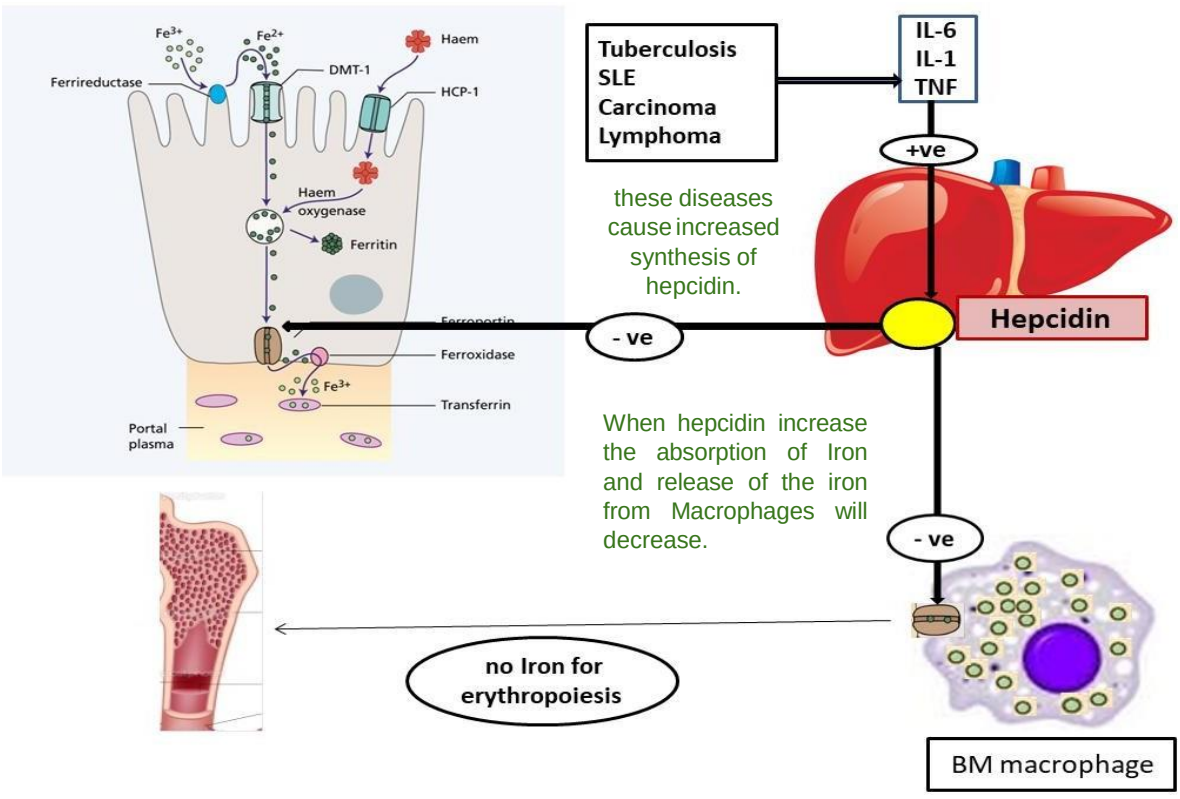
-GIT disturbances, staining of teeth & metallic taste.

-Iron supplementation: For high risk groups.

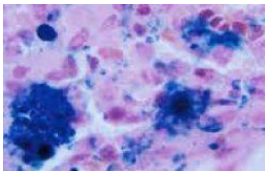
Anemia of chronic disease:

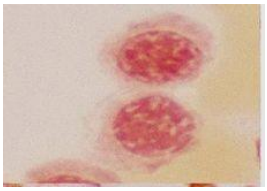
-Normochromic normocytic (usually) anemia caused by decreased release of iron from iron stores and reduction of iron absorption due to raised serum Hepcidin.

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



Work-up and treatment:





-Normocytic normochromic or mildly microcytic anaemia

Findings:-

-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 (erythropoietin)

Summary

Anemia: 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)	**Clinical Features:** Presence or absence of clinical feature depends on: ١ Speed of onset : ٢ Severity: Symptoms appear if Hb less than 9g/dL 3- Age
Clinical Features Weakness, Headache, Pallor, Lethargy, Dizziness, Palpitation (tachycardia), Angina, Cardiac failure	**2-Specific features** Specific signs are associated with particular types of anemia : *Spoon nail with iron deficiency, *Leg ulcers with sickle cell anemia *Jaundice with hemolytic anemia * bone deformities in thalassemia major
Classification of Anemia: Hypochromic microcytic anemia: Related to hemoglobin due to porphyrin,iron,globin chain problems. Macrocytic anemia: Related to DNA synthesis Normocytic normochromic anemia: Related to blood count	**Iron Deficiency Anemia**: the most common disorder(24%). Limited absorption ability Excess blood loss
Treatment of IDA •Treat the underlying cause •Iron replacement therapy:	**Iron Absorption:** Depends on: ١ Body Iron status: ٢ Content and form of dietary iron ٣ Balance between dietary enhancers & Inhibitory factors
Factors favoring absorption Haem iron, Ferrous iron, Acid, Iron def., Pregnancy, Hemochromatosis, Solubilizing agents	**Factor reducing absorption** Inorganic iron, Ferric iron, Alklines, Iron overload, Tea, Increased hepcidin, Precipitating agent
Causes of IDA 1-Chronic blood loss: 2- Increased demands: 3-Malabsorption 4-Poor diet	**PREVENTION OF IDA** •Dietary modification •Food fortification (with ferrous sulphate) •Iron supplementation:

:MCQs

1- Which one of the following consider as the major factor that control Iron absorption and release?

A- Vit. B12
B- Hepcidin
C- Ferrireductase
D- Precipitating Agent

Answer: B

2- The gold standard for investigating IDA is:

A- H&E stain
B- Perl's stain
C- Zheel Neelsen stain
D- PAS

Answer: B

3-The cause of Megaloblastic Anemia is deficiency of:

A- Vit B6
B- Vit A
C- Vit B12
D- Vit E

Answer: C

4- Normochromic normocytic is associated with:

A- Pregnancy
B- HIV
C- Blood loss
D- Poor diet

Answer: B

5- Which ONE of the following consider As transcriptional factors that have a role in cell differentiation from Hematopoietic stem cell :

A- GATA1
B- Myeloid Cells
C- Hepcidin
D- None of the above

Answer: A

Good Luck!

Team members

Girls:

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Wejdan Alzaid

Reema AlOtaibi

Ashwaq Almajed

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Safa AlOsaimi

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