

Hematology

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Anemia



432 Hematology Team

Done By: Ali Saeed Al-Rawdhan

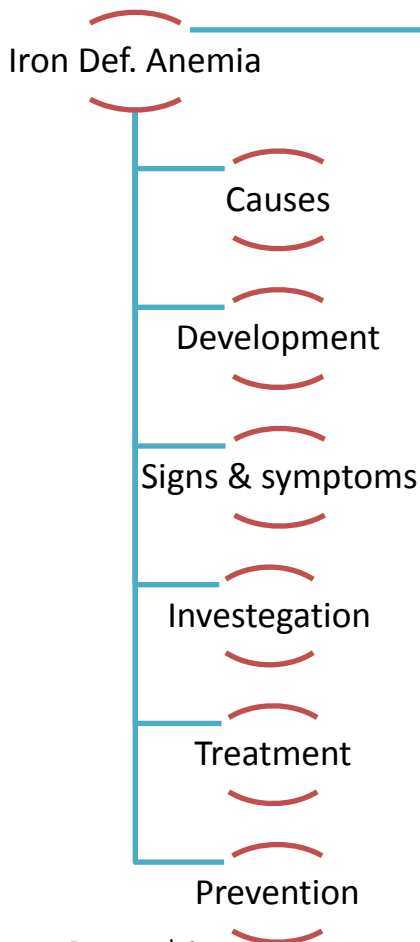
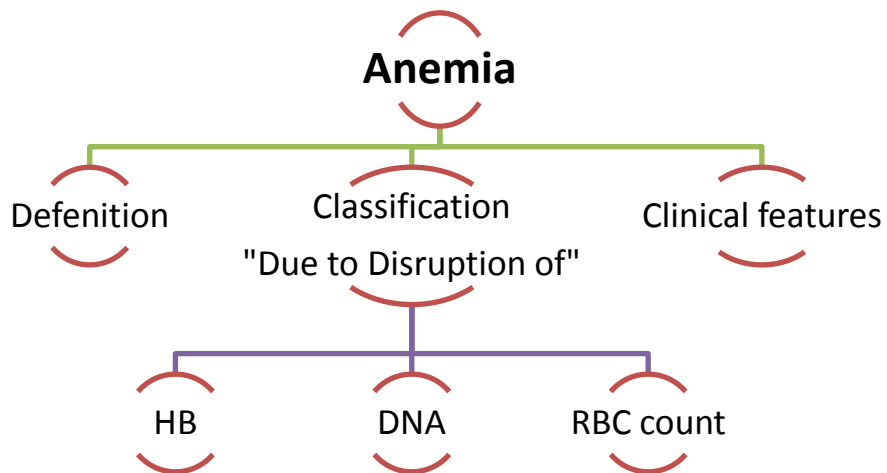
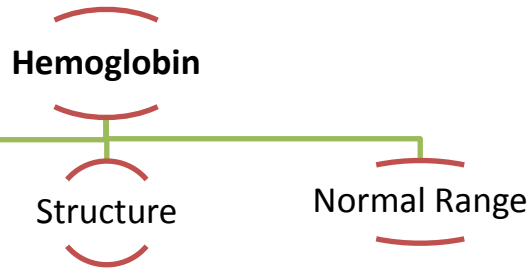
Reviewed By: Rawan Al-Quaiz



Color Index: Female notes are in Green. Male notes are in Blue. Red is important. Orange is explanation.

Anemia

Mind Map:



Hemoglobin

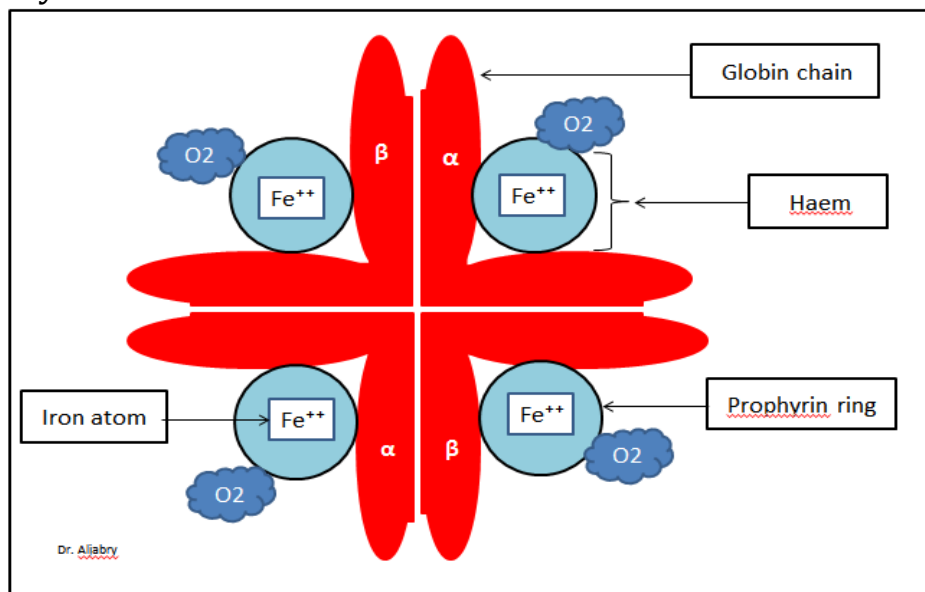
What is Hemoglobin?

- 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. *"flexible, biconcave disc"*

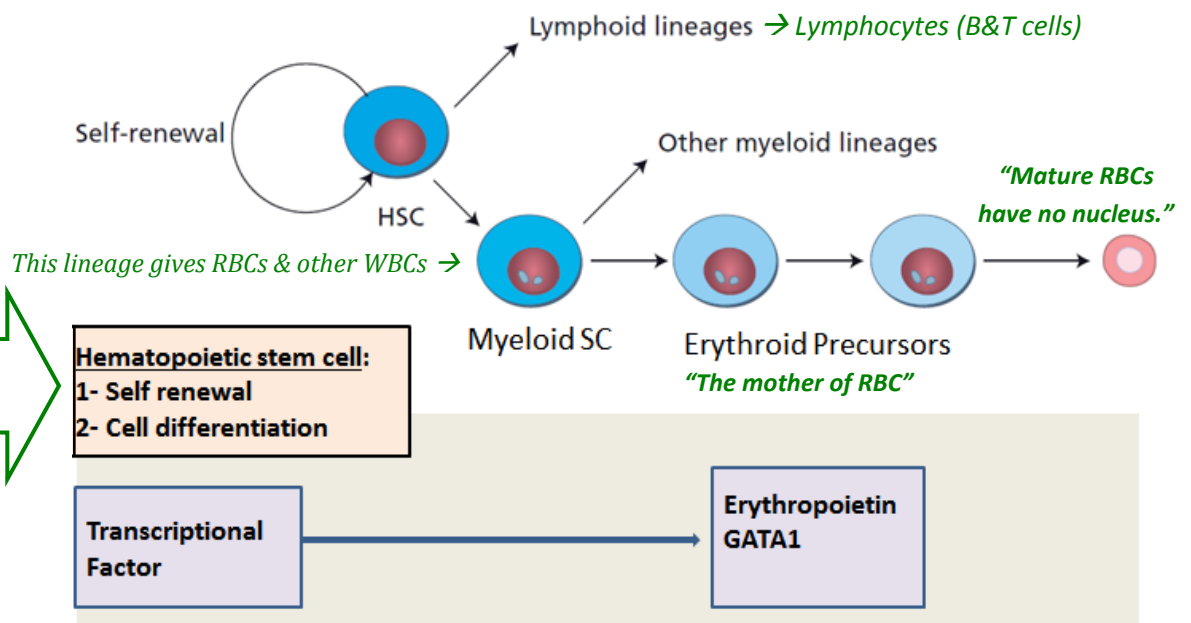
Hemoglobin structure:

Consist of: 4 Iron atoms/ 4 Porphyrin rings/ 4 globin chains.

A single molecule of Hb can carry up to 4 molecules of O₂. It depends on the bioavailability of the O₂.



Hematopoiesis: All cellular blood components are derived from haematopoietic stem cells. In a healthy adult, approximately 10¹¹–10¹² new blood cells are produced daily in order to maintain steady state levels in the peripheral circulation. “Production, Proliferation, specialization and maintain of each blood cell.”

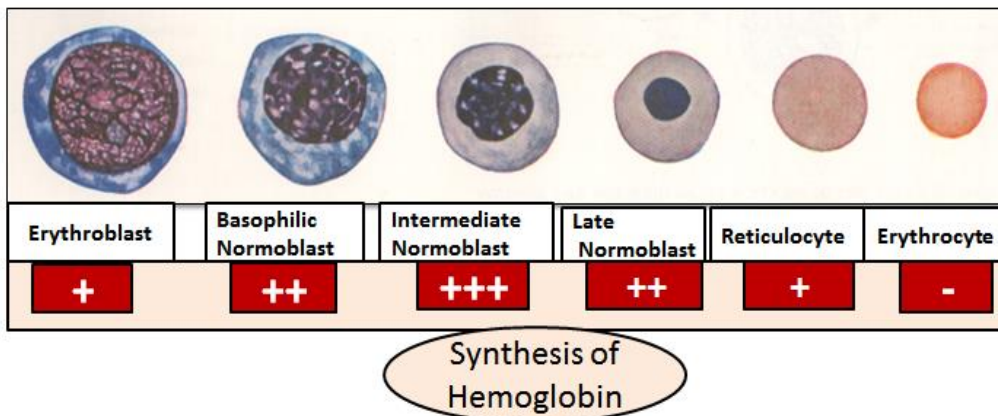


Its self-renewal is tightly regulated, because if it's not controlled, it could lead to diseases including malignancies.

Hemoglobin

Erythropoiesis: It is the process by which red blood cells (erythrocytes) are produced. "Doctor said do not memorize this for the exam it's only for your information"

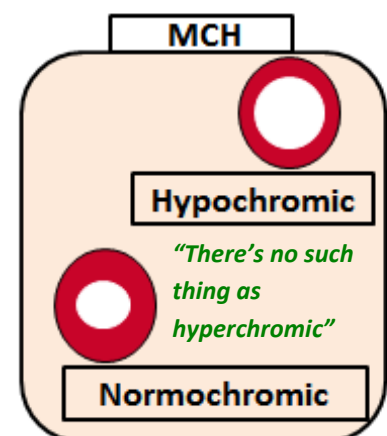
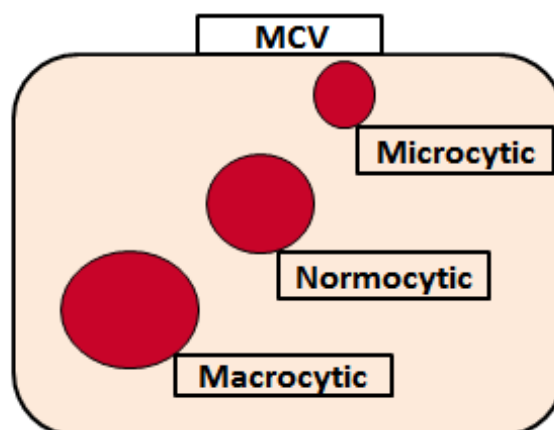
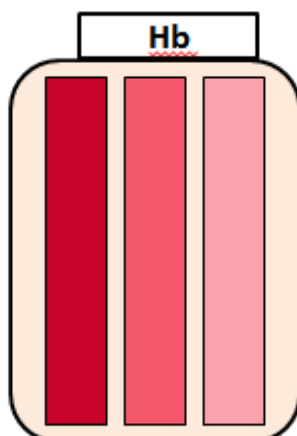
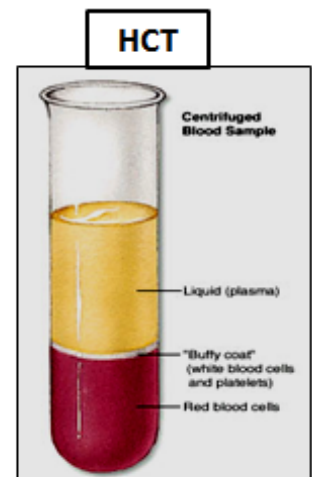
The "Bone Marrow" is the major site with the need of:
 Folic acid – Iron "Ferrous" – Vit B12 – Erythropoietin -Amino acids
 minerals - other regulatory factors



The first 4 stages are found ONLY in the bone marrow, while the last 2 are in the circulation. When the cell reaches the erythrocyte stage, it stops synthesizing

Normal Ranges:

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

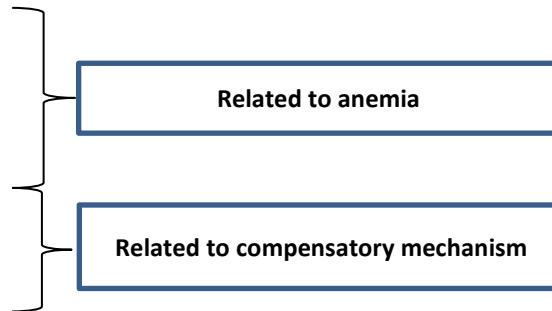


Anemia

- ❖ 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**).

Clinical Features:

- **Weakness**
- **Headache**
- **Pallor**
- **Lethargy**
- **Dizziness**
- **Palpitation (tachycardia)**
- **Angina**
- **Cardiac failure**



NOTE: Presence or absence of clinical features 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 "Bone marrow" & O₂ dissociation curve).

2- Severity:

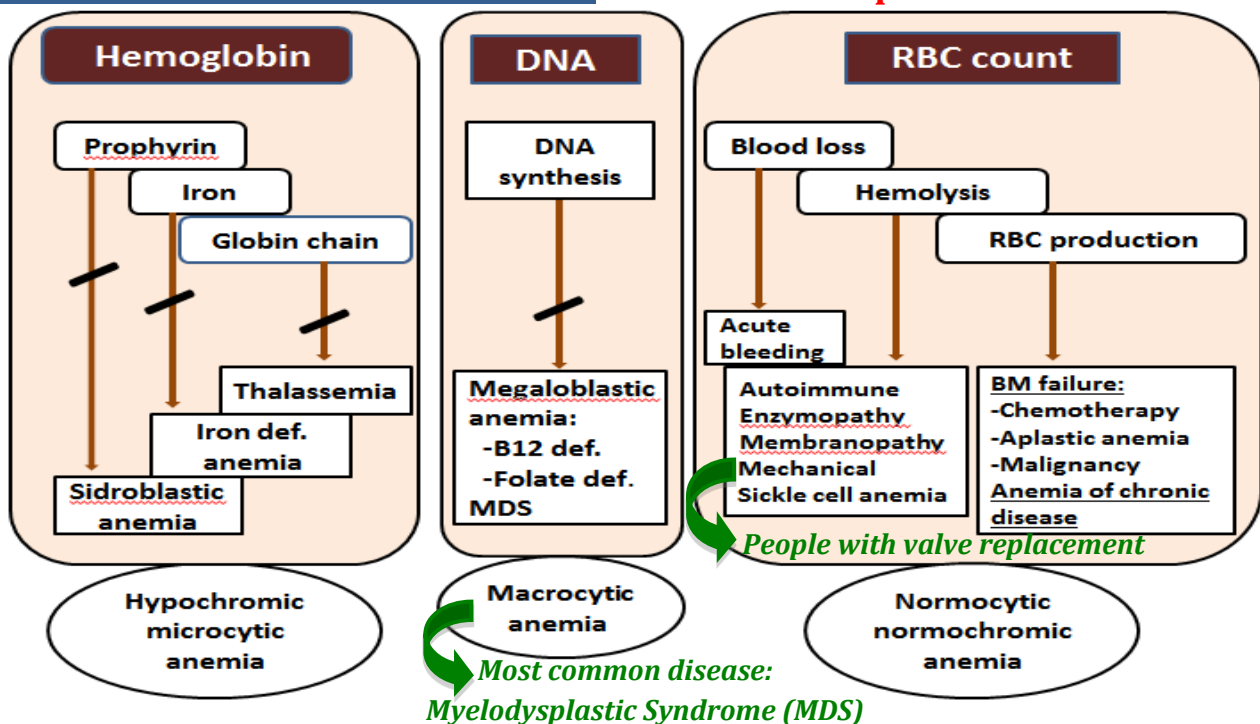
- Mild anemia (Hb = 10 g/dL): no symptoms usually.
- Symptoms appear if Hb less than 9 g/dL.

3- Age:

- Elderly tolerate anemia less than young patients. (Because the body cannot compensate as usual)

Classification of Anemia:

Important to understand!



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. *“Even if your iron intake is high”*
- 2- Inorganic iron cannot be absorbed easily.

- Excess loss due to hemorrhage. *“Iron deficiency can also be caused by pregnancy, lactation, labor & menstruation”*

Iron cycle and storage:

1) Site of absorption:



Daily absorption ~ 1 mg

2) Carried in the blood via transferrin in the ferric state.



Important:

Storage forms:
Ferritin
Haemosiderin

Daily loss ~ 1mg

Urine, faeces, nails, hair, skin

Liver, other parenchymal cells and tissues, especially muscle myoglobin (600-650 mg)

Some of the iron in the blood will travel to the liver & other tissues, where it might be stored or excreted into the urine & feces.

3) Majority will travel to the bone marrow, where it's needed for the RBC maturation.



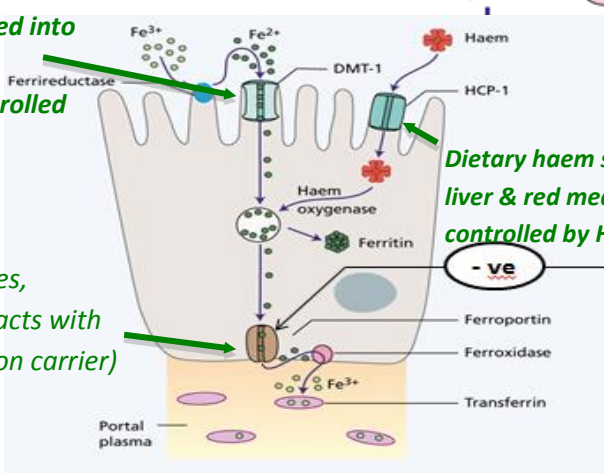
Mature RBCs are released into the blood.

Circulating haemoglobin (1.7-2.4 g)

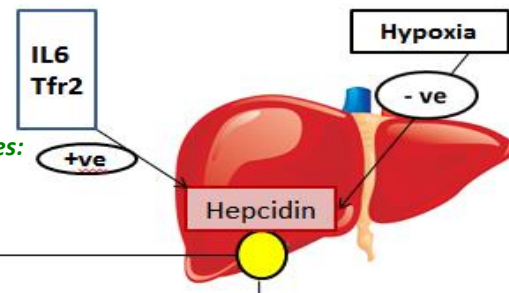
Macrophages (0.5-1.5 g)

4) Macrophages will engulf the old RBCs & recycle the iron by sending it back to the circulation and from there to the bone marrow.

Dietary iron (ferric Fe^{+3}) is converted into (ferrous Fe^{+2}). Its entry is controlled by DMT-1.

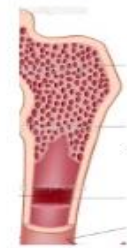


In the intestines, hepcidin interacts with ferroportin (iron carrier) & inhibits iron absorption.

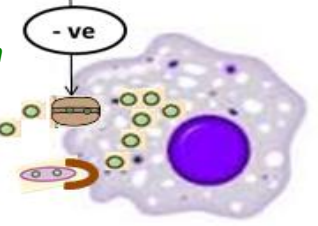


Hepcidin inhibits iron release from the macrophages by interacting with ferroportin.

Hepcidin is produced in the liver & it's the major hormonal regulator of iron.



Iron for erythropoiesis



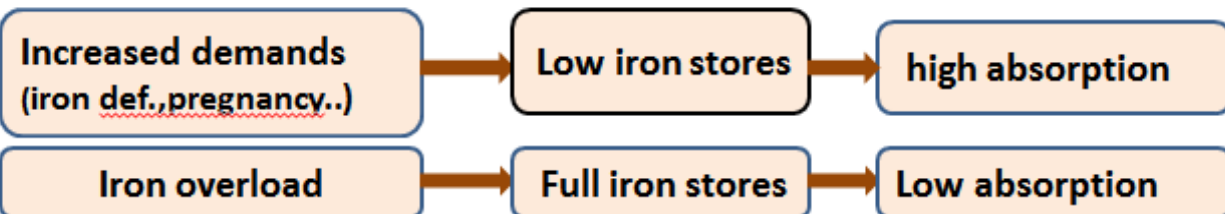
BM macrophage

Iron Deficiency Anemia

Iron Absorption:

Factors favoring absorption	Factor reducing absorption
Haem iron	Inorganic iron
Ferrous Iron (Fe ⁺⁺)	Ferric iron (Fe ⁺⁺⁺)
Acid (vitamin C)	Alkalines
Iron deficiency	Iron overload
Pregnancy	Tea
Hemochromatosis <i>“congenital anomaly leading to increased absorption”</i>	Increased hepcidin
Solubilizing agent (Sugar)	Precipitating agent (phenol)

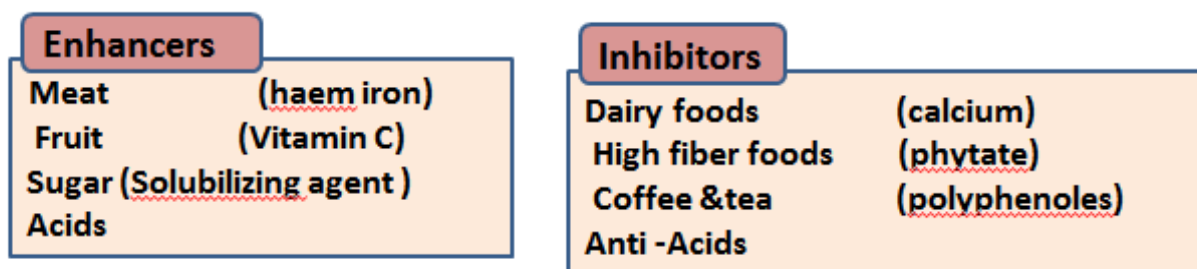
1-Body Iron status:



2- Content and form of dietary iron



3- Balance between dietary enhancers&Inhibitory factors:



Iron Deficiency Anemia

Causes of IDA:

1-Chronic blood loss:

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

2- Increased demands:

- Immaturity "*premature babies*"
- Growth
- Pregnancy
- EPO "Erythropoietin" therapy

3-Malabsorption:

- Enteropathy
- Gastrectomy

4-Poor diet:

- Rare as the only cause (rule out other causes).

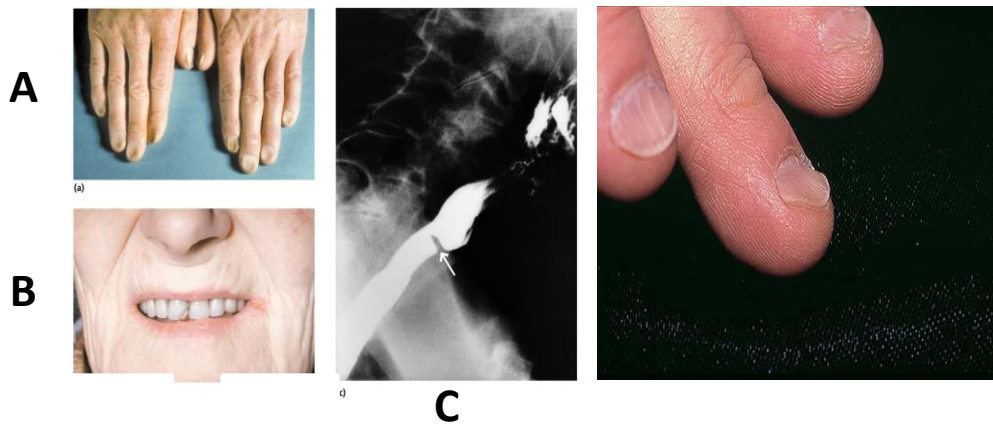
Development of IDA:

	1 Normal	2 Pre-latent	3 Latent	4 Iron def. anemia
Stores (first one affected in iron deficiency)	Normal	Low	Low	Low
MCV/MCH	Normal	Normal	Low	Low
Hemoglobin	Normal	Normal	Normal	Low

Signs of anemia

Iron Deficiency Anemia

Signs and symptoms of IDA:

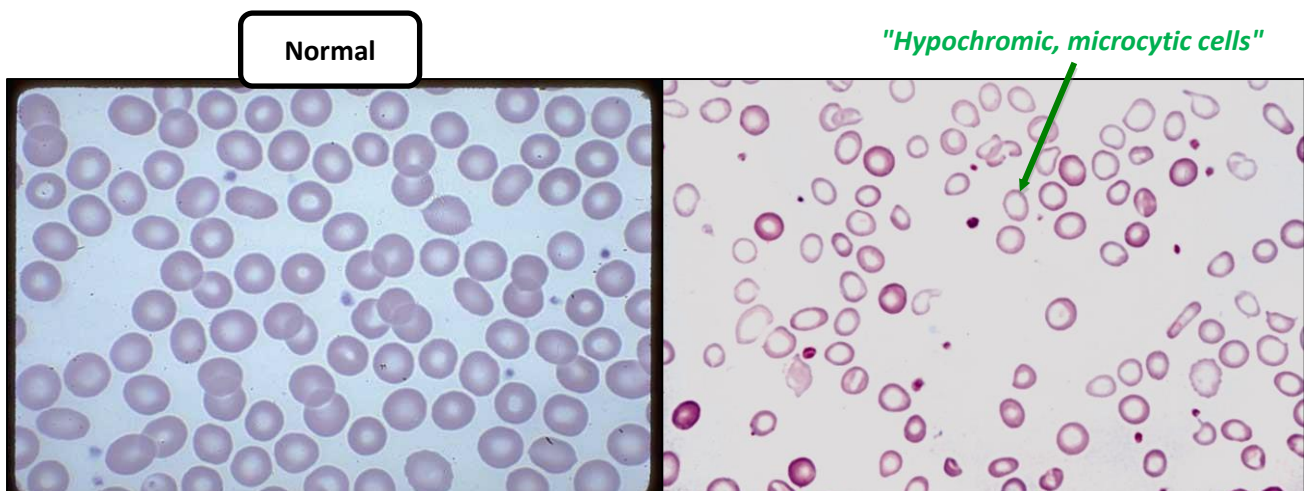


NOTE: Beside symptoms and signs of anaemia +/- bleeding patients present with:

(A): Koilonychia (spoon-shaped nails).

(B): Angular stomatitis and/or glossitis. *"Fissures around the edges of the mouth. It's usually the patient's main complaint"*

(C): Dysphagia due to pharyngeal web (Plummer-Vinson syndrome). *"Difficulty in swallowing"*

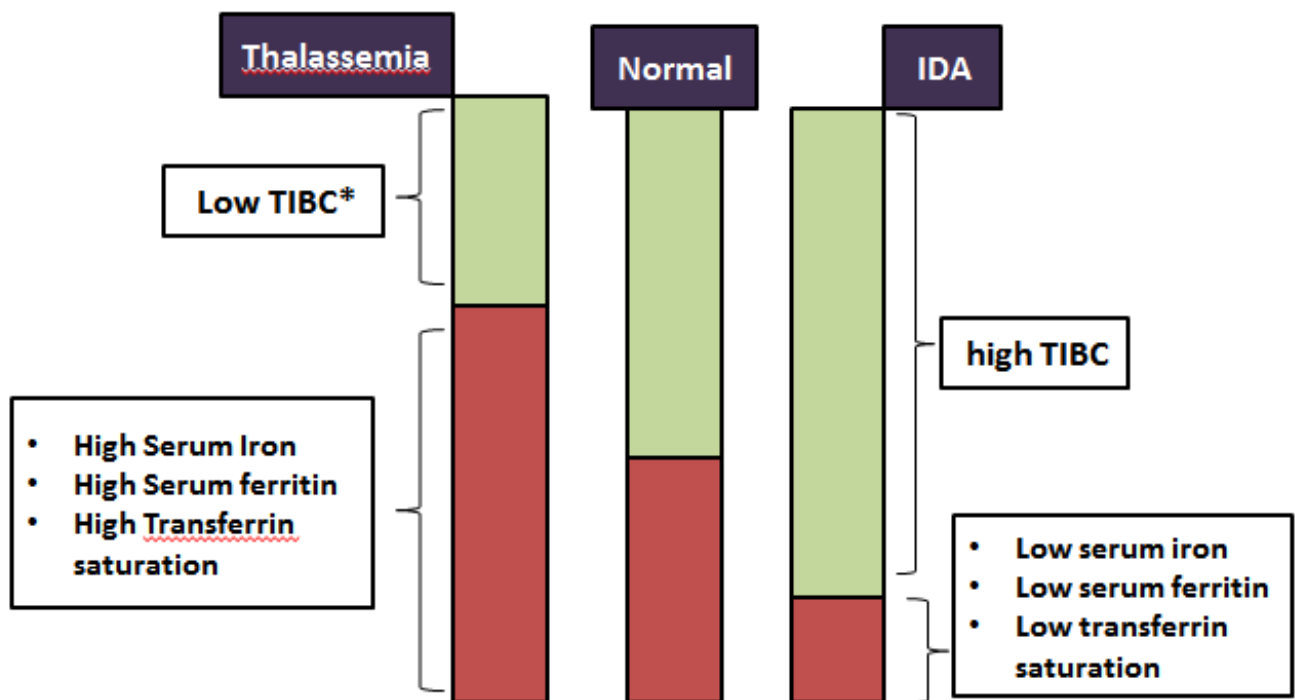
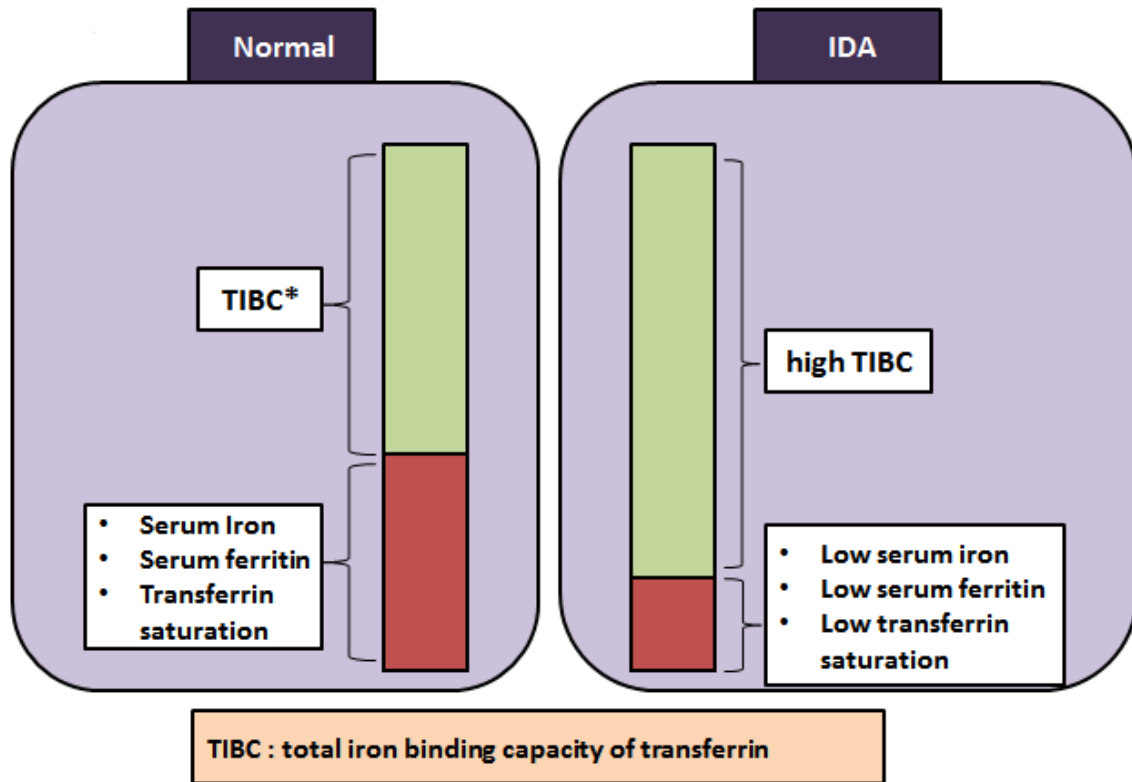


NOTE: Microcytic hypochromic anemia with:

- Anisocytosis (variation in size).
- Pokilocytosis (variation in shape).

Iron Deficiency Anemia

Iron Studies:

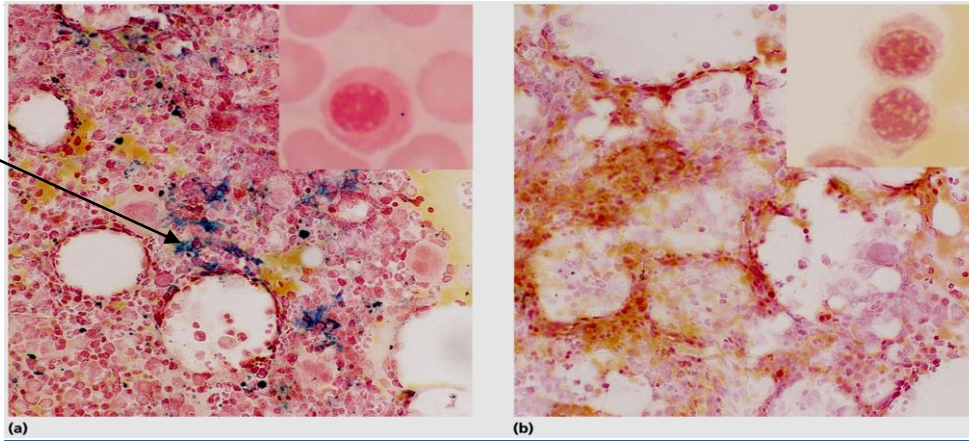


Iron Deficiency Anemia

Investigation:

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

In normal individuals, iron appears blue in Perl's stain.



Normal

IDA: reduced or absent iron stores (Hemosiderin)

Treatment of IDA:

- Treat the underlying cause
- Iron replacement therapy:
 - Oral: (Ferrous Sulphate OD for 6 months) *"if the patients doesn't respond → intravenous"*
 - Intravenous: (Ferric sucrose OD for 6 months)

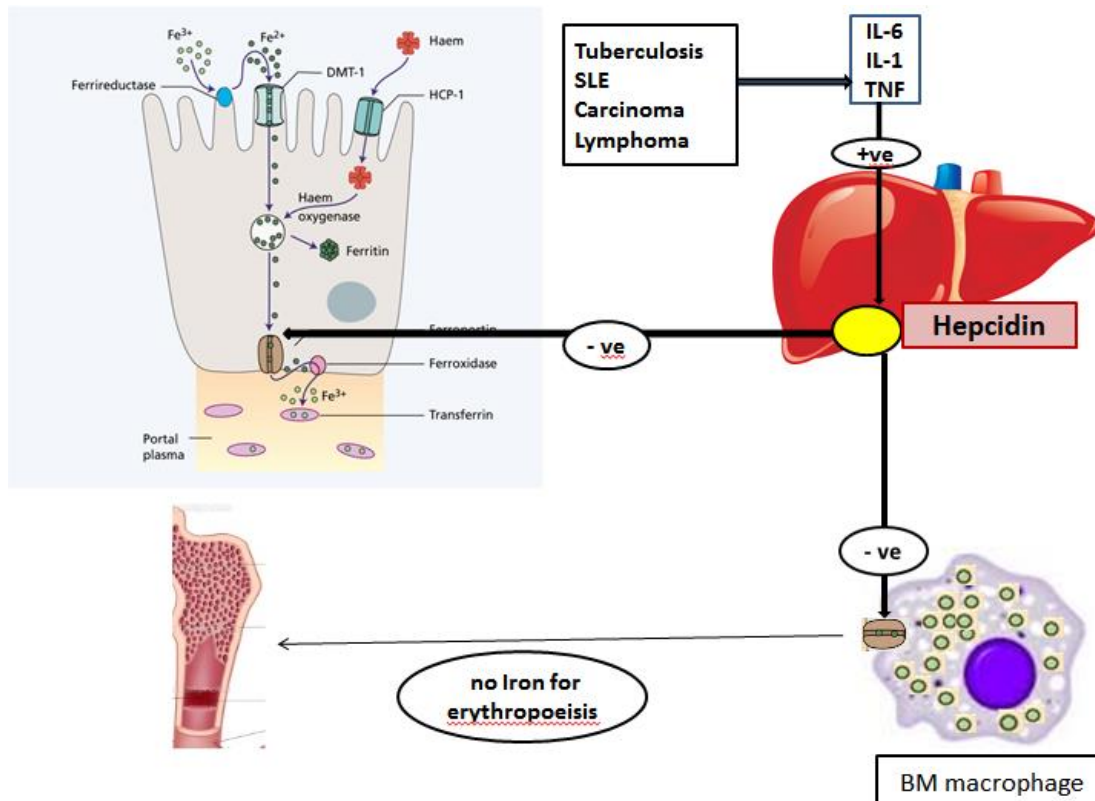
Hb should rise 2g/dL every 3 weeks

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.

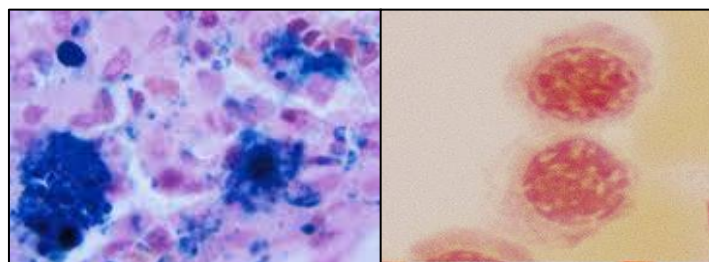
Anemia of Chronic Disease

- Normochromic normocytic (usually) anemia is caused by the decreased release of iron from iron stores due to raised serum Hepcidin levels.
- Associated with:
 - **Chronic infection including HIV, malaria**
 - **Chronic inflammations**
 - **Tissue necrosis**
 - **Malignancy**



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. *"macrophages are unable to release iron"*



NOTE: Management:

- Treat the underlying cause
- Iron replacement +/- EPO *"to increase the formation of Hb"*

Summary

- Hemoglobin is made up of: 4 globin chains, 4 porphyrin rings and 4 iron molecules. Its binding capacity is up to 4 molecules of O₂.
- **Haematopoiesis** is the formation of all the blood cellular components that are derived from the haematopoietic stem cells.
- **Erythropoiesis** is the process by which red blood cells (erythrocytes) are produced.
- It includes 6 stages: The first 4 in the bone marrow, while the last 2 are in the circulation.
- All stages of the RBC can synthesize Hb, except for the **last stage (erythrocyte)**.
- Iron deficiency is the most common cause of anemia.
- Iron is transported in the blood as **transferrin** and stored in the macrophages and other tissues as **ferritin and haemosiderin**.
- **Hepcidin** is produced by the liver. High levels of hepcidin will lead to decreased iron absorption in the intestines. It will also decrease the release of iron from the macrophages.
- **The most important cause of IDA** is chronic bleeding (GIT bleeding).
- Bone marrow iron stain (**perl's stain**) is the gold standard for diagnosing IDA.
- Other frequent causes of hypochromic, microcytic anemia are the anemia of chronic disorders, which occurs in patients with **chronic infections and malignancies**.

Questions

1/In iron deficiency, serum Fe is:

- A- Increased
- B- Decreased
- C- Normal

2/In latent Iron deficiency, the iron stores are:

- A- Normal
- B- Increased
- C- Absent

3/We can consider an adult male anemic if the HB concentration is below:

- A- 13.5gm/dl
- B- 11gm/dl
- C- 11.5gm/dl

4/ A 36-year-old man from China presents with increasing fatigue. He has a 3-year history of tuberculosis, and CBC shows a mild microcytic anemia. Blood work-up demonstrates low serum iron, low iron-binding capacity, and increased serum ferri- tin. The pathogenesis of anemia in this patient is most likely caused by which of the following mechanisms?

- A- Clonal stem cell defect
- B- Hypoxemia
- C- Impaired utilization of iron from storage sites
- D- Synthesis of structurally abnormal globin chain

Answers:

- 1- B
- 2- C
- 3- A
- 4- C

اللهم إني استودعك ما قرأت و ما حفظت و ما تعلمت فرده عليّ عند حاجتي إليه انك على كل شيء قدير

If there is any mistake or feedback please contact us on: 432PathologyTeam@gmail.com

