ANEMIA

BY:

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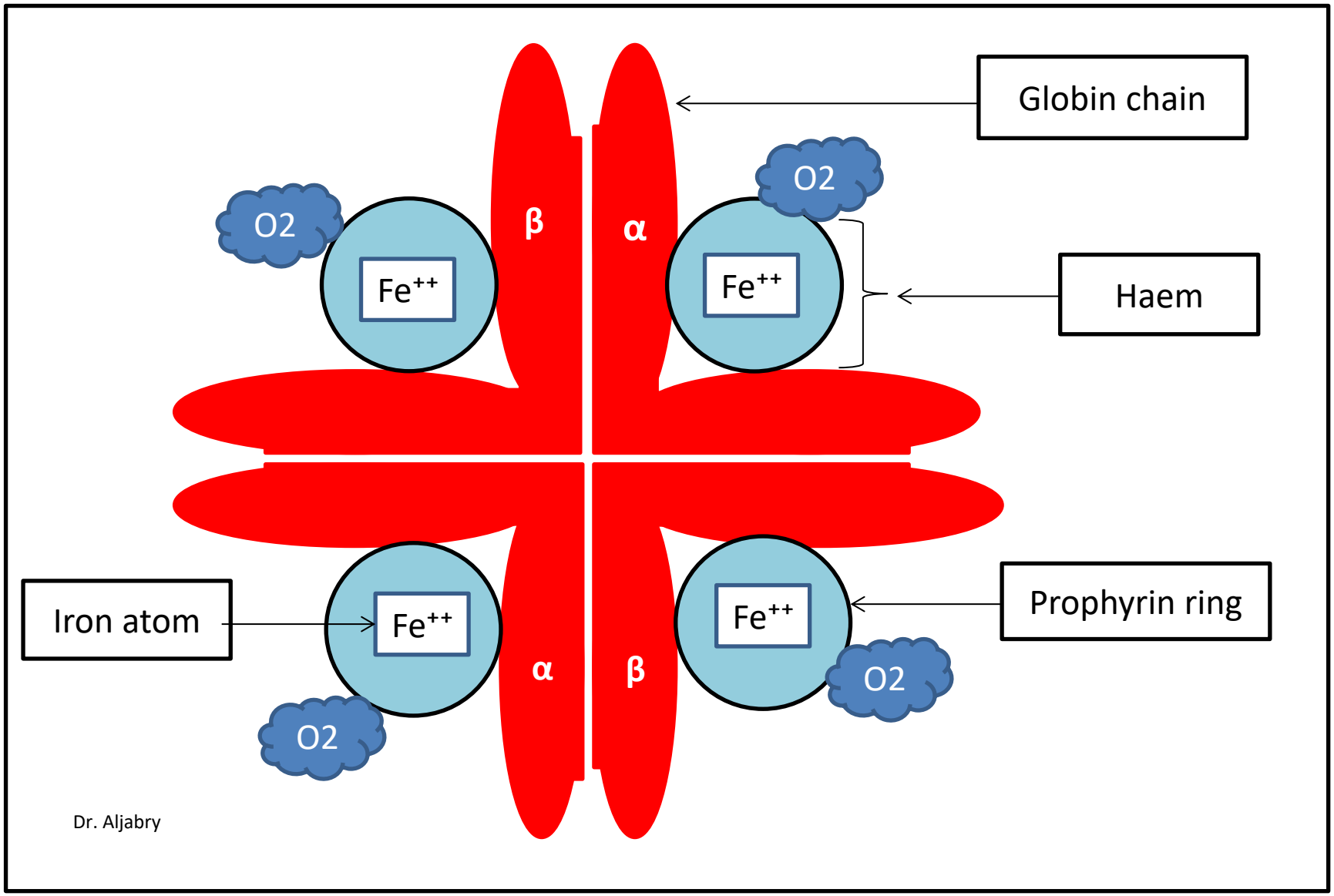
Objectives

- To understand the normal control of erythropoiesis
- To understand the pathophysiology of anemia
- To recognize the general features of anemia
- To understand the basis of anemia classification
- To understand iron metabolism, how iron deficiency and anemia of chronic disease may arise and how to manage it.

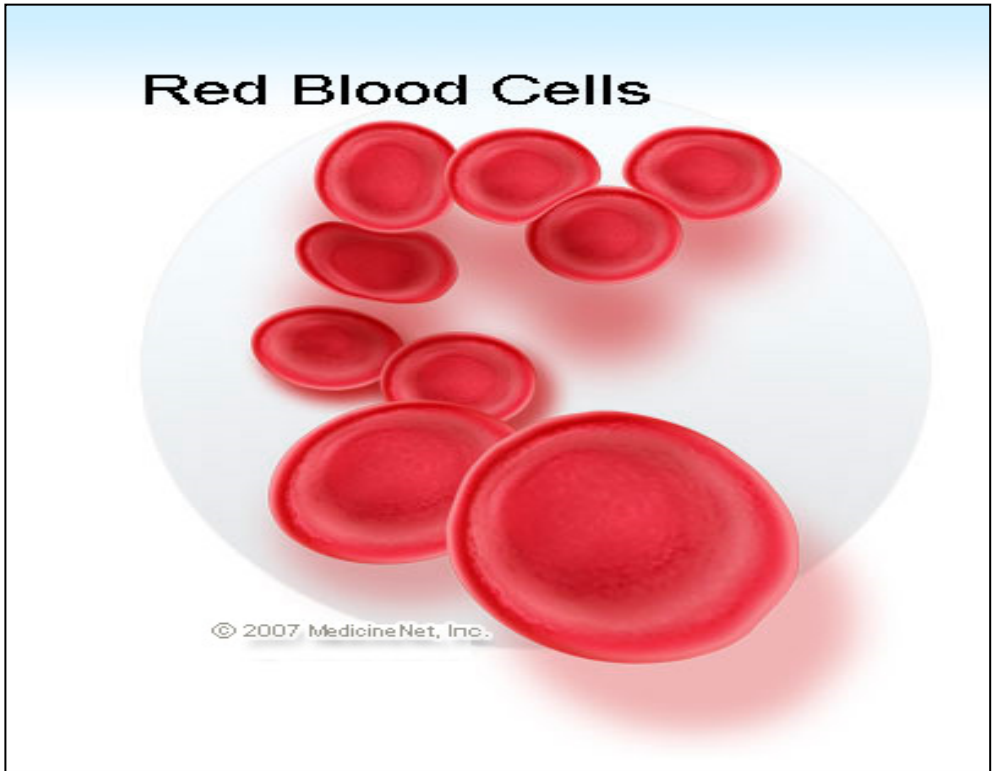
Hemoglobin??

Hemoglobin structure

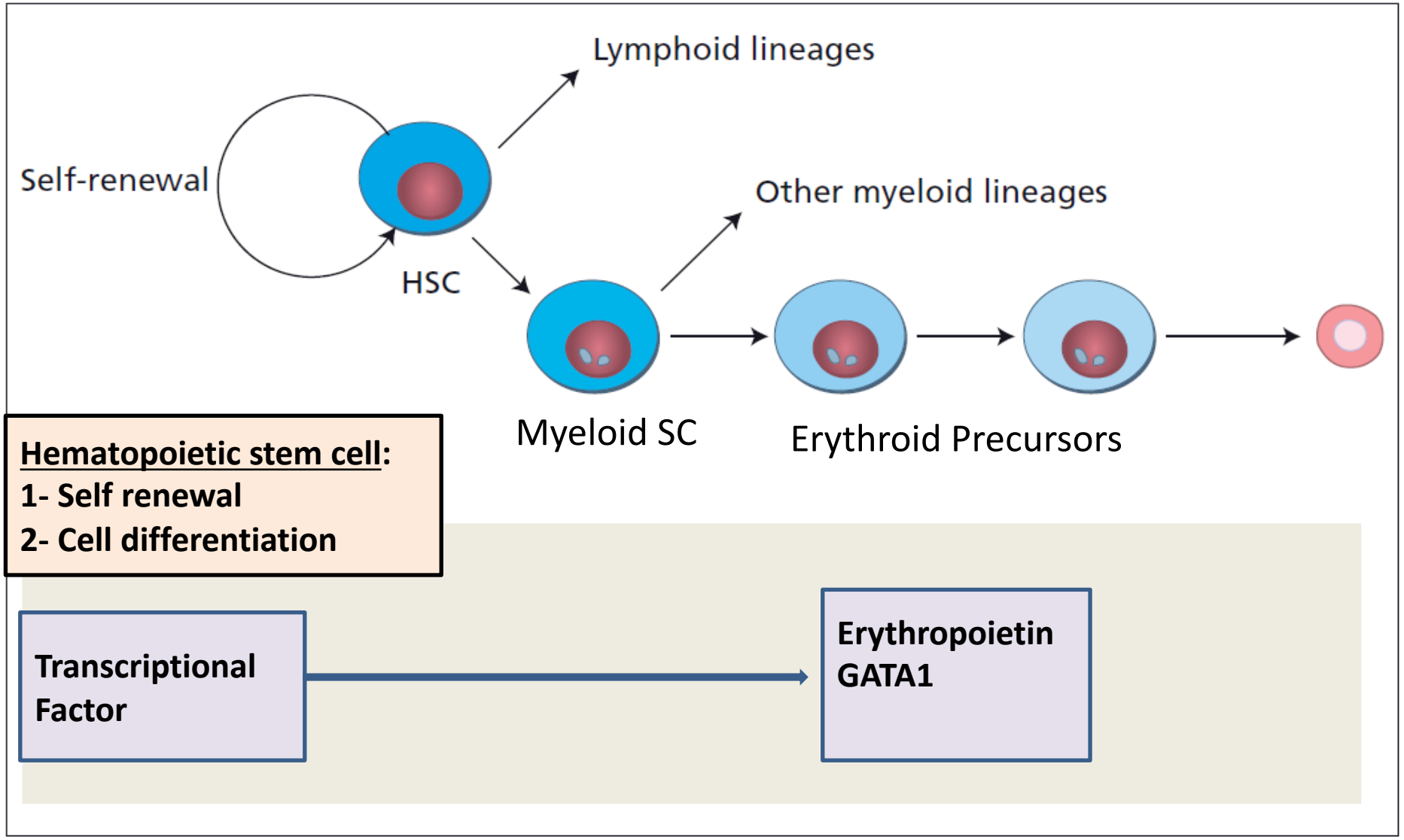


Hemoglobin

- **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.**



Hematopoiesis

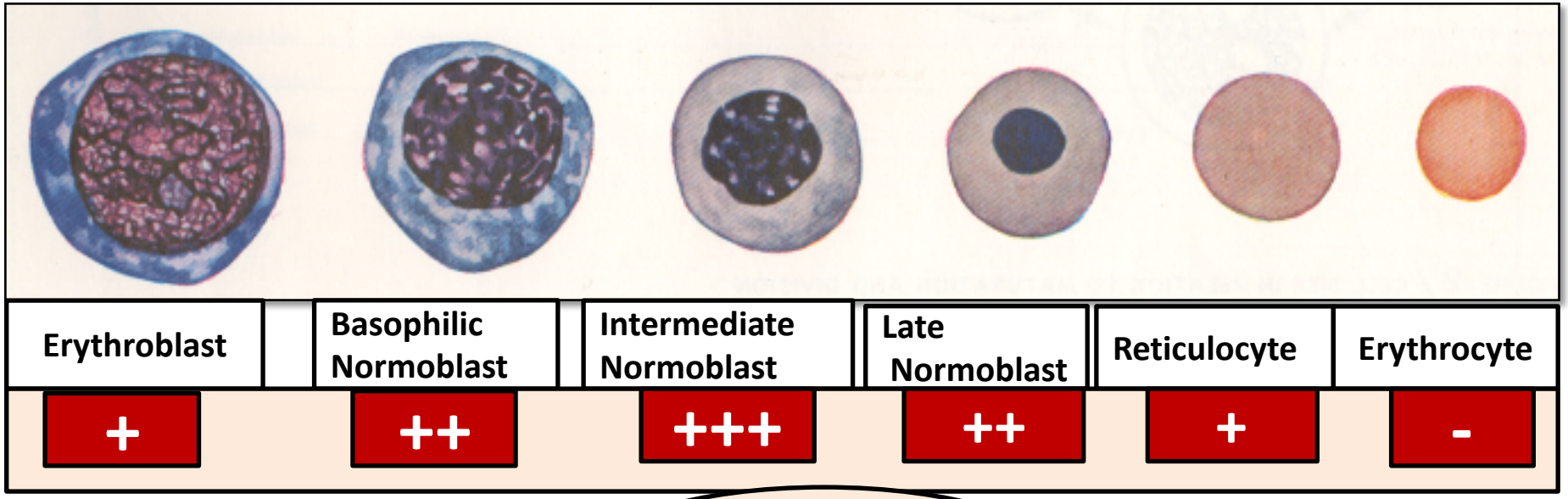


Hematopoietic stem cell:
1- Self renewal
2- Cell differentiation

Transcriptional Factor	→	Erythropoietin GATA1

Erythropoiesis

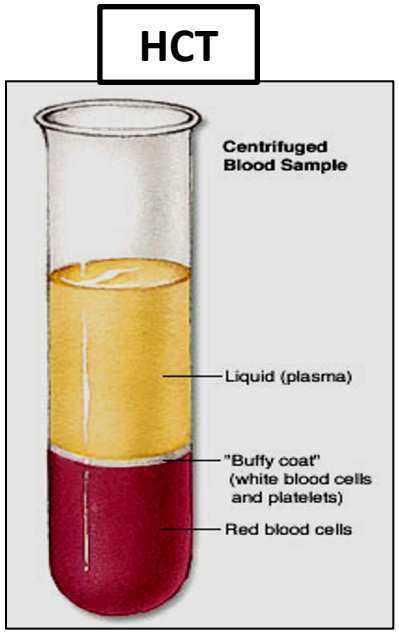
The "Bone Marrow" is the major site with the need of:
Folic acid – Iron "Ferrous" – Vit B12 – Erythropoietin -Amino acids minerals - other regulatory factors

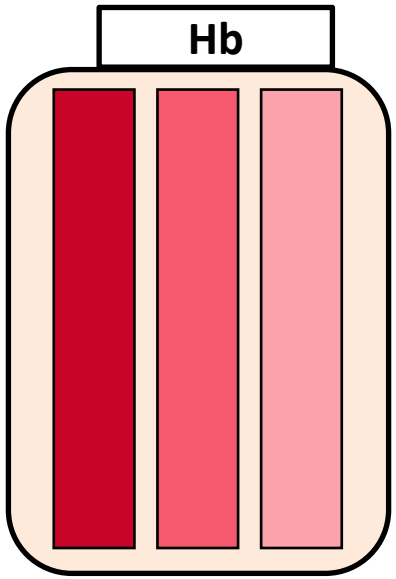


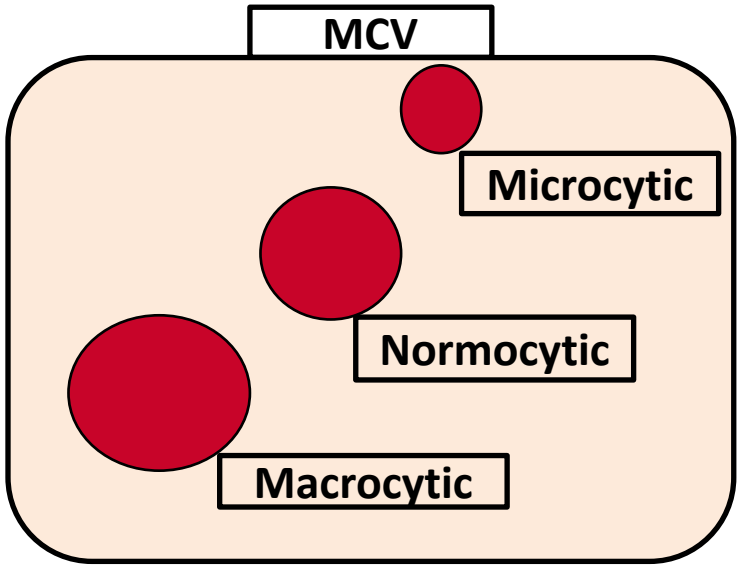
Synthesis of Hemoglobin

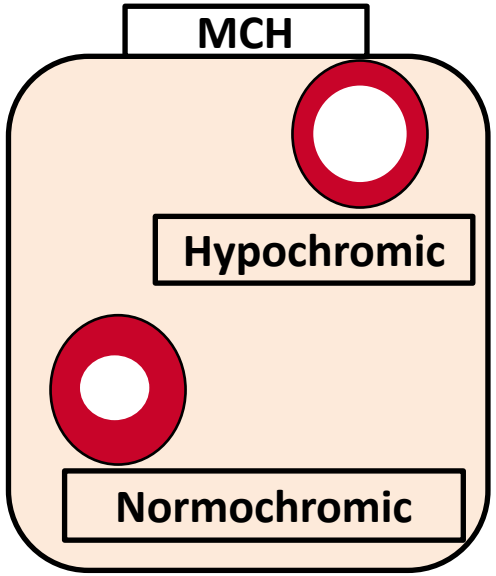
Normal Ranges

Indices	Male	Female
Hemoglobin(g/dL)	13.5-17.5	11.5-15.5
Hematocrit (PCV) (%)	40-52	36-48
Red Cell Count ($\times 10^{12}$)	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) -a*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)

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 &O2 dissociation curve

2-Severity:

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

3- Age:

- **Elderly tolerate anemia less than young patients**

Clinical Features

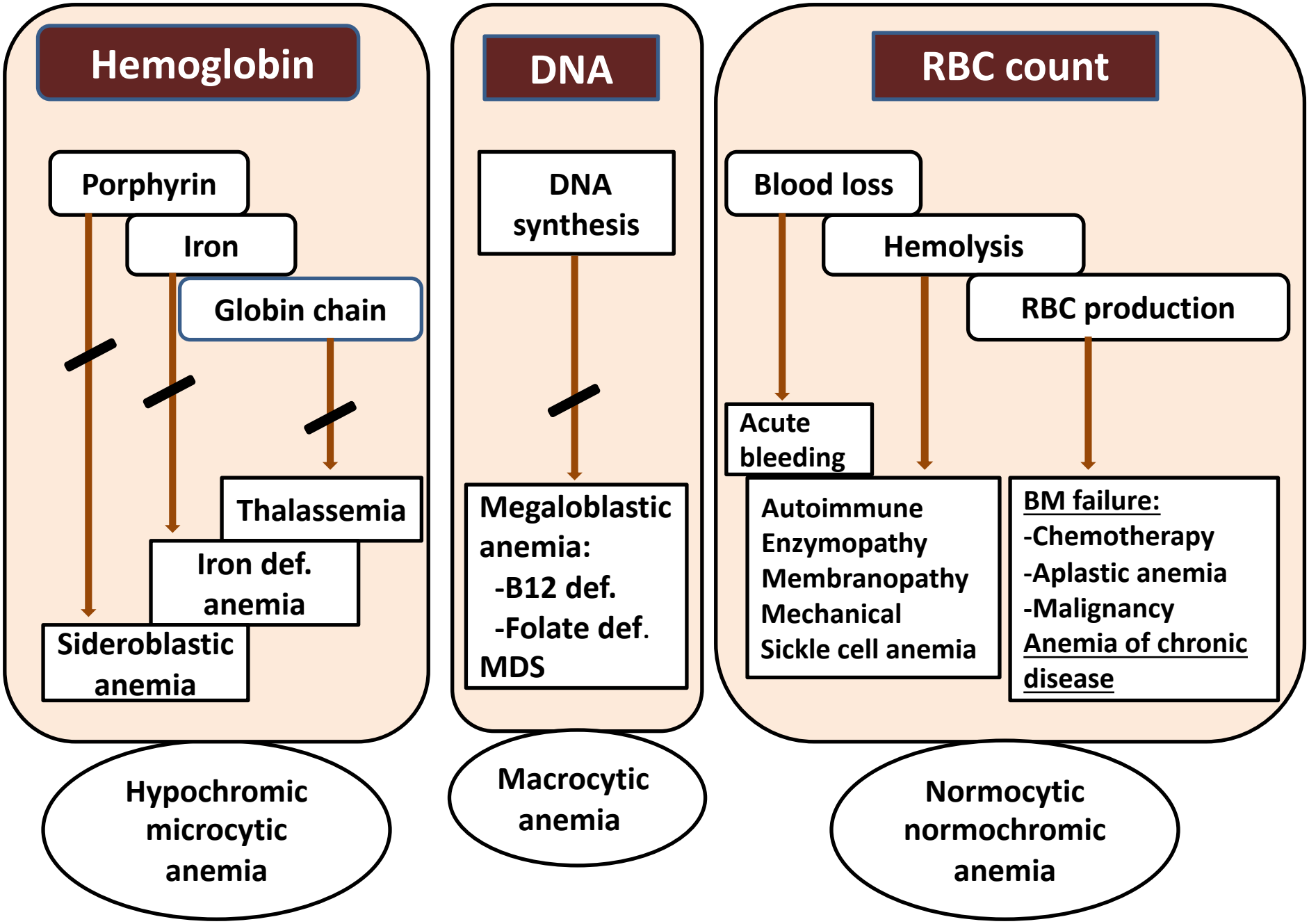
- **Weakness**
- **Headache**
- **Pallor**
- **Lethargy**
- **Dizziness**

Related to anemia

- **Palpitation (tachycardia)**
- **Angina**
- **Cardiac failure**

Related to compensatory mechanism

Classification of Anemia

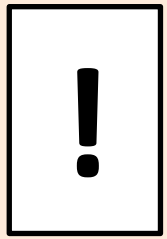

Hemoglobin
Porphyrin
Iron
Globin chain
Thalassemia
Iron def. anemia
Sideroblastic anemia
Hypochromic microcytic anemia
DNA
DNA synthesis
Megaloblastic anemia:
-B12 def.
-Folate def.
MDS
Macrocytic anemia
RBC count
Blood loss
Hemolysis
RBC production
Acute bleeding
Autoimmune
Enzymopathy
Membranopathy
Mechanical
Sickle cell anemia
BM failure:
-Chemotherapy
-Aplastic anemia
-Malignancy
Anemia of chronic disease
Normocytic normochromic anemia

Iron Deficiency Anemia

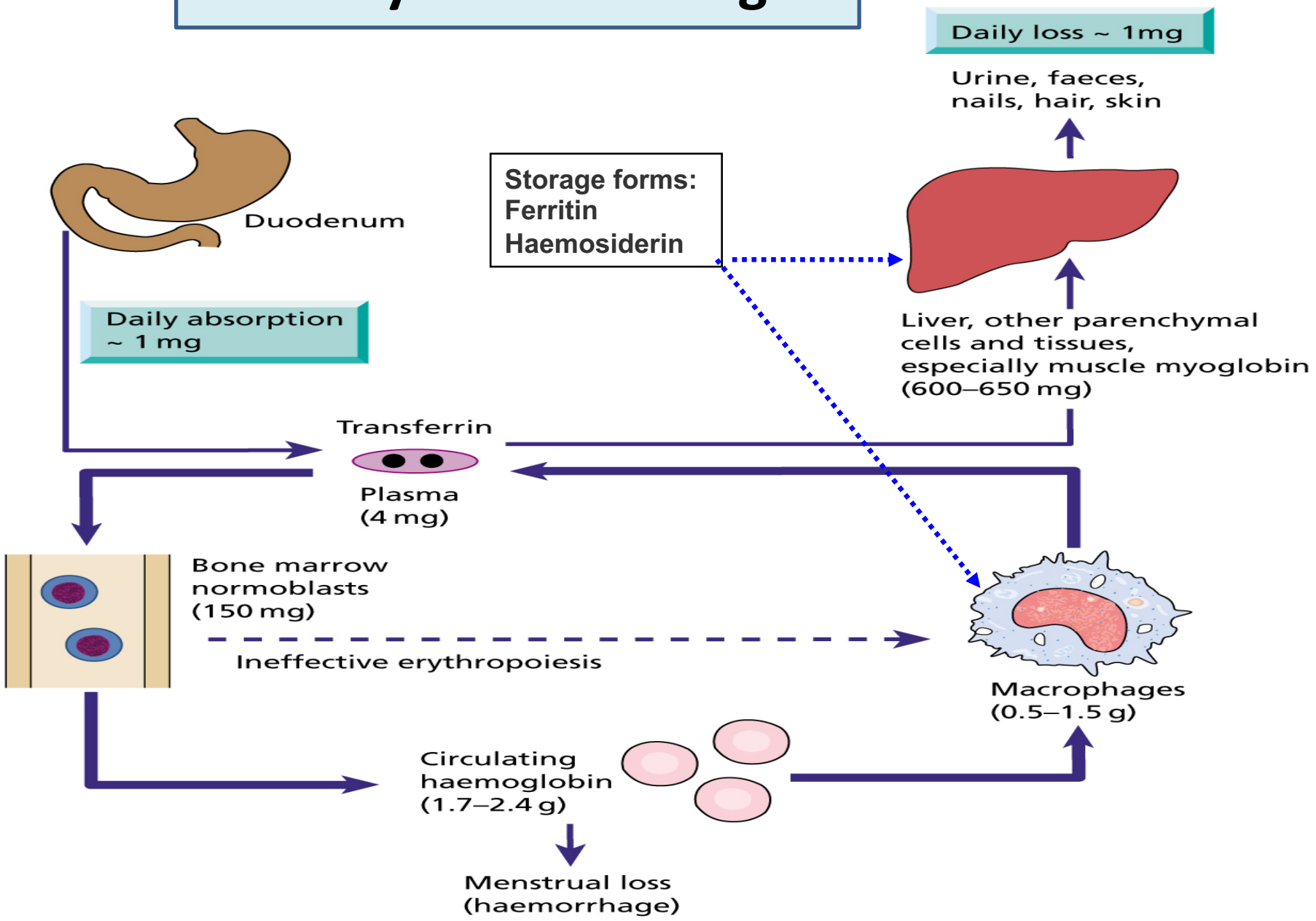
- **Iron is among the abundant minerals on earth (6%).**
- **Iron deficiency is the most common disorder(24%).**
- **Limited absorption ability :**

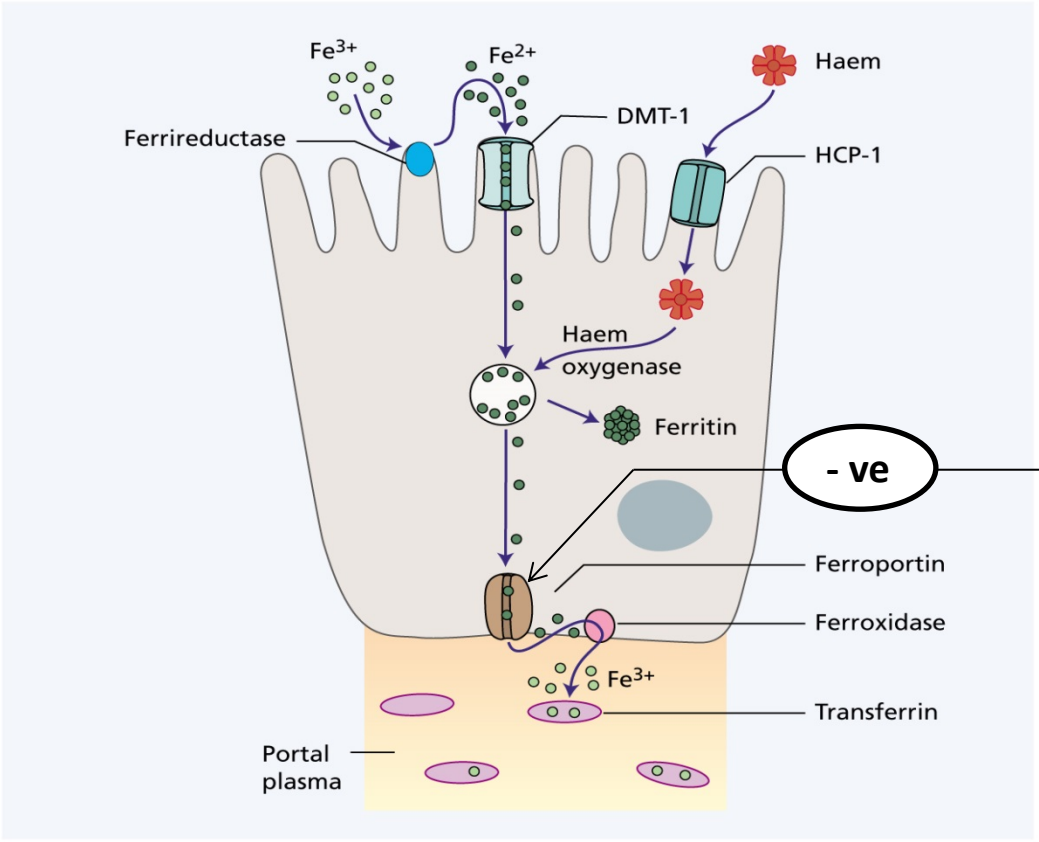
  1-Only 5-10% of taken iron will be absorbed
  2- Inorganic iron can not be absorbed easily.

- **Excess loss due to hemorrhage**



Iron cycle and storage





IL6
Tfr2

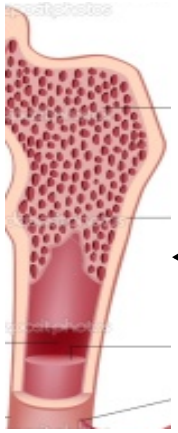
+ve

Hypoxia

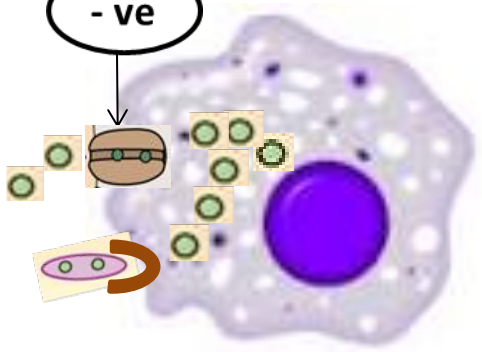
- ve

Hepcidin

- ve



Iron for
erythropoeisis



BM macrophage

Iron Absorption

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

Iron Absorption

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
Heam Iron
Ferrous Iron
→ More absorption

3- Balance between dietary enhancers&Inhibitory factors:

Enhancers

Meat (haem iron)
Fruit (Vitamin C)
Sugar (Solubilizing agent)
Acids

Inhibitors

Dairy foods (calcium)
High fiber foods (phytate)
Coffee &tea (polyphenoles)
Anti -Acids

Causes of IDA

1-Chronic blood loss:

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

2- Increased demands:

- Immaturity
- Growth
- Pregnancy
- EPO therapy

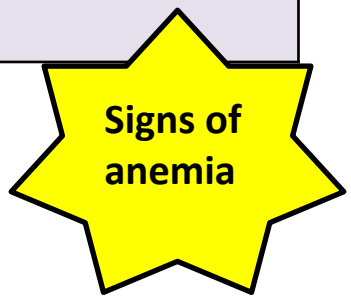
3-Malabsorption:

- Enteropathy
- Gastrectomy

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

Development of IDA

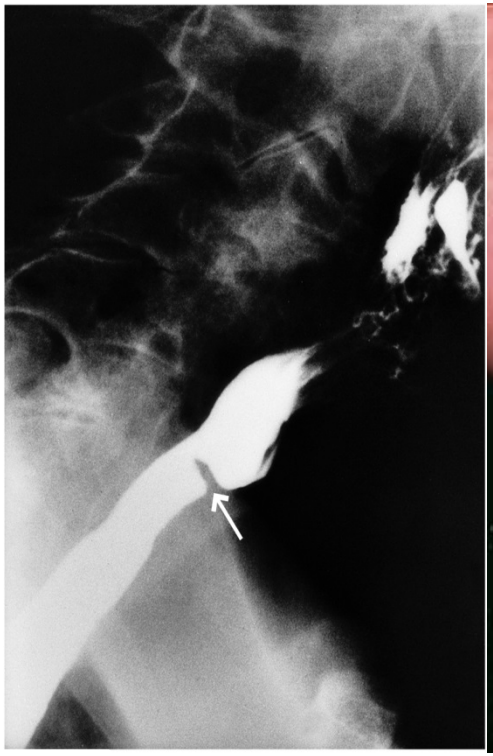
	1 Normal	2 Pre-latent	3 Latent	4 Iron def. anemia
Stores	Normal	Low	Low	Low
MCV/MCH	Normal	Normal	Low	Low
Hemoglobin	Normal	Normal	Normal	Low



Signs and symptoms of IDA

a

b



c

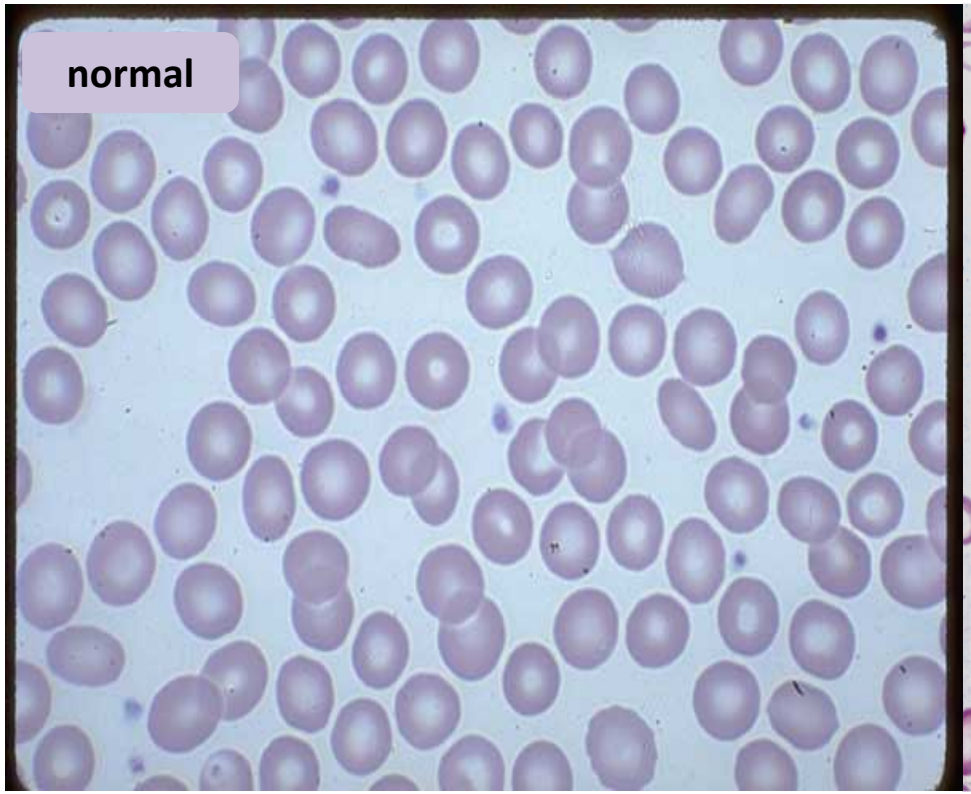
Beside symptoms and signs of anaemia +/- bleeding patients present with:

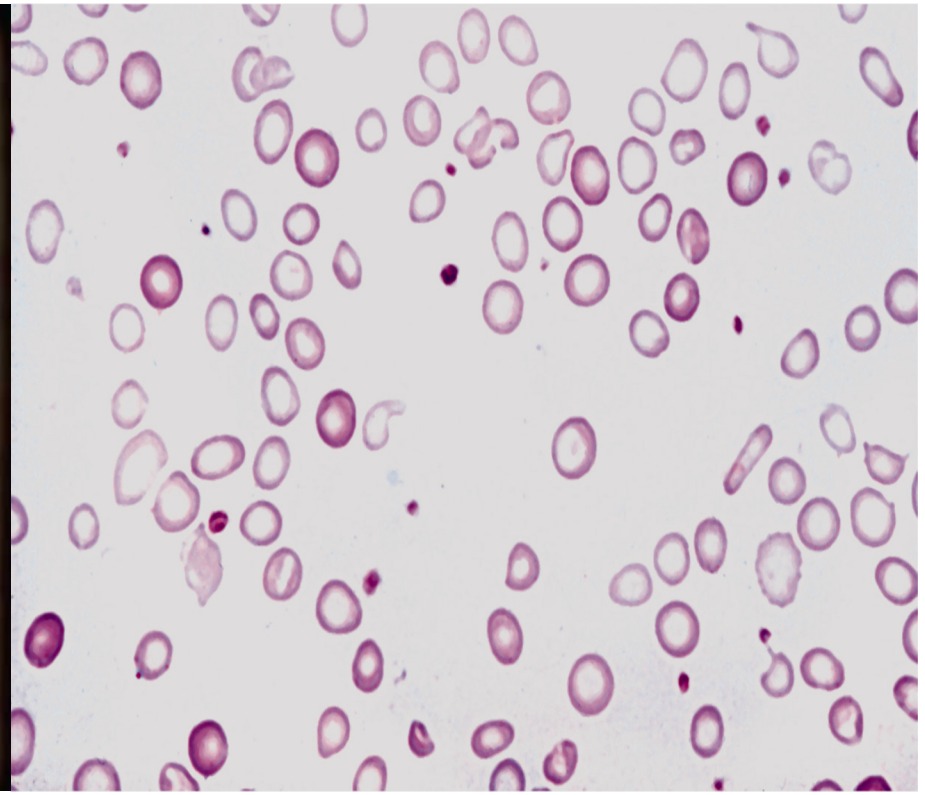
(a): Koilonychia (spoon-shaped nails)

(b): Angular stomatitis and/or glossitis

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

Investigation

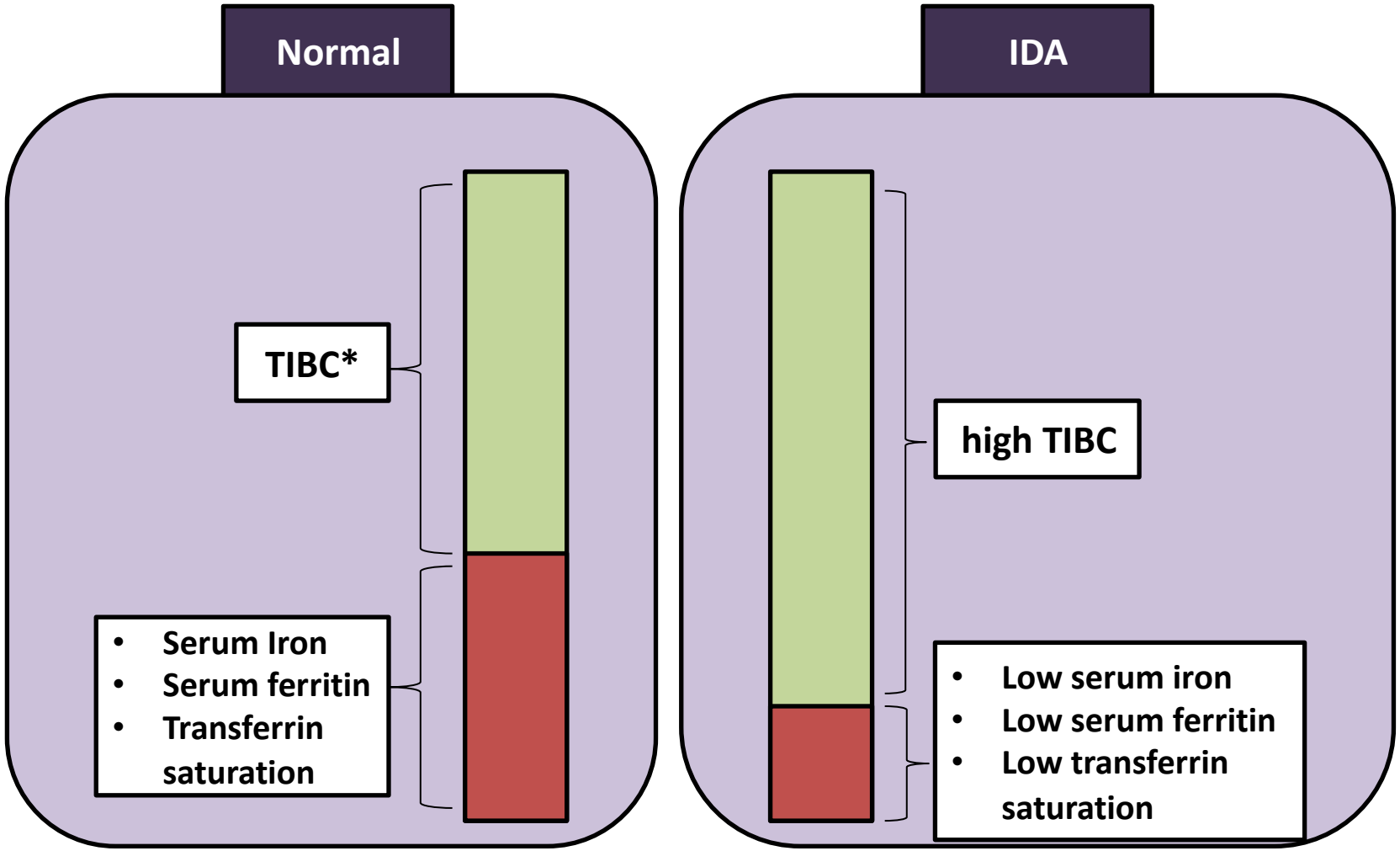




Microcytic hypochromic anemia with:

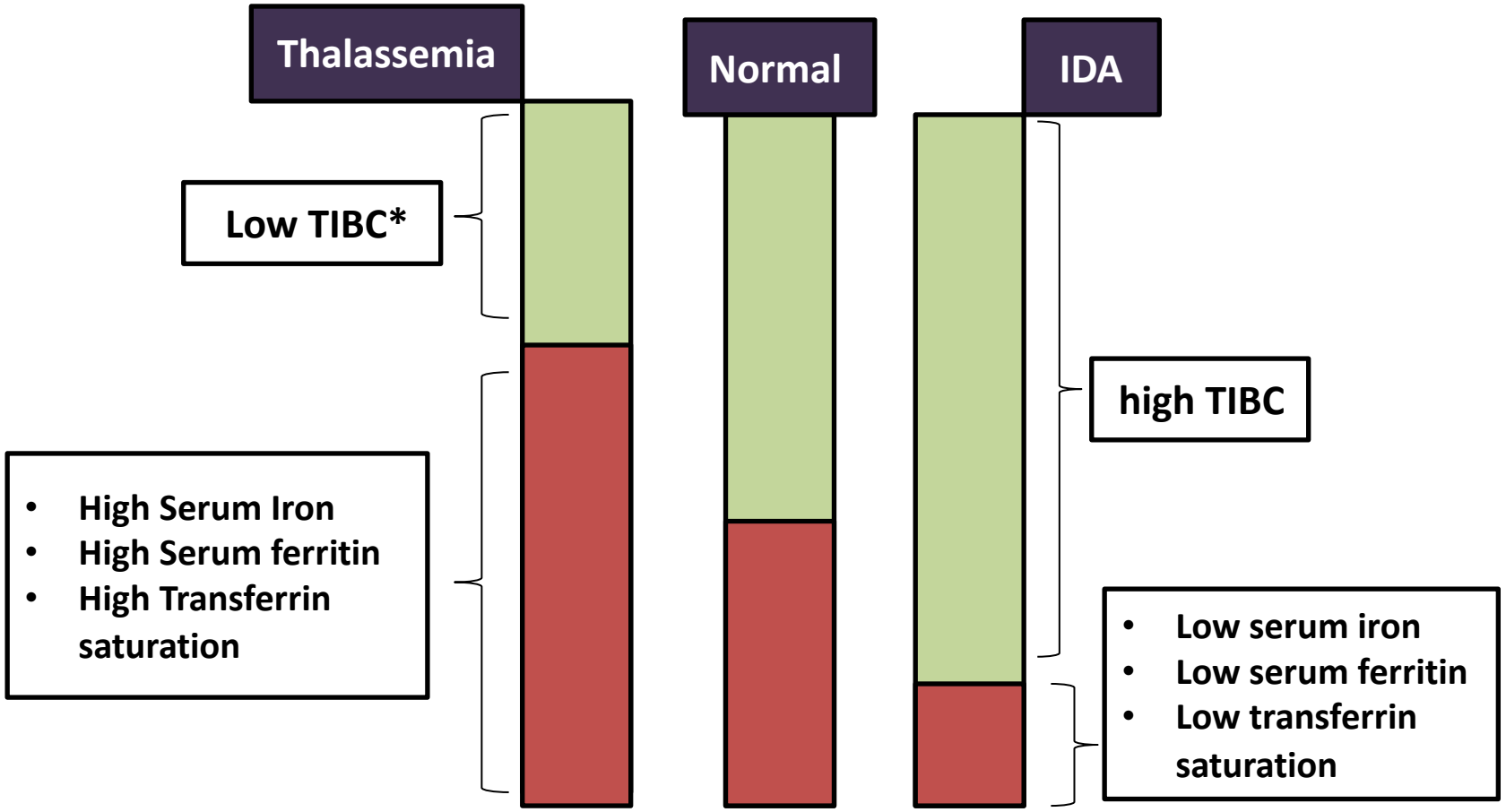
- **Anisocytosis(variation in size)**
- **Poikilocytosis (variation in shape)**

Iron Studies



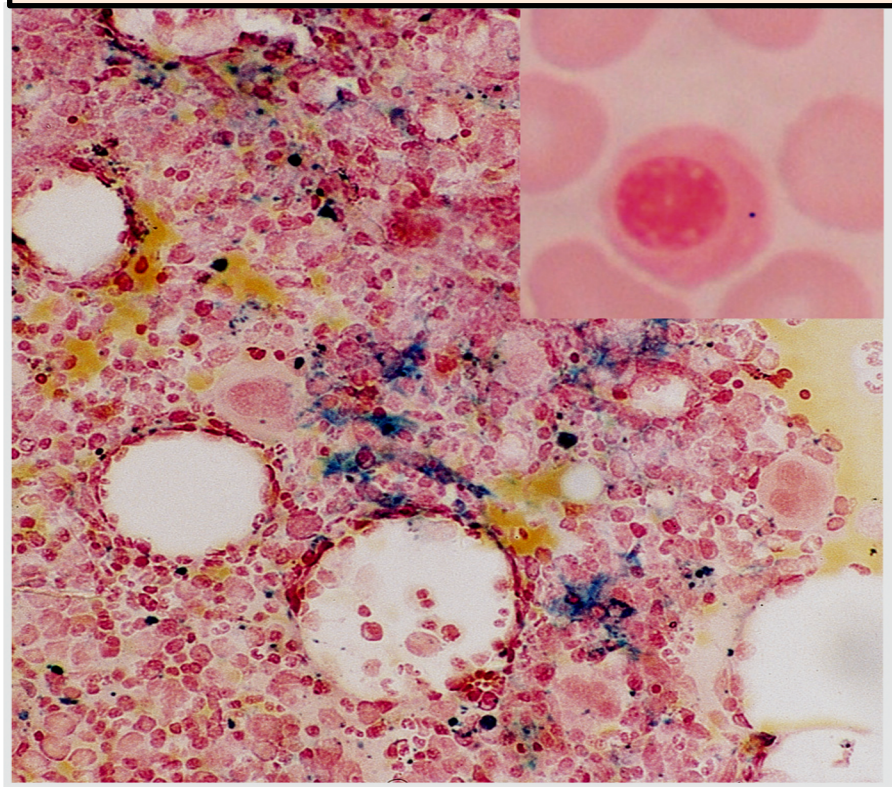
TIBC : total iron binding capacity of transferrin

Iron Studies



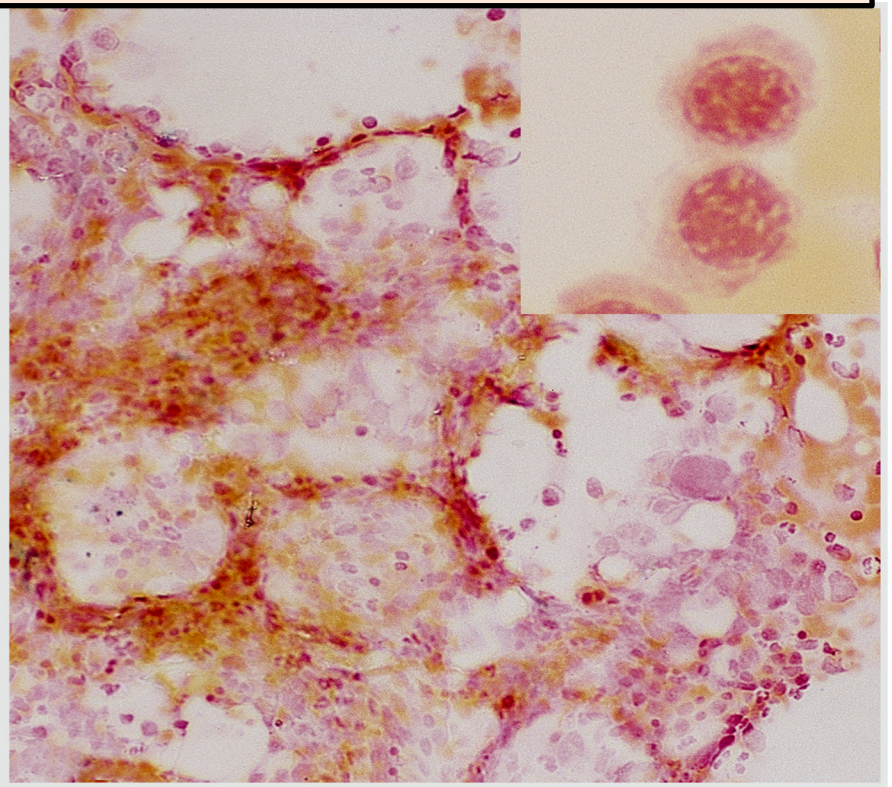
Investigation

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



(a)

Normal



(b)

IDA: reduced or absent iron stores (hemosiderin)

Treatment of IDA

- **Treat the underlying cause**
- **Iron replacement therapy:**

Oral :(Ferrous Sulfate 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 sulfate)**
- GIT disturbances ,staining of teeth & metallic taste.

- **Iron supplementation:**
  For high risk groups.

Anemia of chronic disease

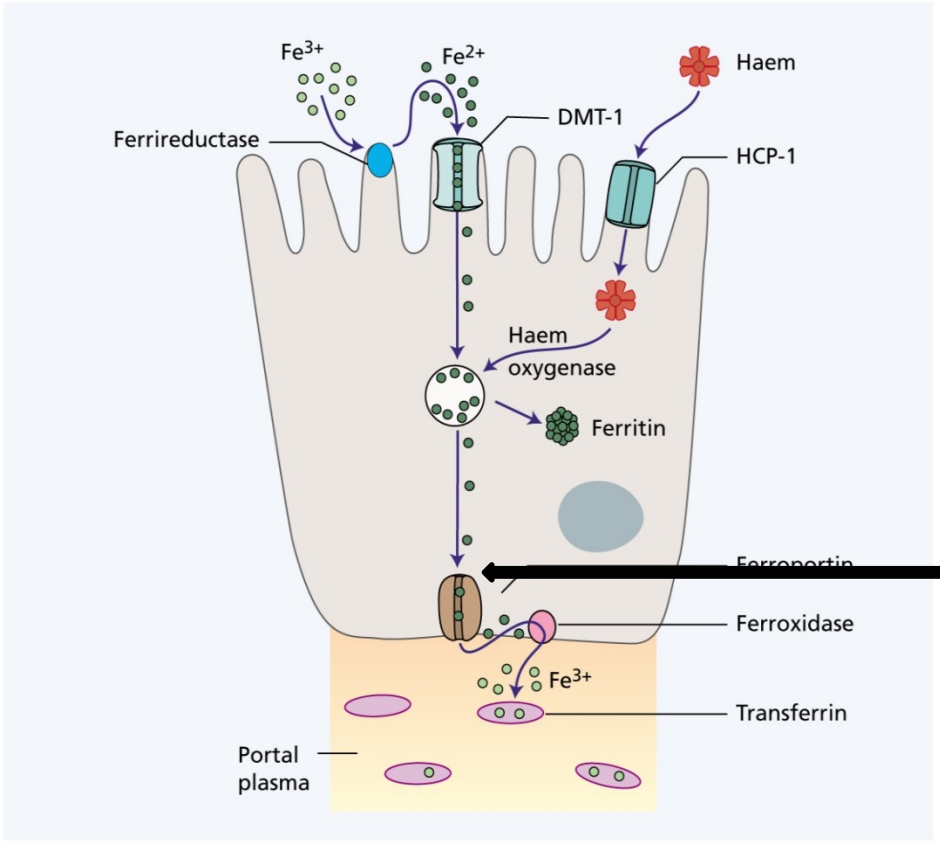
- Normochromic normocytic (usually) anemia caused by decreased release of iron from iron stores due to raised serum Hepcidin .
- Associated with

  - Chronic infection including HIV, malaria

  - Chronic inflammations

  -Tissue necrosis

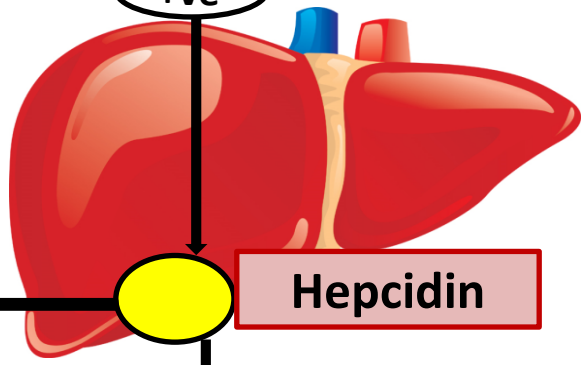
  -Malignancy



Tuberculosis
SLE
Carcinoma
Lymphoma

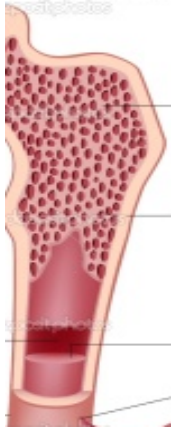
IL-6
IL-1
TNF

+ve



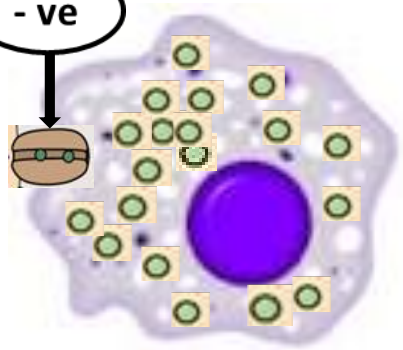
Hepcidin

- ve



no Iron for
erythropoiesis

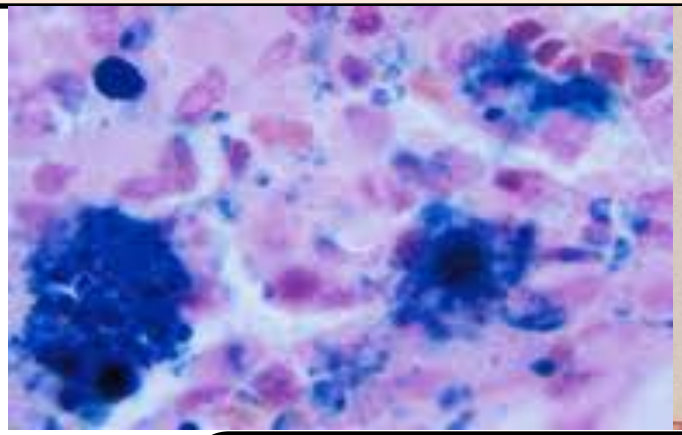
- ve

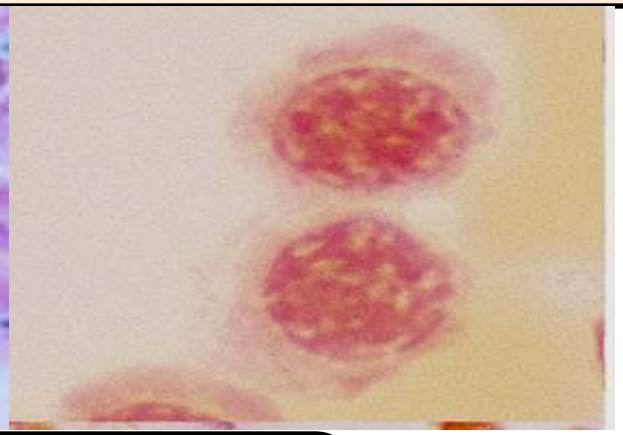


BM macrophage

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