

ANEMIA

BY:

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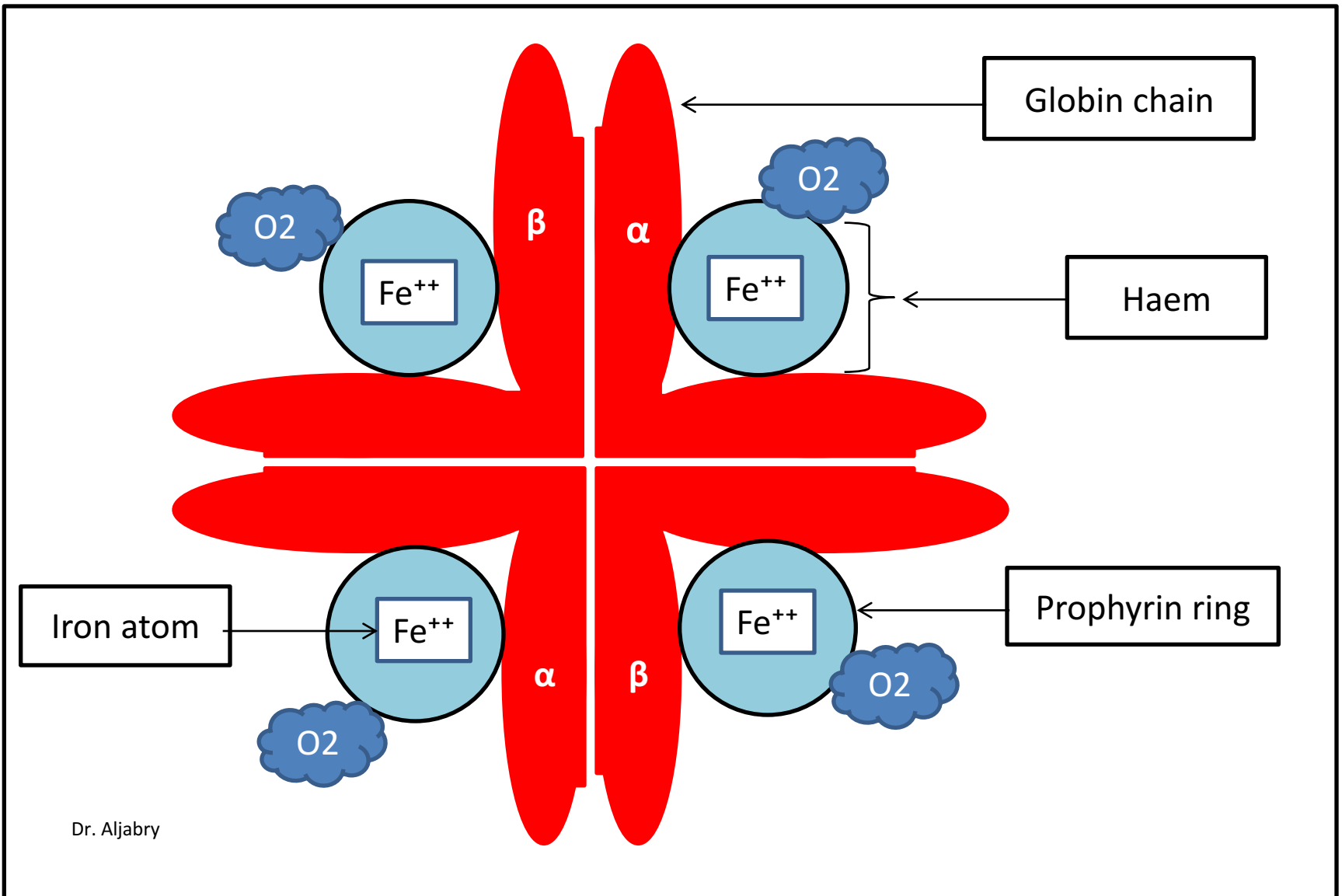
DEPARTMENT OF PATHOLOGY

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

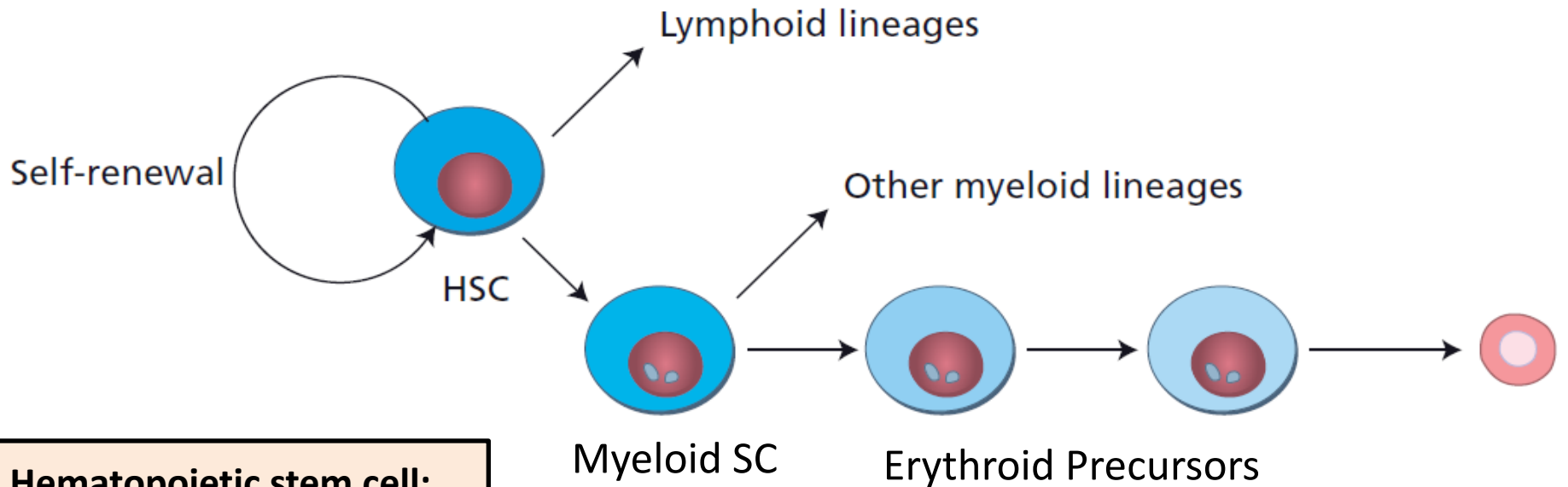
- Hemoglobin is the protein molecule in RBC that carries O₂ from the lungs to the body's tissues and returns carbon CO₂ from the tissues back to the lungs.
- Hemoglobin maintains the shape of RBC also.

Red Blood Cells



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Hematopoiesis



Hematopoietic stem cell:

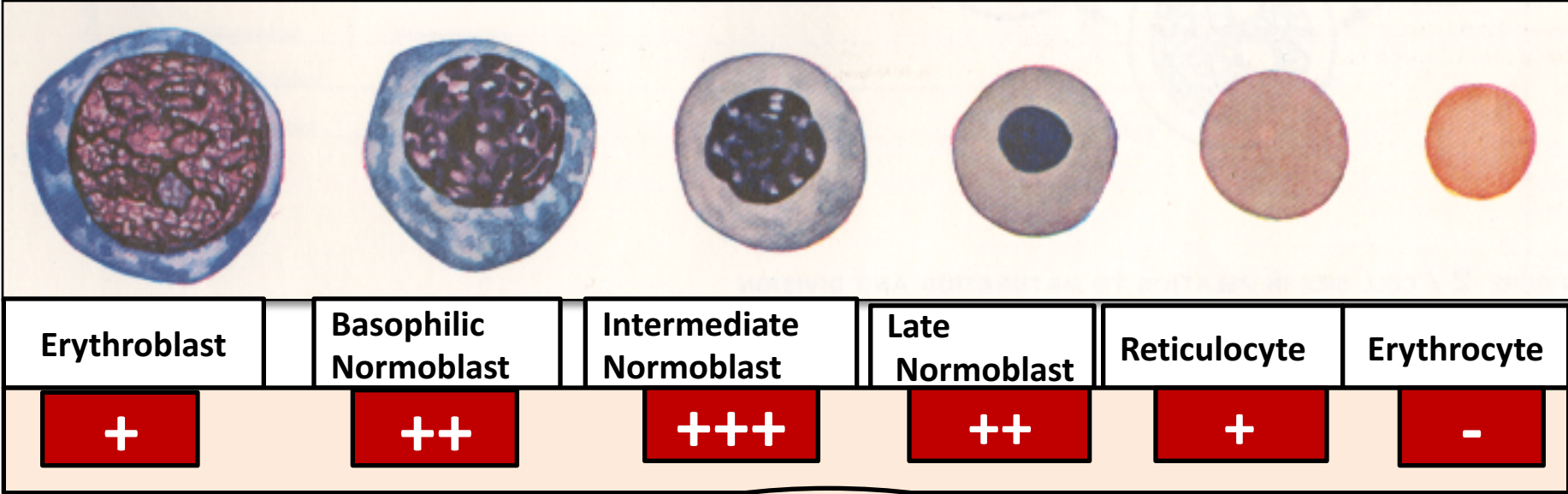
- 1- Self renewal
- 2- Cell differentiation

Transcriptional
Factor

Erythropoietin
GATA1

Erythropoiesis

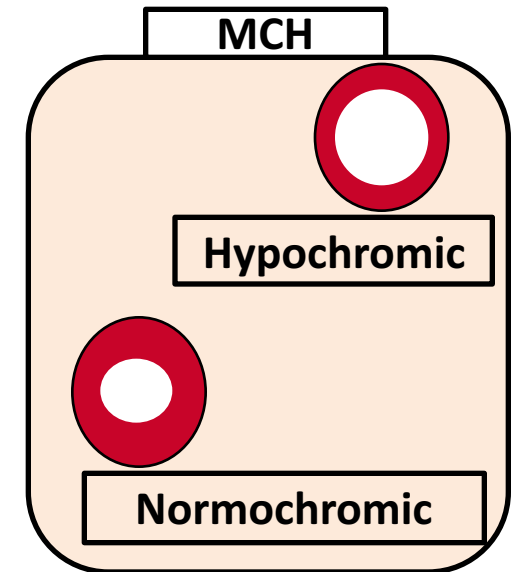
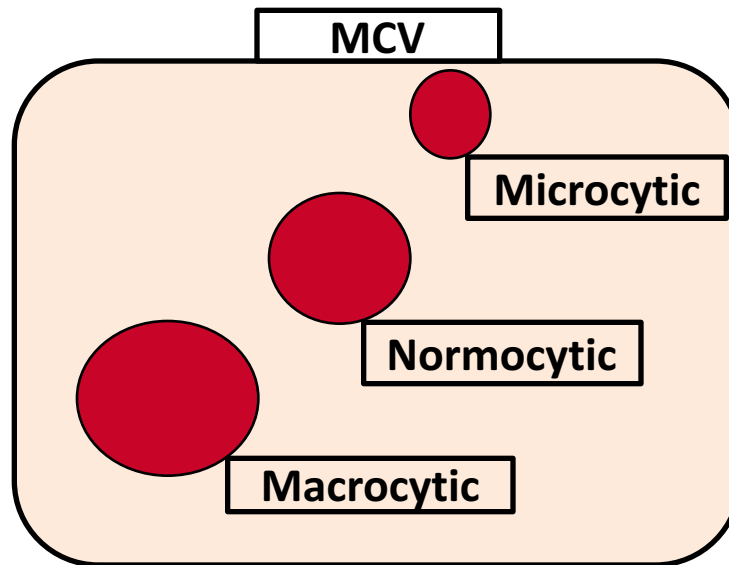
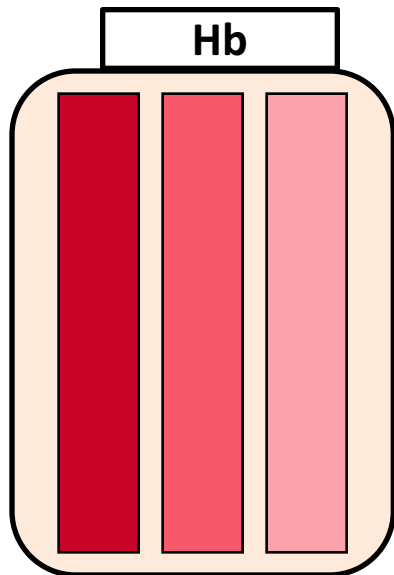
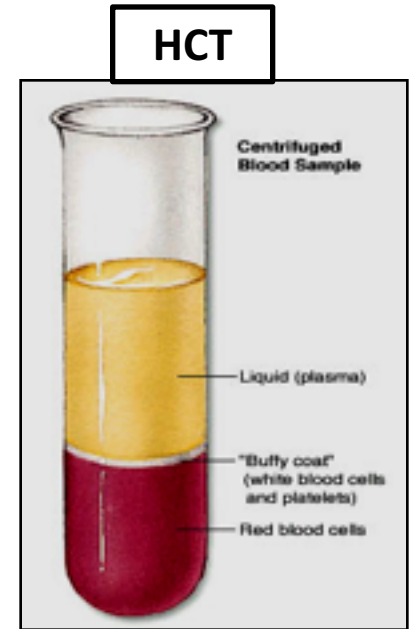
The “Bone Marrow” is the major site with the need of:
Folic acid – Iron “Ferrous” – Vit B12 – Erythropoietin -Amino acids
minerals - other regulatory factors



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) -*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

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**

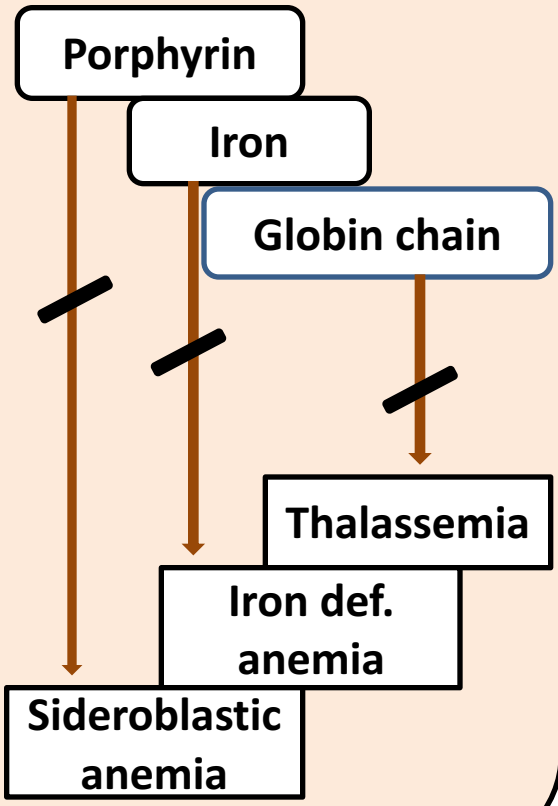
Related to anemia

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

Related to compensatory
mechanism

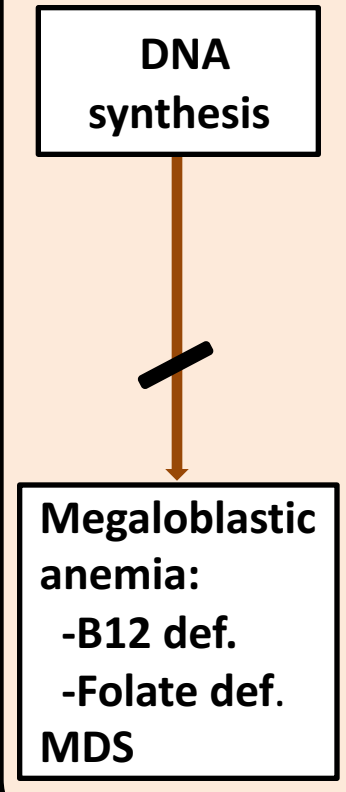
Classification of Anemia

Hemoglobin



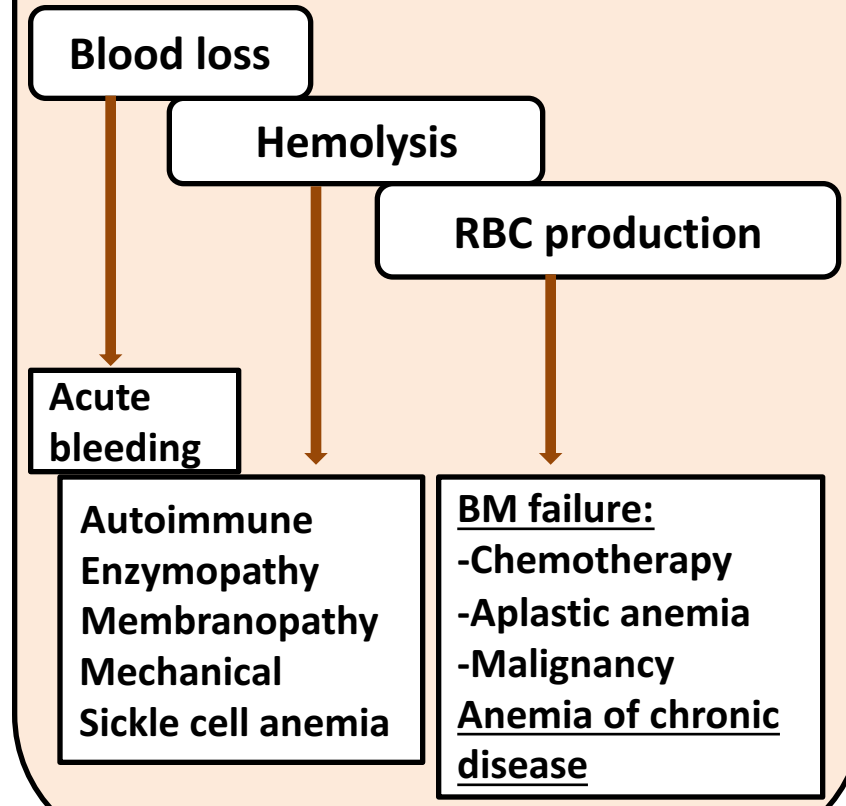
Hypochromic microcytic anemia

DNA



Macrocytic anemia

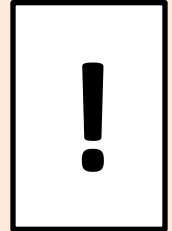
RBC count



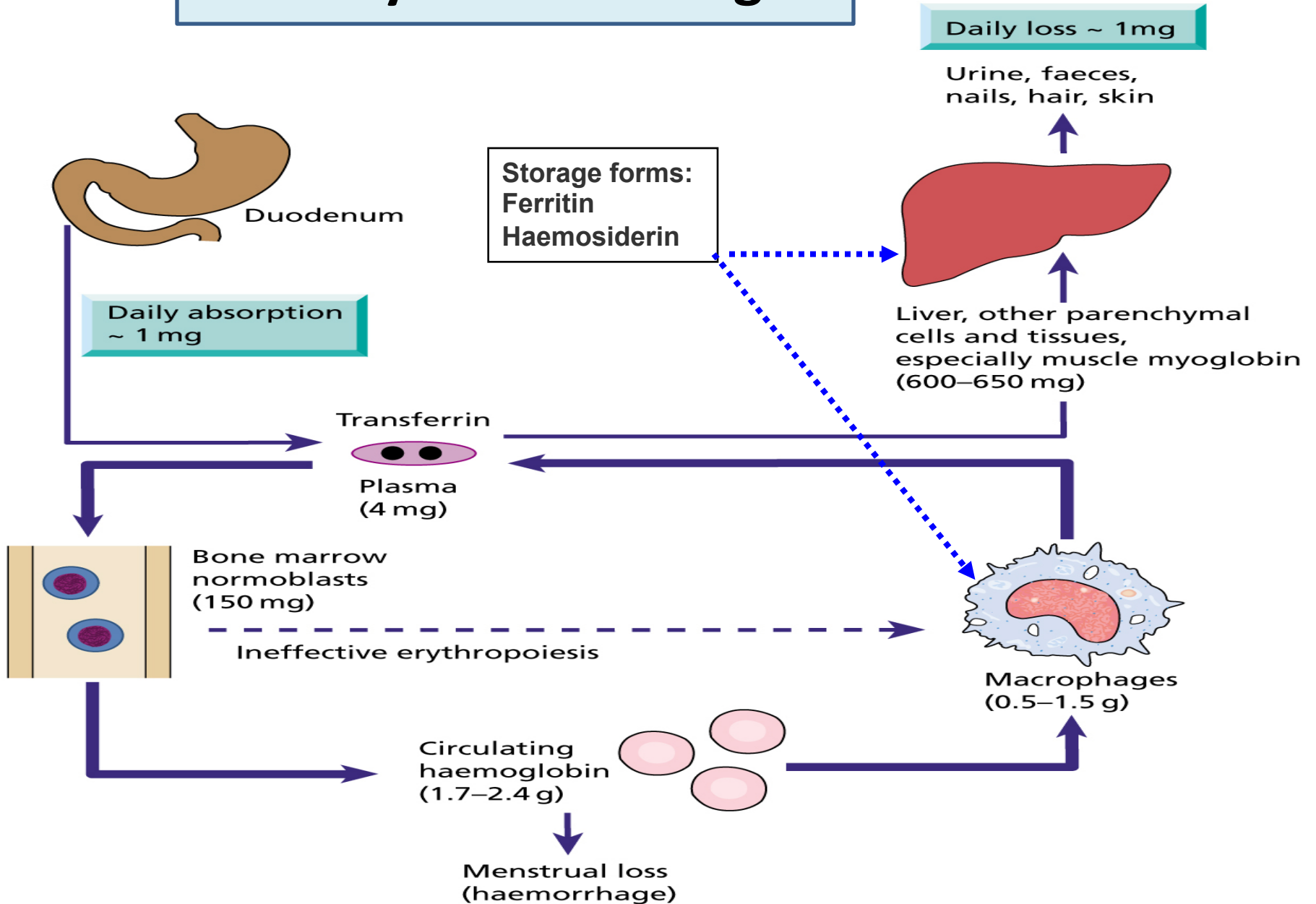
Normocytic normochromic anemia

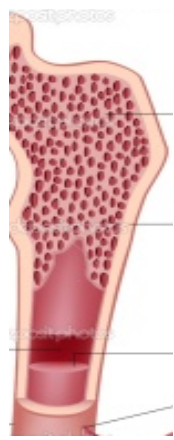
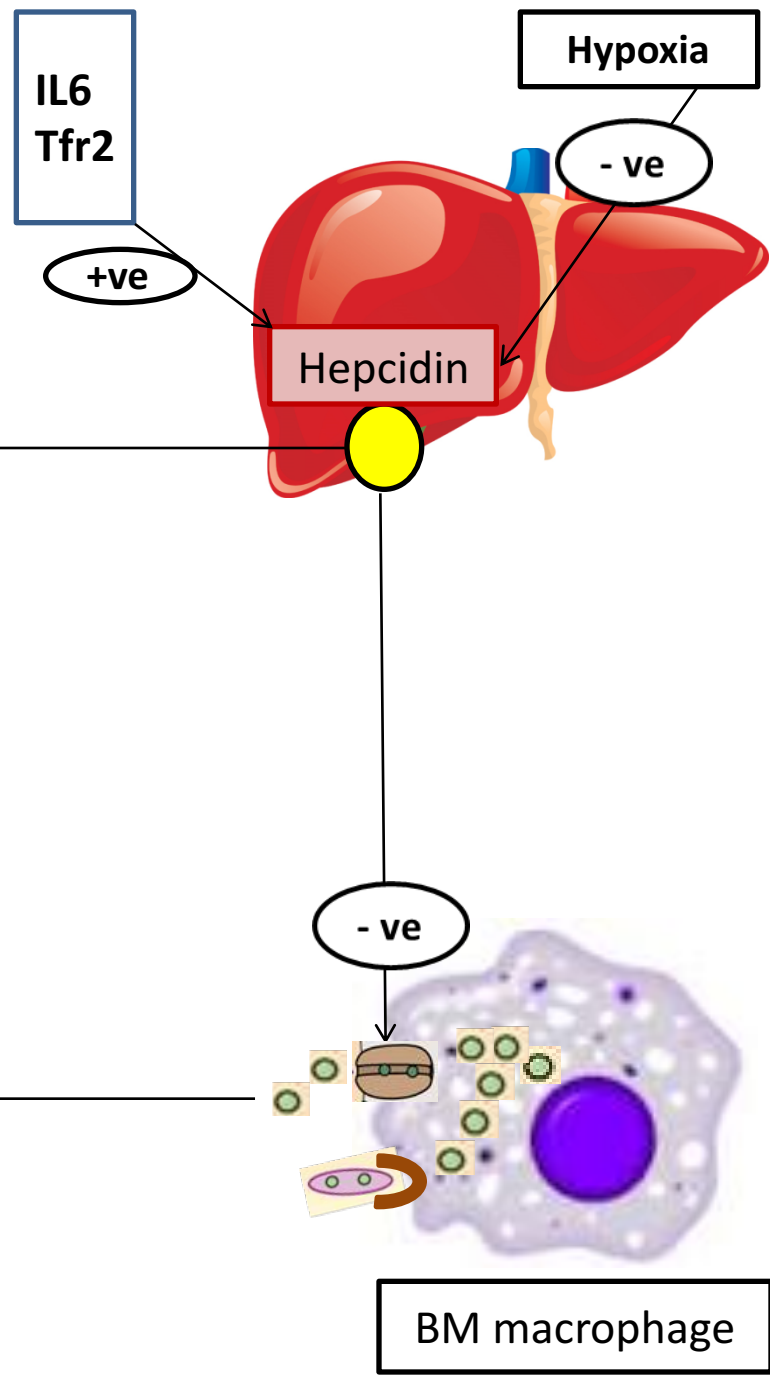
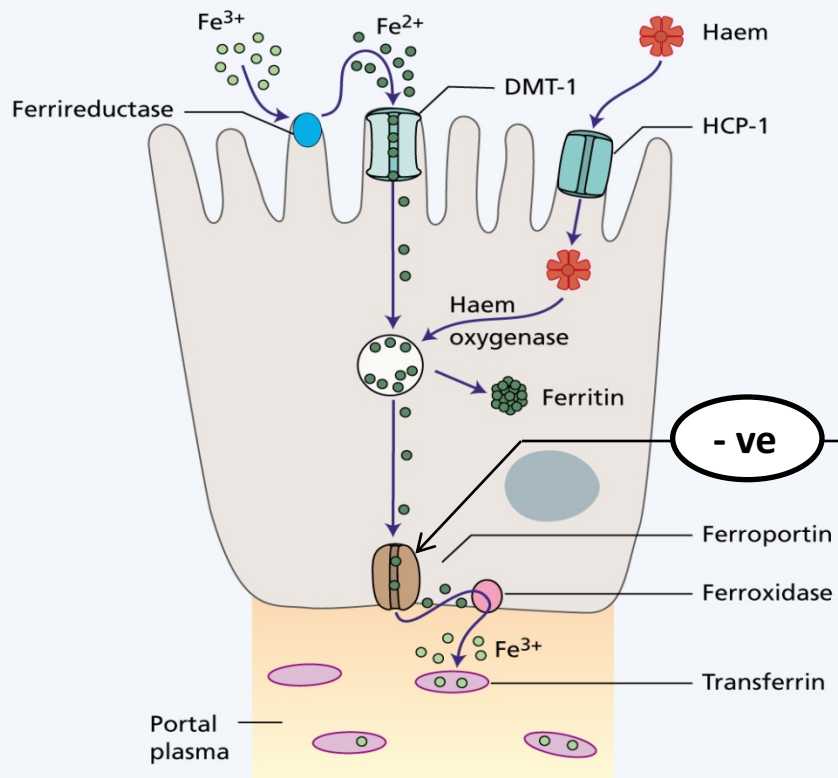
Iron Deficiency Anemia

- **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





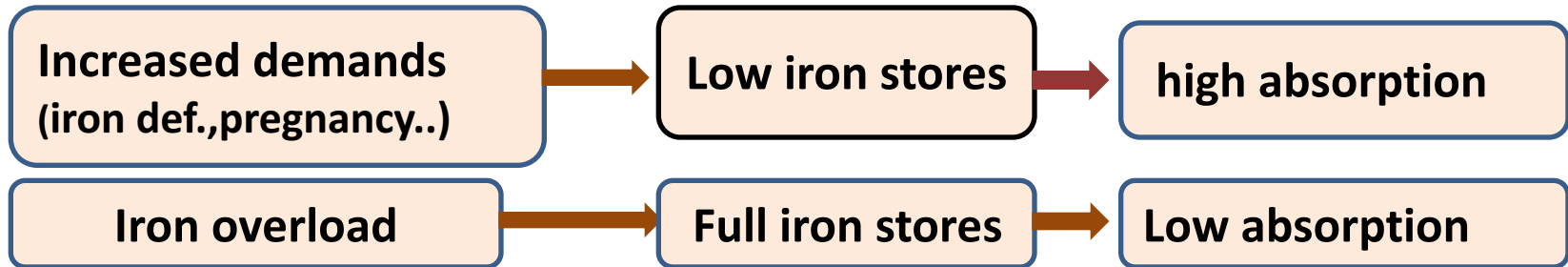
Iron for erythropoiesis

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

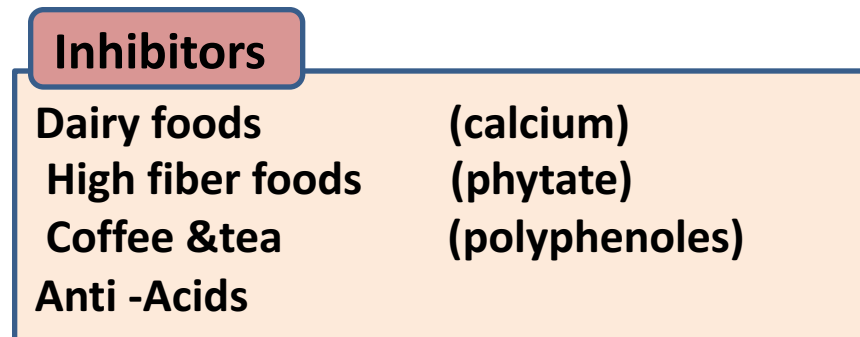
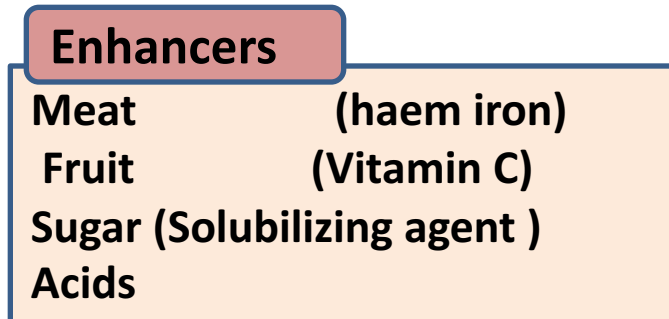
1-Body Iron status:



2- Content and form of dietary iron



3- Balance between dietary enhancers&Inhibitory factors:



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 of
anemia**

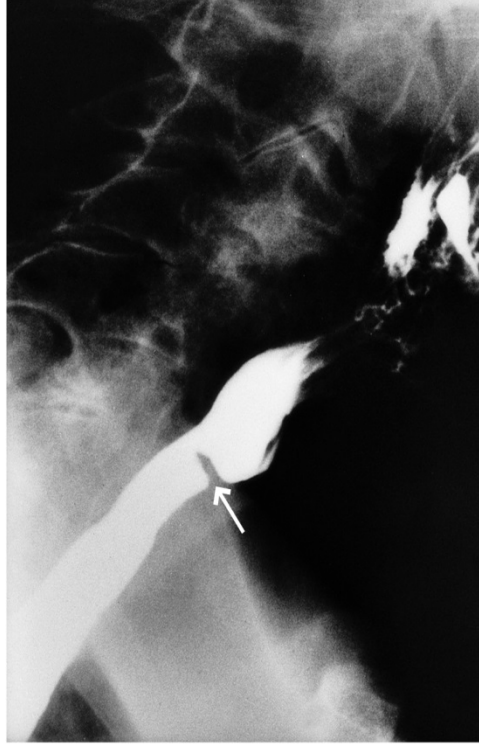
Signs and symptoms of IDA



a



b



c



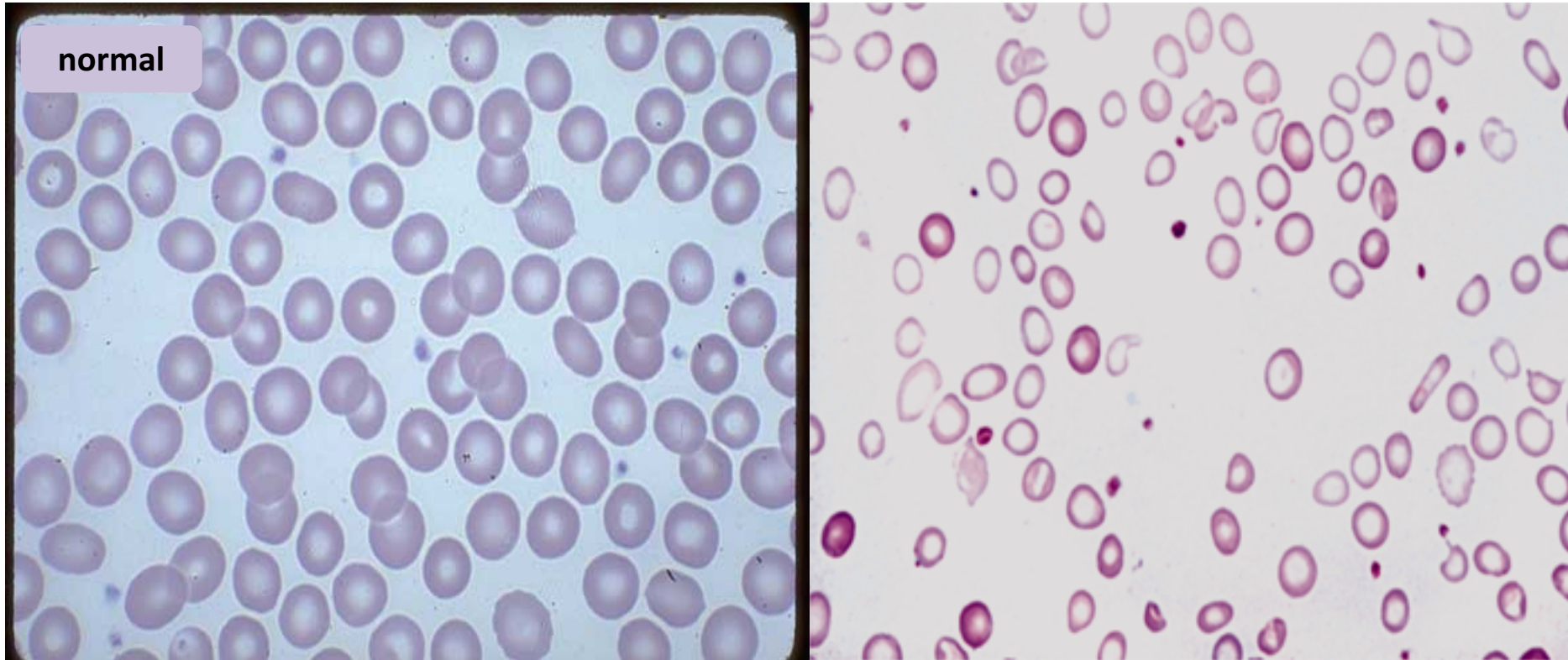
Beside symptoms and signs of anaemia +/- bleeding patients present with:

(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

Normal

IDA

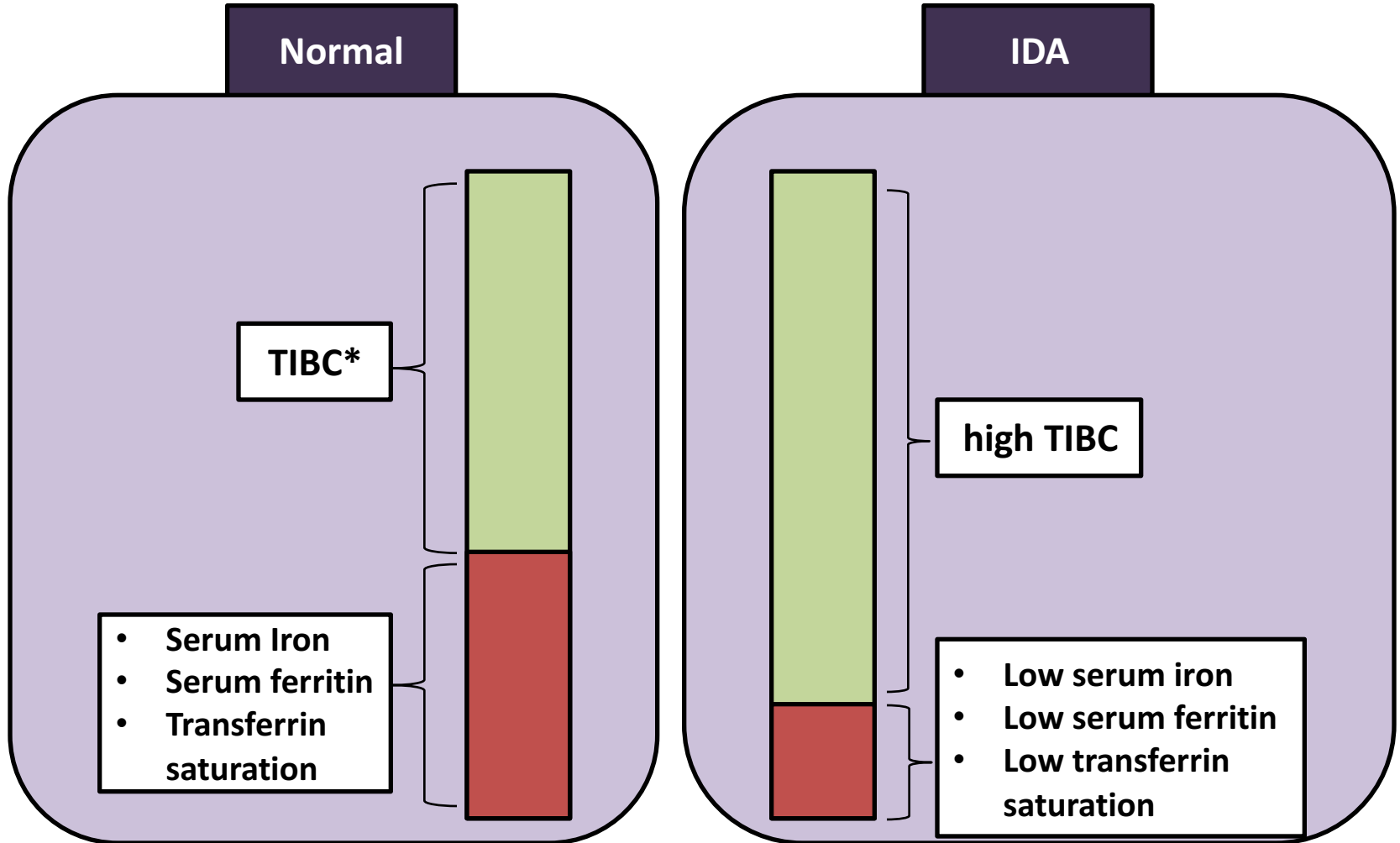
TIBC*

high TIBC

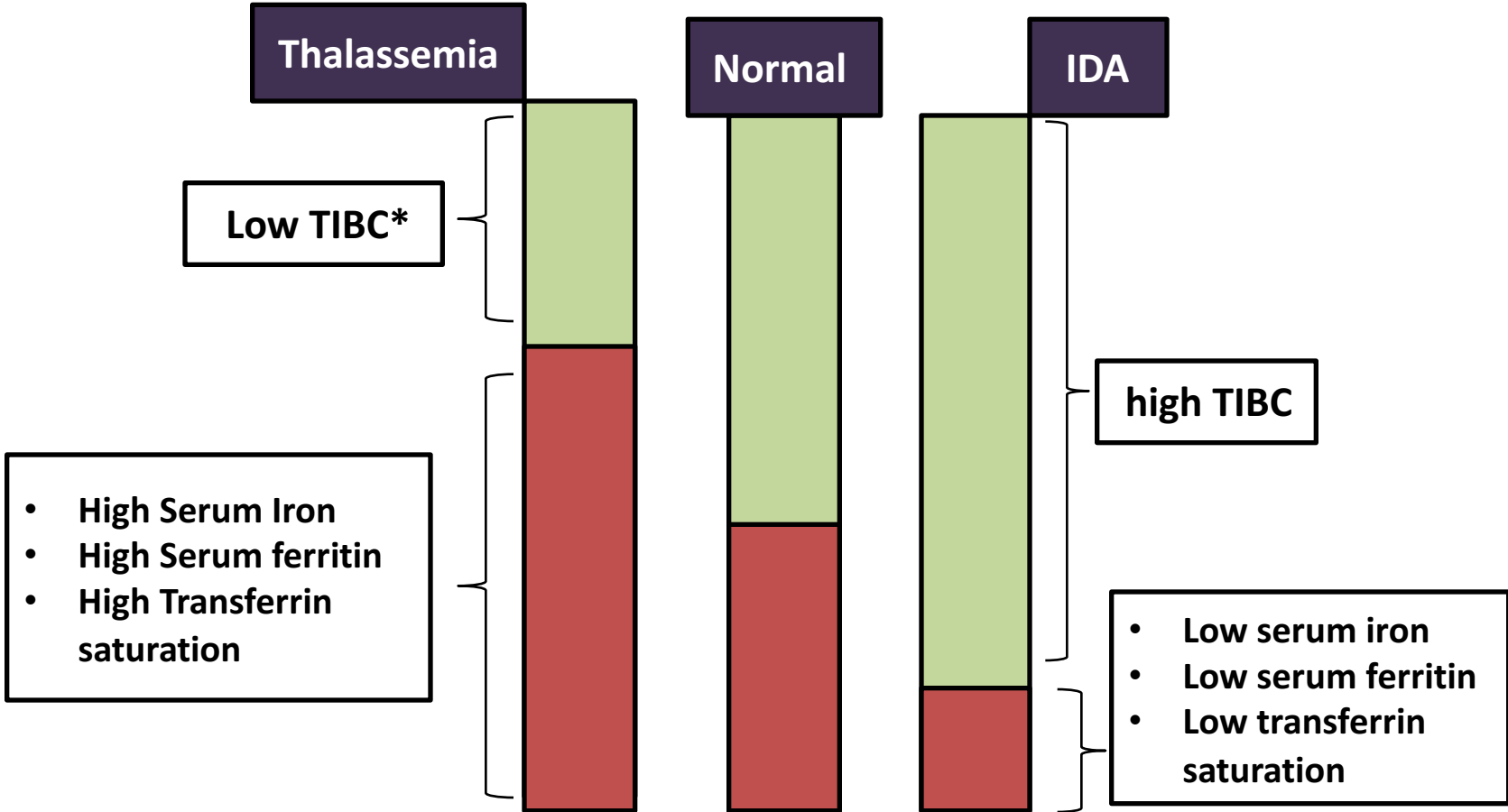
- Serum Iron
- Serum ferritin
- Transferrin saturation

- Low serum iron
- Low serum ferritin
- Low transferrin saturation

TIBC : total iron binding capacity of transferrin

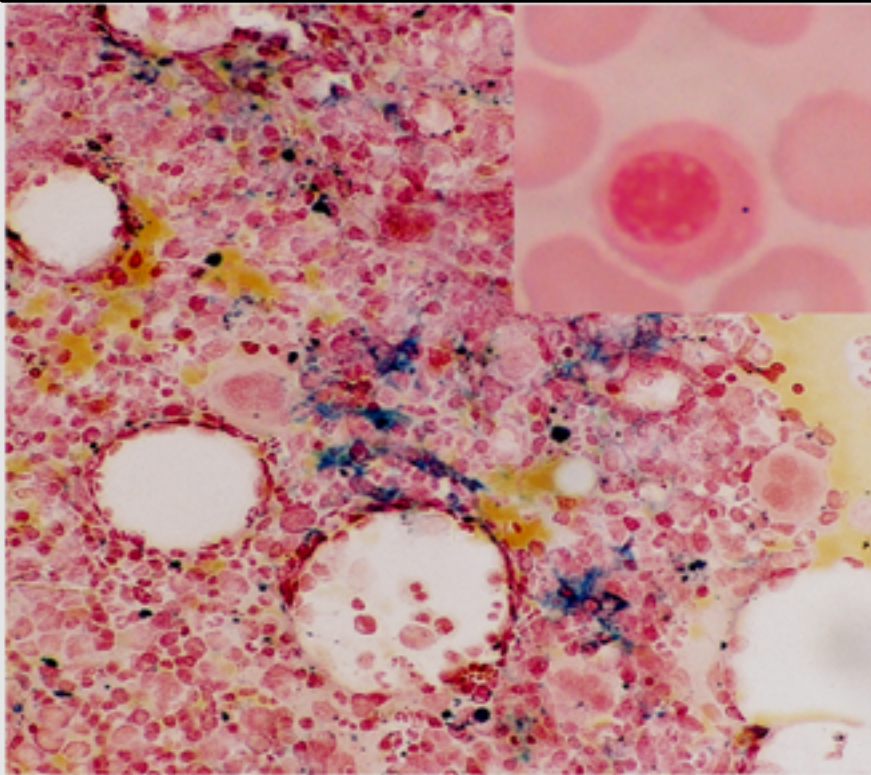


Iron Studies



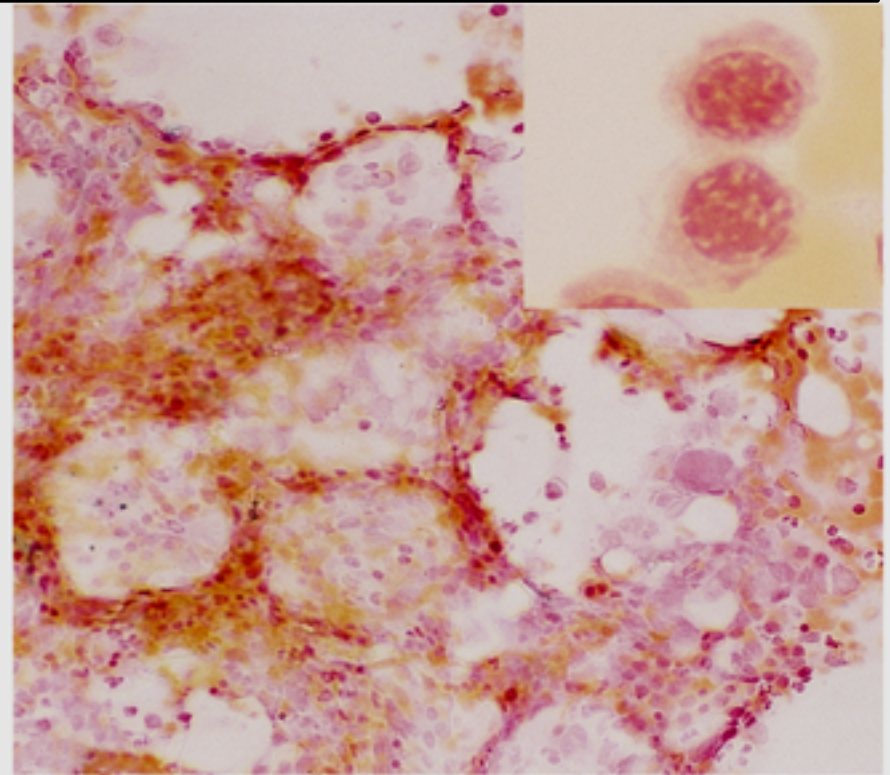
Investigation

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.

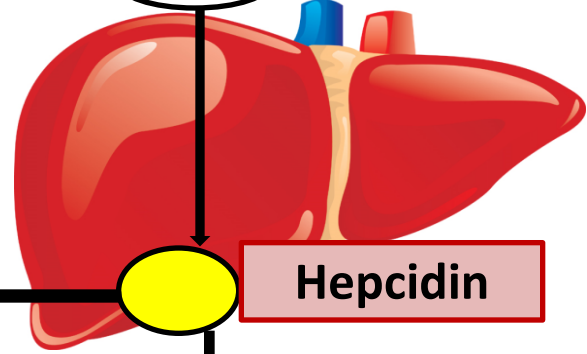
Anemia of chronic disease

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

Tuberculosis
SLE
Carcinoma
Lymphoma

IL-6
IL-1
TNF

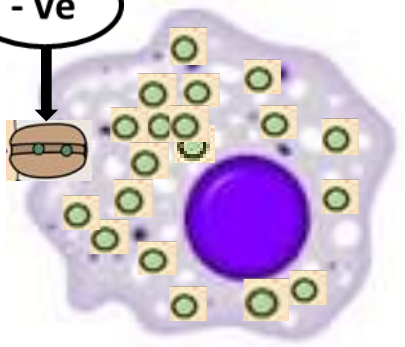
+ve



Hepcidin

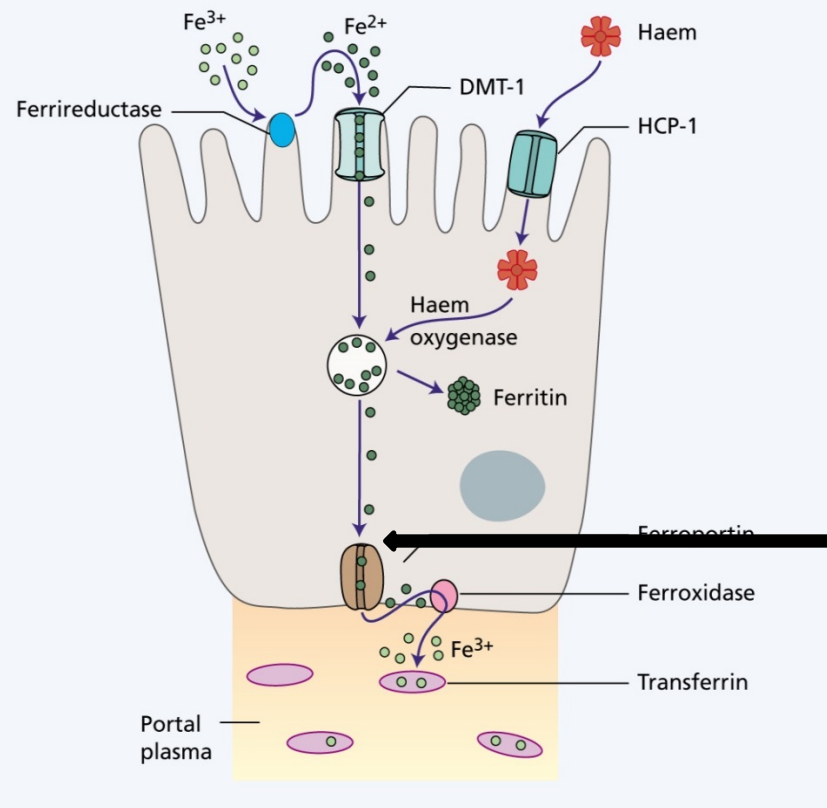
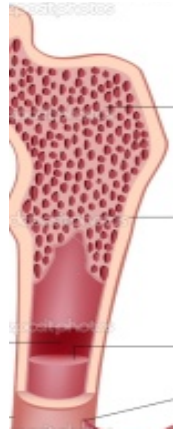
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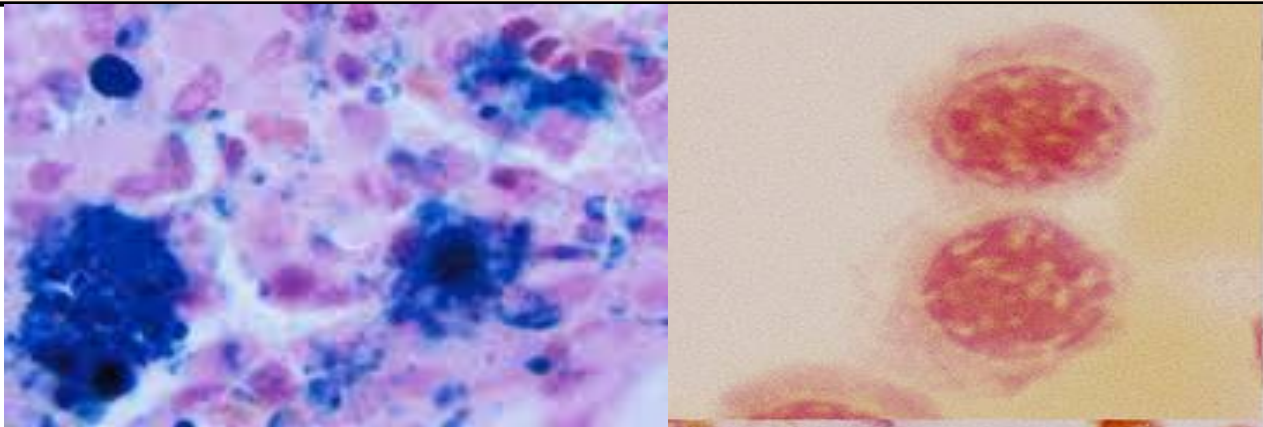
BM macrophage

no Iron for erythropoiesis



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