

# Haematology

## Team <sup>431</sup>

1/4



## Anemia

Team Leaders

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RevisedBy

Shatha Al-mweisheer

- ◆ very important
- ◆ mentioned by doctor
- ◆ team notes
- ◆ not important

**Anemia:** is a reduction of the hemoglobin concentration of the peripheral blood below the lower limit of certain range and gender.

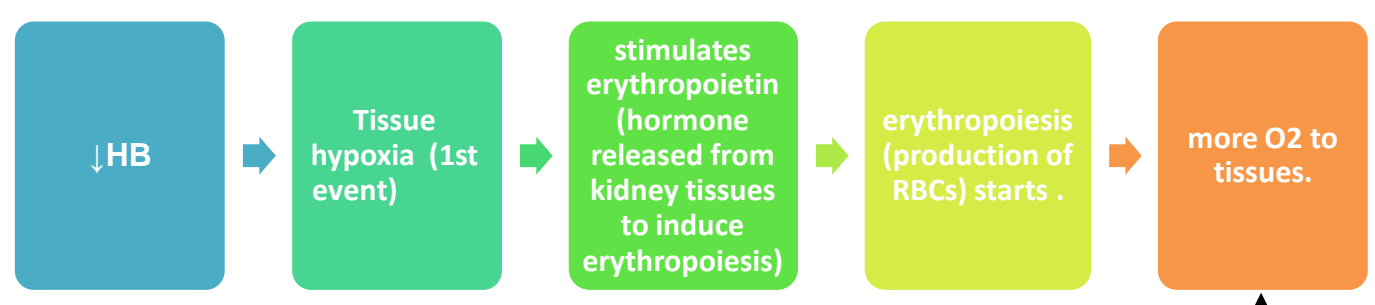
You can label the person as anemic if the Hb concentration is below:

	13.5 gm/dl in adult male
	11.5 gm/dl in adult female
	11 gm/dl in the age group between ( 2 years - until puberty)
	14 gm/dl in neonates* & infants

\*Neonatal period: the interval from birth to 28 days of age.

**Pathophysiology and how the body compensates anemia**

1)



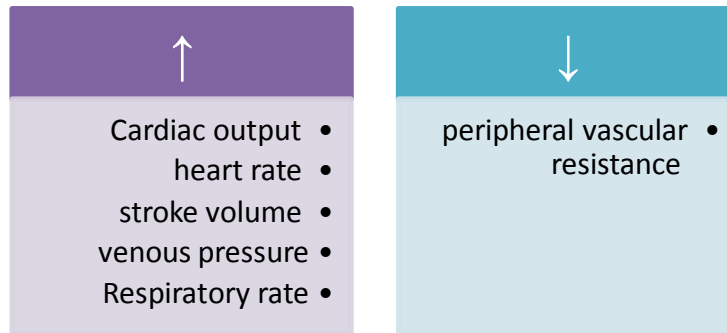
2) Redistribution of blood flow: **non vital organs like the skin will develop a compensatory vasoconstriction leading to pallor\***(deficiency of color)

2, 3 DPG molecules attach to the HB and lower the HB affinity to O2 molecules → more O2 to tissues

\*Pallor start to appear when the HB drop between 9-10

3) Maintenance of blood flow by expansion of the plasma volume.

4)



### Signs and symptoms

Anemia can be so mild that it goes unnoticed. But signs and symptoms increase as the condition worsens. The main symptom of **most types** of anemia is **fatigue (weakness)**.

- 🔥 **Rapidly progressive anemia is associated with more signs and symptoms because the body doesn't have enough time to compensate.**
- 🔥 **Elderly patients tend to tolerate the anemia less than adult or healthy people**

#### symptoms :

1- Headache	2- Exercise induced dyspnea (Shortness of breath)
3- Pale skin	4- Numbness or coldness in your extremities
5- Palpitation (A fast or irregular heartbeat) caused by increased hyper dynamic circulation.	6- Dizziness
7- Chest pain	8- Cognitive problems: seen in <b>pediatrics and elderly</b> .

#### Signs:

1-Black and tarry stools (sticky and foul smelling)	2- Maroon, or visibly bloody stools: is dark red color of the stool.
3- Tachycardia / Heart murmur/ Bounding pulse (is a leaping and forceful pulse that quickly disappears): caused by increased <b>hyper dynamic circulation</b> .	4- Pale or cold skin (when HB drops between 9-10 gm/dl ) / Jaundice (more frequent <b>in hemolytic anemia</b> )
5- Low blood pressure.	6- Postural hypotension
7- Enlargement of the spleen.	8- Constipation: caused by iron deficiency anemia treatment.
9- Sweating, thirst and air hunger.	10- Syncope (particularly following exercise).
11- Tinnitus or vertigo irritability	12- Restlessness ( <b>more frequent in severe chronic anemia</b> )
13- difficulty sleeping or concentrating → more frequent in <b>severe chronic anemia</b>	

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Pat.No: | Name: | Page No.: 1  
 Hospital: KING KHALID UNIVERSITY HOSPITA | Sex: F  
 Location: (OBG03) Booking Clinic | DOB: 08 Jun 72  
 Doctor: |

Xref:  
 Req No.: | Date Coll.: 22/12/29 (20/12/08) | Date Recd.: 22/12/29 (20/12/08)  
 Printed: 22/12/1429 (20/12/08) 11:53 | Time Recd.: 10:10

EDTA Whole Blood

Parameter	Value	Unit	Reference Range
WBC	10.2	x10.e9/L	4 - 11
RBC	4.59	x10.e12/L	4.2 - 5.5
HGB	132	g/L	120 - 160
HCT	39.5	%	37 - 47
MCV	86.0	fL	80 - 94
MCH	28.8	pg	27 - 32
MCHC	335	g/L	320 - 360
RDW	14.9	%	11.5 - 14.5
PLT	PEND	x10.e9/L	140 - 450
MPV	9.4	fL	7.2 - 11.1
%NEUT	76.7	%	40 - 75
%LYMP	19.0	%	20 - 45
%MONO	2.3	%	3 - 9
%EOS	1.8	%	0 - 6
%BASO	0.2	%	0 - 1
#NEUT	7.8	x10.e9/L	2 - 7.5
#LYMP	1.9	x10.e9/L	1 - 5
#MONO	0.2	x10.e9/L	0.2 - 0.8
#EOS	0.2	x10.e9/L	0.0 - 0.8

Morphology  
 Flag Comments  
 Flag Comment 1  
 ANISO  
 MICRO  
 MACRO  
 POIKILO  
 HYPO  
 Polychromasia  
 LSHIFT

REQUEST COMMENTS:  
 F

Technician on Duty | Consultant

Complete Blood Count (CBC)

Differential

Normocytic cell  
 (if ↓ → microcytic cell  
 If ↑ → macrocytic

Normochromic cell  
 (if ↓ → microchromic cell  
 If ↑ → macrochromic cell)

There are three main types of anemia: 1-Microcytic Hypochromic. 2- normocytic normochromic. 3- Macrocytic Hyperchromic.

**\*Important Hypochromic, Microcytic Anemia**

Any defect in heme or globin will give rise to it. Eg. Thalassemia (globin defect) and the most common one is iron deficiency anemia (defect in heme)

Serum Fe reduced	1-low ferritin & absent bone marrow macrophages → <b>Iron deficiency (MCV is in the lower limit of normal range).</b>
	2- Normal or increased ferritin & normal bone marrow macrophages → <b>Anemia of chronic disorders</b> (infections, malignancies, C.T disease). <b>Caused by decreased release of iron from the stores.</b>
Serum Fe Normal	Electrophoresis → <b>THALASSEMIA (MCV is severely low 65-70) or HEMOGLOBINOPATHIES (S,C,D,E)</b> both affect the globins.
Serum Fe Increased	Bone marrow Sideroblast Fe Increased > <b>SIDEROBLASTIC ANAEMIA</b>

**Note:** Serum iron test is the second step should be done to figure out if it is iron deficiency anemia since it is the most common type. (After the blood film is done and before electrophoresis)

## Macrocytic Hyperchromic, Macrocytic anemia

<b>Megaloblastic</b>	<b>1- FOLATE DEFICIENCY: diet or drug induced</b>
	2- B12 DEFICIENCY: caused by defect in digestion, absorption & medication. 3- NO DEFICIENCY
<b>Non-megaloblastic</b>	Increased RETICULOCYTES* : 1- Hemolytic Anemia.      2-Hemorrhage.
	Normal or decreased RETICULOCYTES: 1- <b>Hepatic Disease.</b> 2- <b>Myxaedema (hypothyroidism).</b> 2- 3-Myelophthisic Anemia.      4- physiological during pregnancy& neonatal period.

\* Reticulocytes: immature red blood cells, typically composing about 1% of the red cells in the human body. Reticulocytes develop and mature in the red bone marrow. They are a compensation from the rapid bone marrow turnover of RBC.

## Normocytic, normochromic anaemia

<b>Increased Erythrocyte Production (RETICULOCYTES)</b>	1- <b>Hemolytic Anemia.</b> 2- <b>Acute blood loss.</b>
<b>Normal Erythrocyte Production (RETICULOCYTES)</b>	Bone Marrow Aspirate and Biopsy should be taken: 1- To reveal any infiltrations like in <b>Leukemia , Myeloma , myelofibrosis and metastasis</b> that can interfere with bone marrow functions→ anemia of chronic disease 2- If it is normal, investigate serum iron, Liver function test ,test for renal and endocrine functions.

**Note:** chronic diseases may cause either Hypochromic Microcytic or NORMOCYTIC, NORMOCHROMIC ANEMIA.

### Functional causes of anemia( 3 Hs)

1- Hypofunctioning (the bone marrow): due to lack of RBCs components e.g.iron,folic acid and B12

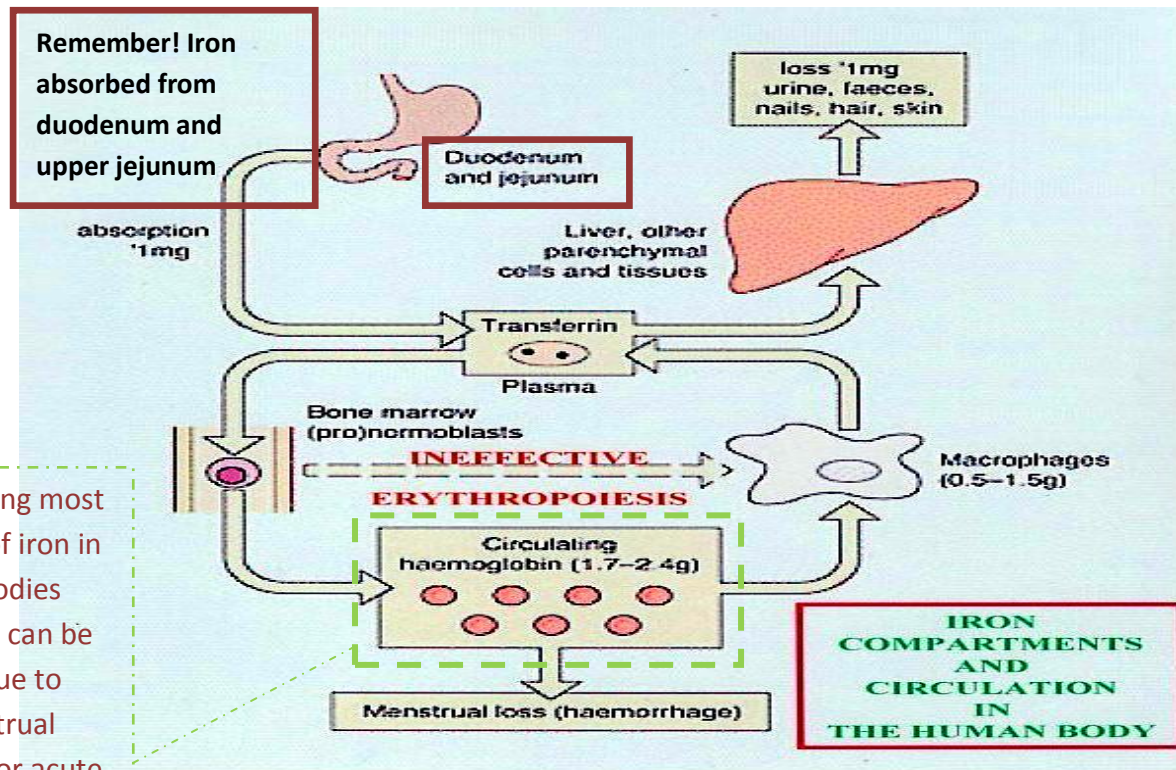
2- Hemorrhage

3- Hemolysis in tissue

## IRON DEFICIENCY ANAEMIA

The most common cause of hypochromic microcytic anemia

There is a regular physiological 1mg loss of iron (feces, urine, and skin). This loss is compensated by absorbing 1mg iron. Hemorrhage is an extra source of iron loss that can't be compensated by the 1mg absorbed iron, result in iron deficiency anemia



Carrying most part of iron in our bodies which can be lost due to menstrual cycle or acute hemorrhage

- 1- **Transferrin**: is a protein that transfers 2 atoms of iron in the circulation to different organs which either utilized iron in the formation of erythroblast where iron will be incorporated to HB (**bone marrow**) or which lost iron physiologically. These organs have **Transferrin receptors**.
- 2- Circulating HB carries the most iron in our bodies.
- 3- When the RBCs died in macrophage, iron will be released and reutilized by the transferrin that delivers iron to different organs.
- 4- Iron stored mainly in macrophages as **ferritin & hemosidrhén**.

## IRON ABSORPTION

	<b>Favored by:</b>	<b>Reduced by:</b>
Dietary factors	<b>Increased</b> Haem iron <b>Increased</b> animal iron <b>Ferrous</b> iron salts	<b>Decreased</b> haem iron <b>Decreased</b> animal iron <b>Ferric</b> iron salts
Luminal factors	<b>Acid</b> pH (e.g. gastric HCl)  Low molecular weight soluble chelates (e.g. Vit. C, sugars, amino acids)	<b>Alkalines</b> (e.g. pancreatic secretions)  Insoluble iron complexes (e.g. phytates, tannates in tea, bran)
Systemic factors* <b>important</b>	<b>Iron deficiency</b> <b>Increased</b> erythropoiesis Ineffective erythropoiesis Pregnancy / Hypoxia Ligand in meat (unidentified)	<b>Iron overload</b> <b>Decreased</b> erythropoiesis Inflammatory disorders

### ETIOLOGICAL FACTORS IN IRON DEFICIENCY

#### A. NEGATIVE IRON BALANCE

##### 1. DECREASED IRON INTAKE

- a. INADEQUATE DIET
- b. IMPAIRED ABSORPTION
  - 1) ACHLORHYDRIA
  - 2) GASTRIC SURGERY
  - 3) CELIAC DISEASE

##### 2. INCREASED IRON LOSS

- a. GASTROINTESTINAL BLEEDING
  - 1) UNKNOWN SITE
  - 2) HEMORRHOIDS
  - 3) SALICYLATE INGESTION
  - 4) PEPTIC ULCER
  - 5) HIATAL HERNIA
  - 6) DIVERTICULOSIS
  - 7) NEOPLASM
  - 8) ULCERATIVE COLITIS
  - 9) HOOKWORM
- b. EXCESSIVE MENSTRUAL BLEEDING
- c. HEMOGLOBINURIA
- d. SELF INFLECTED BLEEDING
- e. IDIOPATHIC PULMONARY HEMOSIDEROSIS
- f. HEREDITARY HEMORRHAGIC TELANGIECTASIA
- g. DISORDERS OF HEMOSTASIS

#### B. INCREASED REQUIREMENT

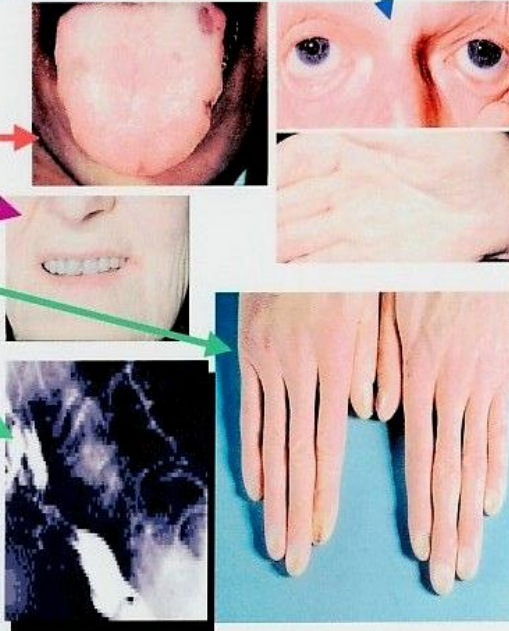
- 1. INFANCY
- 2. PREGNANCY
- 3. LACTATION

The age between 3-6 months they tend to develop negative iron balance. After 6 months until 1 year, infants prone to develop iron deficiency anemia if their diet is a pure milk from the breastfeeding. Mixed food and infant formula insure adequate intake of dietary iron.

Means they are consuming stores without replacing

## IRON DEFICIENCY ANAEMIA CLINICAL FEATURES

- SIGNS & SYMPTOMS OF ANAEMIA
  - PAINLESS GLOSSITIS
  - ANGULAR STOMATITIS
  - BRITTLE NAILS - KOILONYCHIA
  - DYSPHAGIA
  - PHARYNGEAL WEB
- [PATERSON-KELLY OR PLUMMER VINSON SYNDROME]
- PICA
  - ATROPHIC GASTRITIS & DECREASE GASTRIC SECRETION ( REVERSIBLE)



The most important are:

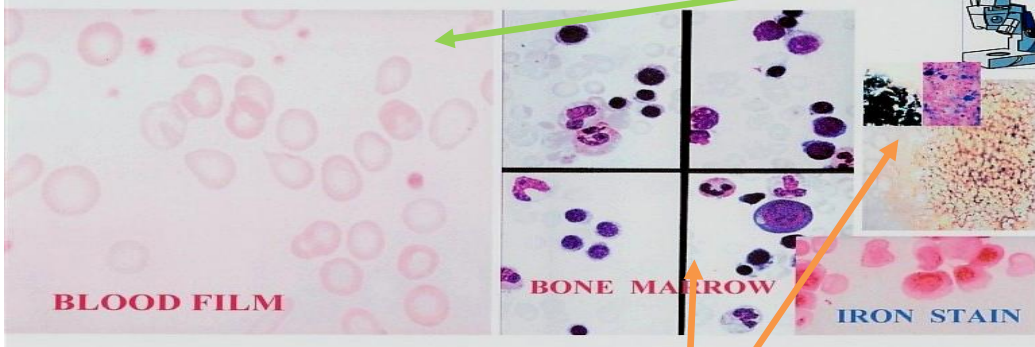
- 1- Painless glossitis
- 2- Koilonychias (spoon nails): rarely seen & only with chronic and very severe cases.
- 3- Angular stomatitis: an inflammatory lesion at the labial commissure, or corner of the mouth.



- 4- Dysphagia & pharyngeal web (esophageal webs are thin membranes located in the middle or upper esophagus)

**Plummer-Vinson syndrome/ Paterson-Kelly syndrome:** presents as a triad of dysphagia (due to esophageal webs), glossitis, and iron deficiency anemia.

## IRON DEFICIENCY ANAEMIA



- 1- Hypochromic microcytic RBCs are clearly seen in the blood film.

- 2- Target cells: more pronounced in thalassemia.

- 3- Pencil shaped RBCs or "Cigar cells"

Platelets increased with iron deficiency anemia.

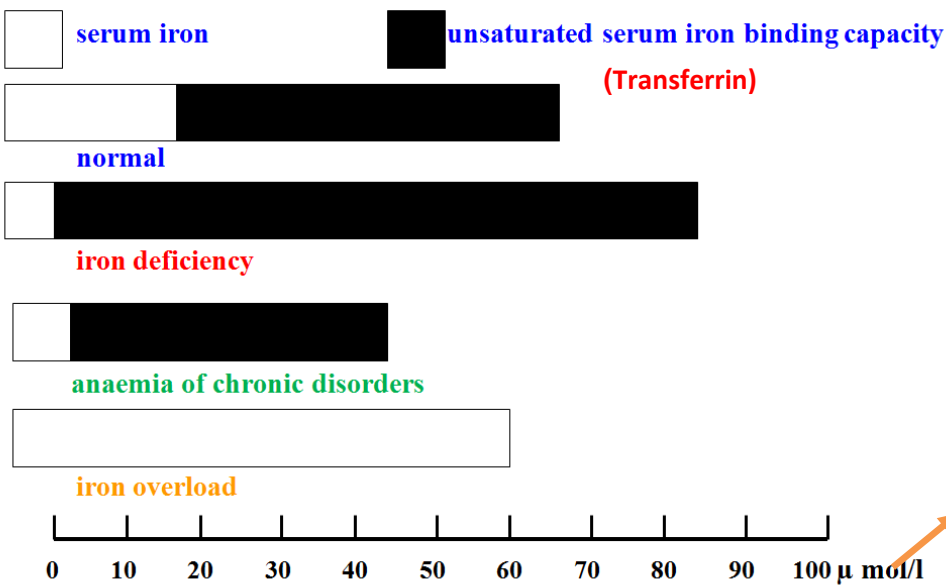
The bone marrow stained with Perls' Prussian blue to assess ferritin storage in bone marrow. The bluish dots indicate that the macrophages have adequate iron stores. Absences of iron stores in macrophages is seen in iron deficiency anemia.



-	Normal	Latent Iron deficiency	Iron deficiency anaemia
Red cell iron (peripheral film And indices)	Normal	Normal	hypochromic, microcytic MCV↓MCH↓MCHC↓
Iron stores (bone marrow Macrophage iron)	+++++	Absent	Absent (low serum iron & low ferritin) Complete depletion. <b>(The development of iron deficiency anaemia Reticuloendothelial (macrophage)iron stores are lost completely before anaemia develops)</b>









**Total Iron Binding Capacity (TIBC)**  
 (Serum iron + unsaturated iron binding capacity)  
 A measure of transferrin concentration in serum or plasma

TIBC is a blood test to see if you may have too much or too little iron in the blood. Iron moves through the blood attached to a protein called transferrin. This test helps your doctor know how well that protein can carry iron in the blood.



TIBC: is the serum iron (transferrin loaded with 2 iron atoms) + unsaturated serum iron (unloaded transferrin).  
 Iron deficiency stimulates transferrin synthesis in liver, causing an **increased TIBC**, although **the serum iron decreased**.  
 In chronic disorders both TIBC & serum iron is increased.

The serum iron and unsaturated serum iron binding capacity in normal subjects, iron deficiency, the anaemia of chronic disorders and iron overload. **The total iron binding capacity (TIBC) is made up by the serum iron and the unsaturated iron binding capacity.**

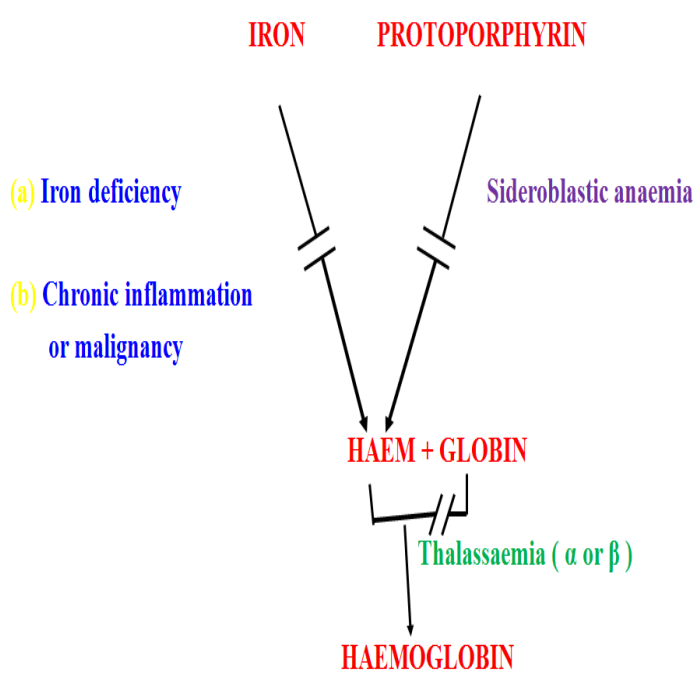
	Normal	Iron Depletion	Iron Deficient Erythropoiesis	Iron Deficiency Anaemia
Iron Stores →				
Erythron Iron →				
RE Marrow Fe (O-6)	2-3+	0-+†	0	0
Transferrin IBC (µmol/l)	60±5	65	70	75
Plasma Ferritin (µg/l)	100±60	20	10	<10
Iron Absorption	Normal	↑	↑	↑
Plasma Iron (µmol/l)	20±9	20	<10	<7
Transferrin Saturation (%)	35±15	30	<15	<10
Sideroblasts (%)	40 – 60	40-60	<10	<10
RBC Protoporphyrin (µg/dl RBC)	30	30	100	200
Erythrocytes	normal	normal	normal	Microcytic and hypochromic

- **Depletion:** the stores are completely lost before developing neither symptoms nor RBC changes. Plasma ferritin is low. Iron absorption is increased. Serum iron is normal. MCV and MCH normal.

- **Iron deficient erythropoiesis:** Plasma ferritin and plasma Iron are more reduced. Transferrin saturation is low.

- **Iron deficiency anaemia:** Low ferritin + Iron + Transferrin saturation. Increased absorption. And complete absence of stores.

The sequence of changes induced by a gradual reduction in the iron content of the body.



The causes of a hypochromic microcytic anaemia include: **(DDx of Iron deficiency Anemia)**

- lack of iron (iron deficiency) or of iron release from macrophages to serum (anaemia of chronic inflammation or malignancy)
- Failure of protoporphyrin synthesis (sideroblastic anaemia)
- Failure of globin synthesis (alpha or beta-thalassaemia)
- **Lead** (الرصاص) also inhibits haem and globin synthesis.

**TREATMENT:** Iron supplements (orally or parentally which is faster) used in acute blood loss, chronic renal failure with erythropoietin therapy, malabsorption.

## Questions

1- In iron deficiency, serum Fe is:

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

2- Iron absorption is favored by:

- A- Ferrous iron salts
- B- Ferric iron salts
- C- Alkalines
- D- Tannates

3- In latent Iron deficiency, the iron stores are:

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

4- We can consider an adult male anemic if the HB concentration is below:

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

Answers: 1)B 2) A 3) C 4) A