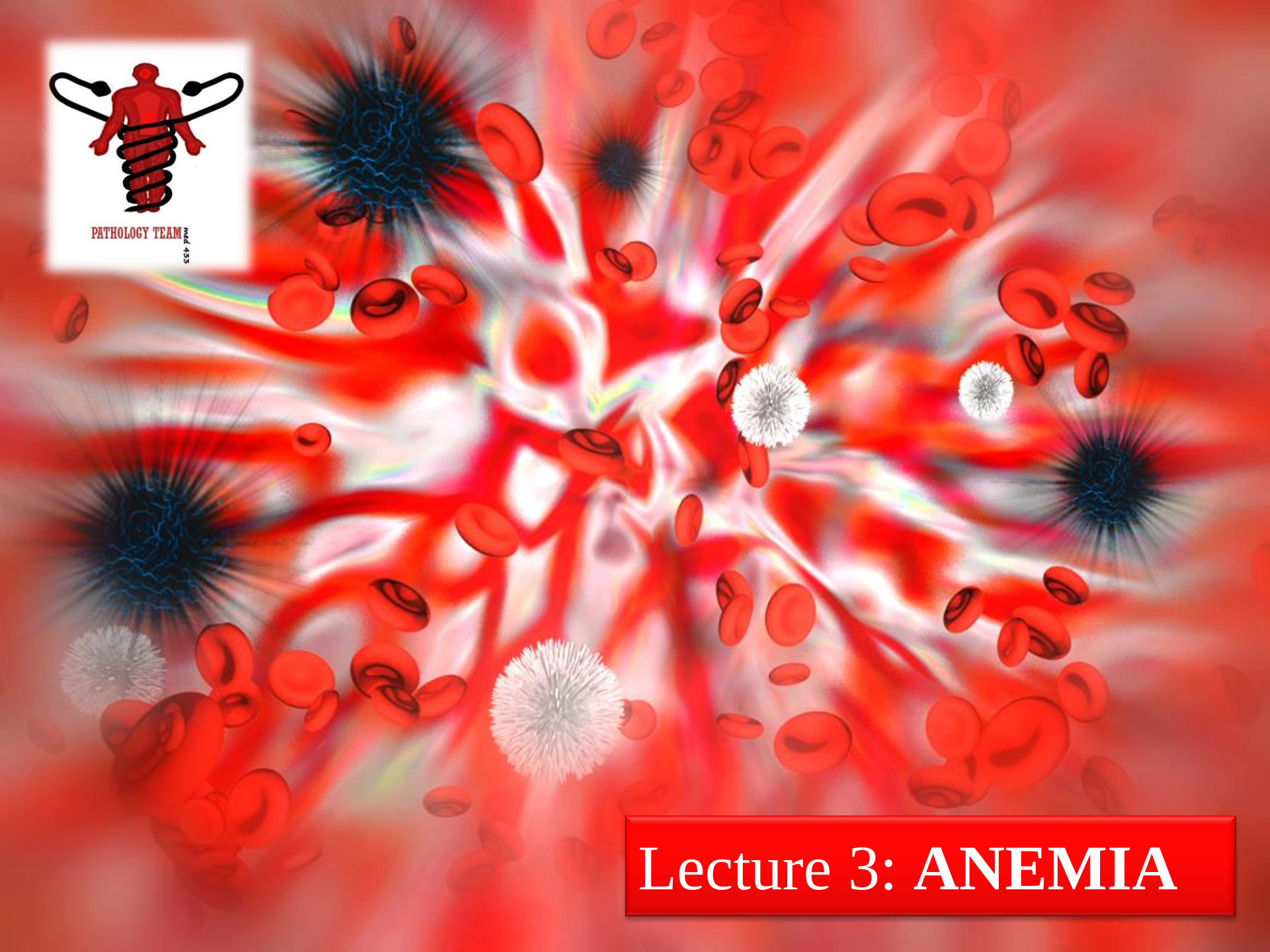
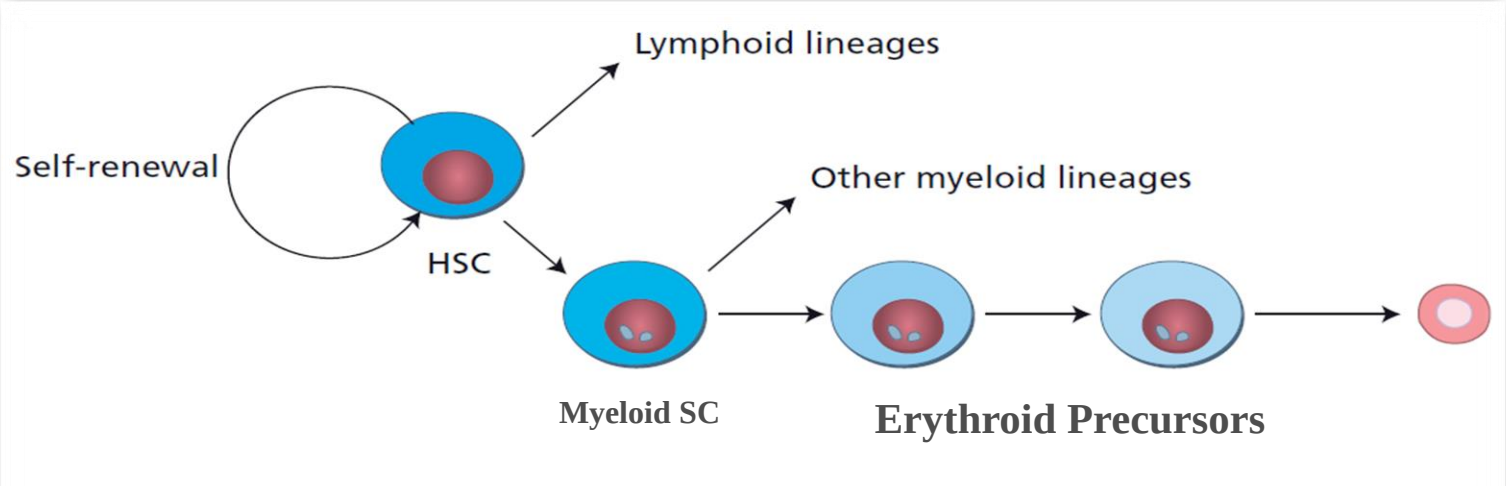


Lecture 3: **ANEMIA**

Hematopoiesis: Formation of blood cells.



Hematopoietic stem cells (HSC) characteristic:

- Self-renewal.
- Cell differentiation.

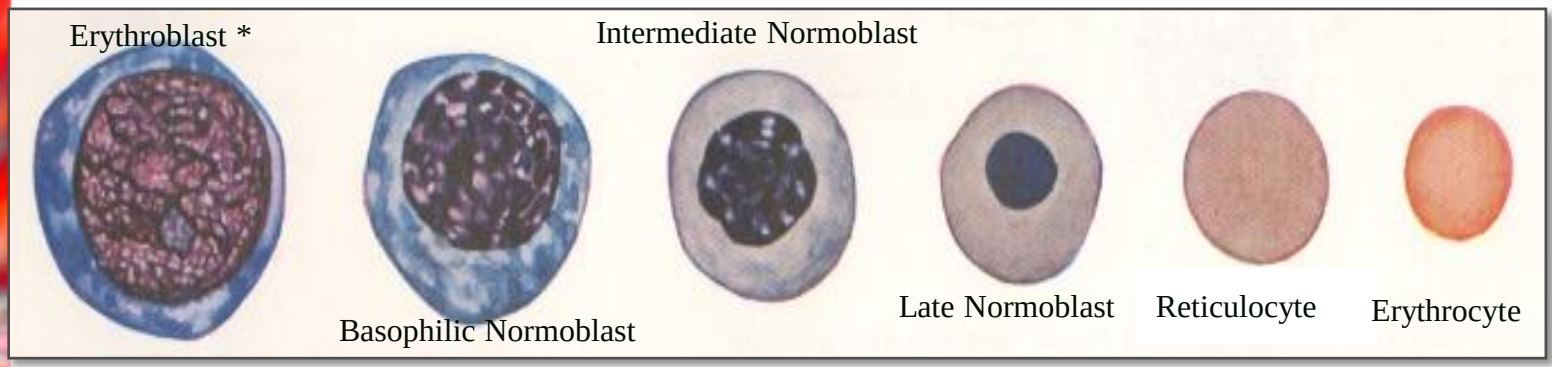
Transcriptional factors:

Lead to proliferation of HSC, and it can push the differentiation to one side.
Like erythropoietin → Erythrocyte.

Erythropoiesis: Formation of RBCs

The Bone Marrow is the major site with the need of:

- Folic acid (DNA synthesis)
- Vit B12 (DNA synthesis),
- Amino acids (globin chain)
- Iron Ferrous (haem synthesis)
- Erythropoietin (growth factor)
- minerals and other regulatory factors.



Notes:

- Hb synthesis begin at erythroblast and stop at reticulocyte, but it is highly active at normoblasts (especially intermediate normoblast).
- Hemoglobin maintains the shape of RBC also

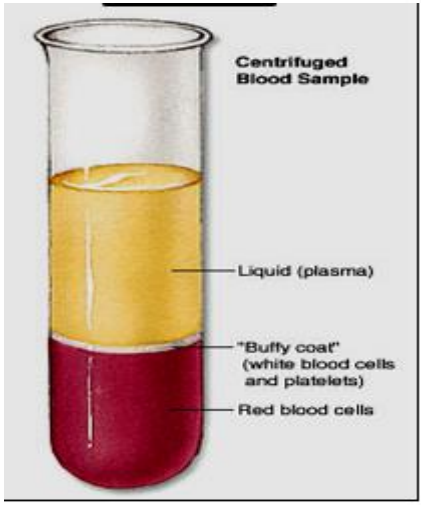
* Erythroblast is the early recognizable erythroid precursor.

❖Reticulocyte & Erythrocyte = will be found in the circulation

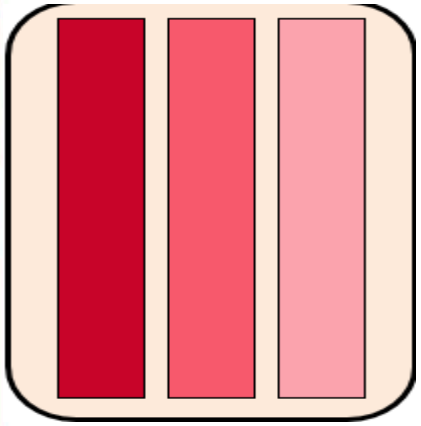
Normal ranges:

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	

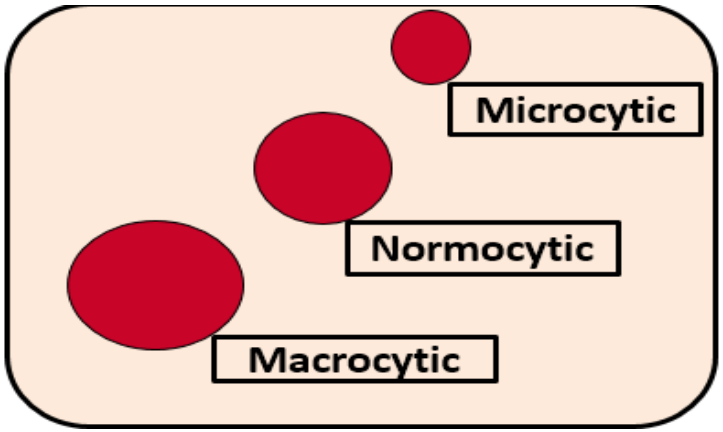
HCT



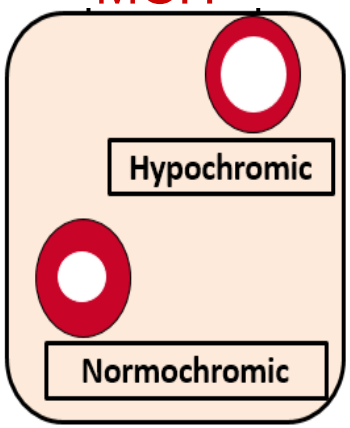
Hb

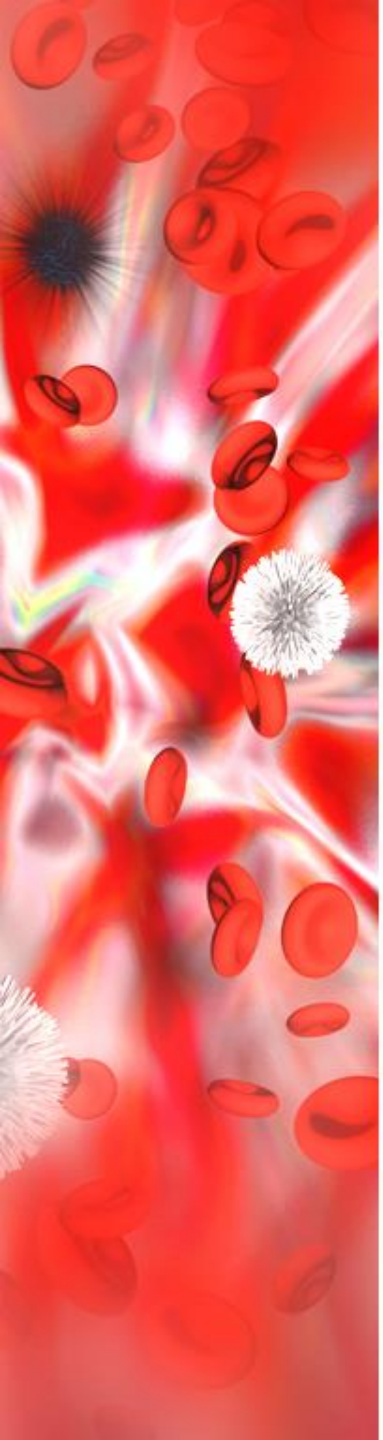


MCV



MCH





ANEMIA

Reduction of Hb concentration 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:

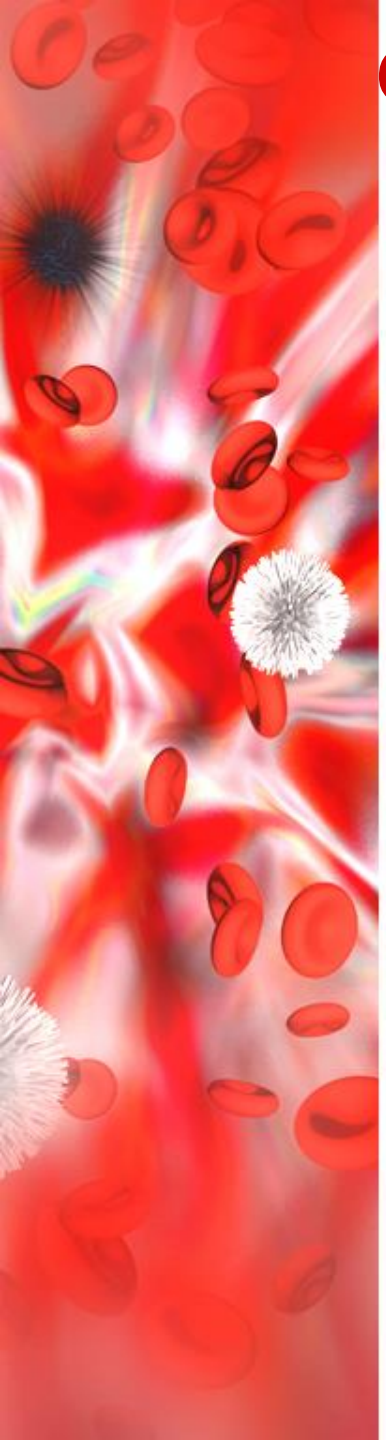
(cardiovascular system, bone marrow and O2 dissociation curve right shifting)

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		
General	**Specific**	
Related to anemia: Weakness, headache, pallor, lethargy, and dizziness.	Spoon nail	iron deficiency.
	Leg ulcers	sickle cell anemia.
Related to compensatory mechanism: Palpitation (tachycardia) Angina, Cardiac failure.	Jaundice	hemolytic anemia.
	bone deformities	thalassemia major.



Classifications of anemia

HEMOGLOBIN	Reduction of prophyrin → sidroblastic anemia	Hypochromic microcyticanemia
	Iron deficiency → IDA	
	Reduction of globin chain → thalassemia	
DNA	DNA synthesis → megaloblastic anemia due to : folate, vit B12 def. ↓ Myelodysplastic syndrome (MDS).	Macrocytic anemia
RBC COUNT	Blood loss due to acute bleeding.	Normocytic normochromic anemia
	Hemolysis due to: Autoimmune, Enzymopathy, Membranopathy Mechanical, Sickle cell anemia.	
	Reduction of RBCs production :- -BM failure: Chemotherapy, aplastic anemia, Malignancy -Anemia of chronic disease	

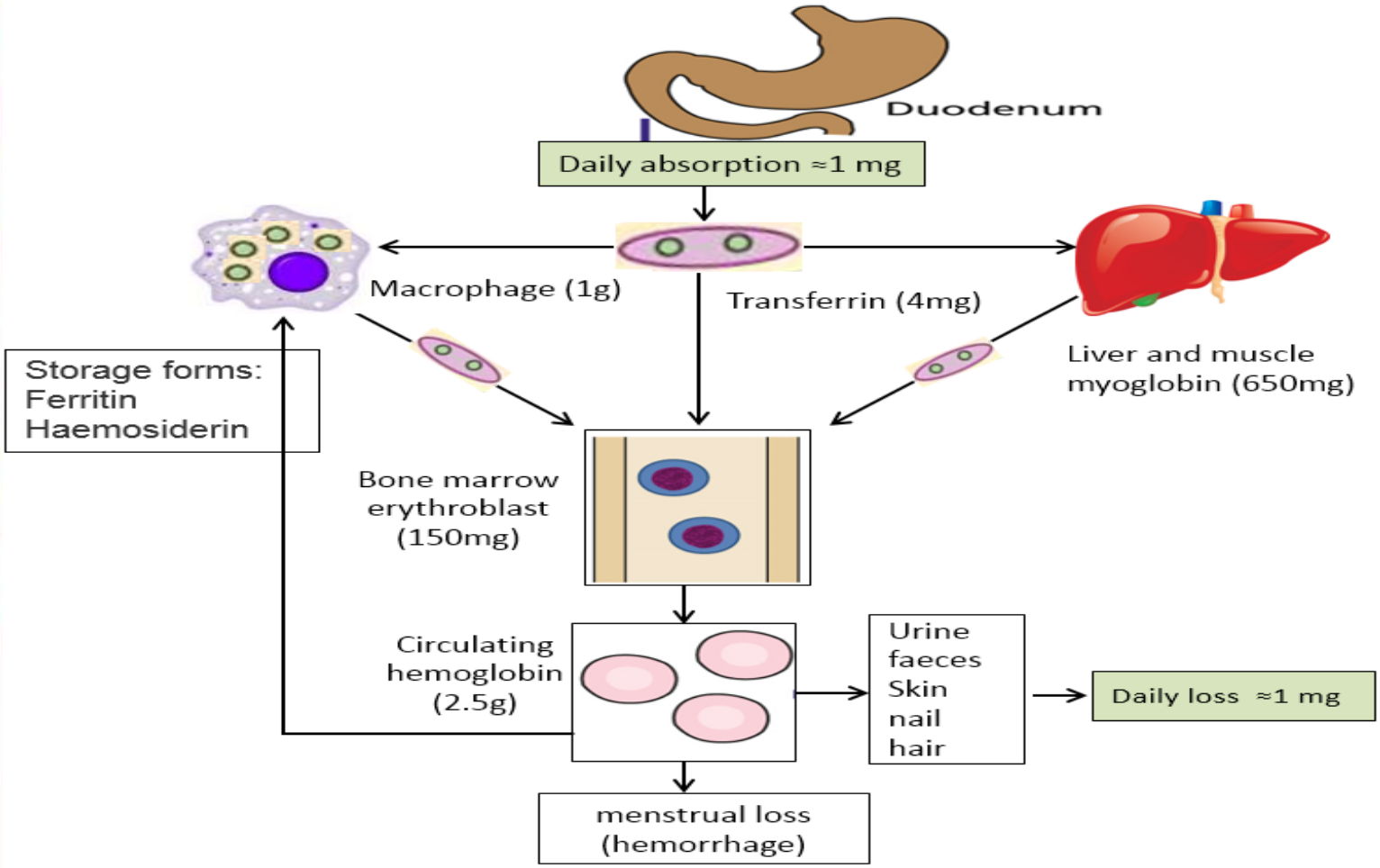
	Hypochromic microcytic anemia	Macrocytic anemia	Normocytic normochromic anemia
MCV	low	high	normal
MCH	low	___	normal
HB	low	high	low
Red cell count	___	___	low

Iron Deficiency Anemia

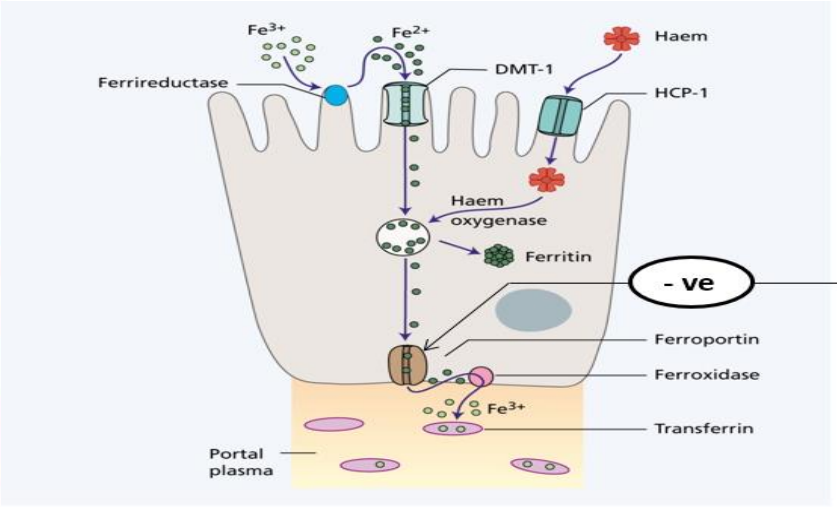
- ✓ Iron is among the abundant minerals on earth (6%).
- ✓ Iron deficiency is the most common disorder(24%). Due to limited absorption ability :

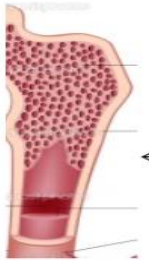
  1-Only 5-10% of taken iron will be absorbed.

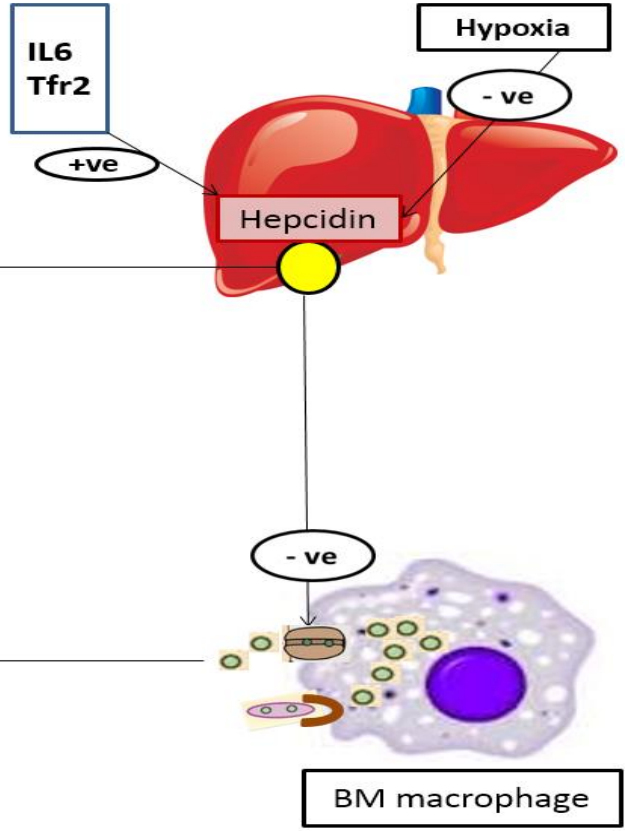
  2- Inorganic iron can not be absorbed easily.
- ✓ Or due to excess loss due to hemorrhage



Iron absorption and regulation:







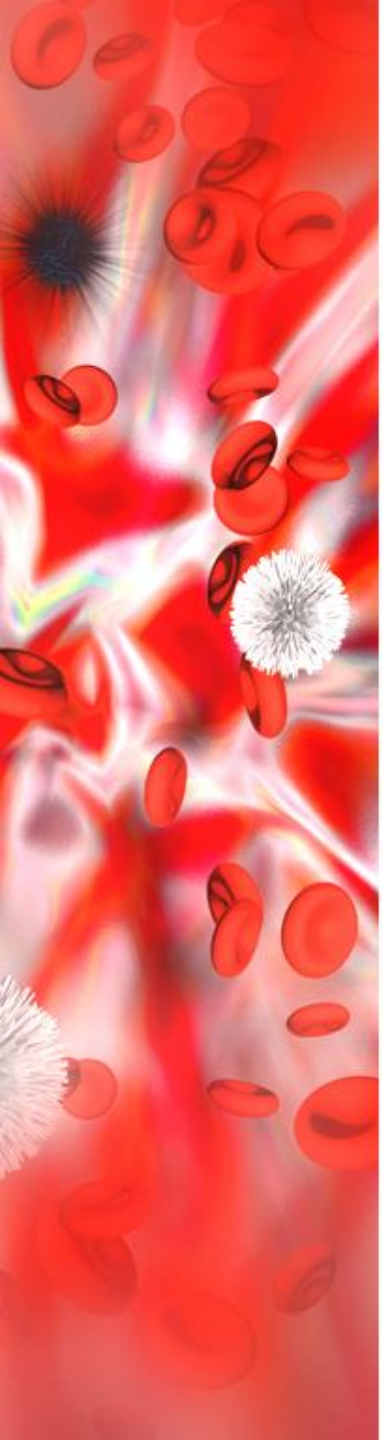
*Duodenum is the site of absorption.

*Dietary iron (ferric fe3+) converted to ferrous (fe2+) before its absorption, and its entry controlled by DMT-1.

*dietary haem source : liver and red meat, its absorption controlled by HCP-1

*Hepcidin produced in liver and it's the major hormonal regulator of iron, it interfere with ferroportin either in intestine or macrophages so it inhibits iron absorption and release.

*ferroportin is a protein responsible for the exit of iron (the only exit pathway).



Continue..

Factor affecting iron absorption:-

1- iron body 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, 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
Inhibitory: Dairy foods (calcium), high fiber foods (phytate), coffee and tea (polyphenoles), and anti-acids.

Causes of IDA:

1- chronic blood loss:

GIT Bleeding: peptic ulcer, esophageal varices , hookworm cancer.
Uterine bleeding, and hematuria.

2-increased demand:

Immaturity, growth, pregnancy, and EPO (erythropoietin) therapy.

3- Malabsorption:

Enteropathy and gastrectomy.

4- poor diet:

Rare as the only cause.

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**

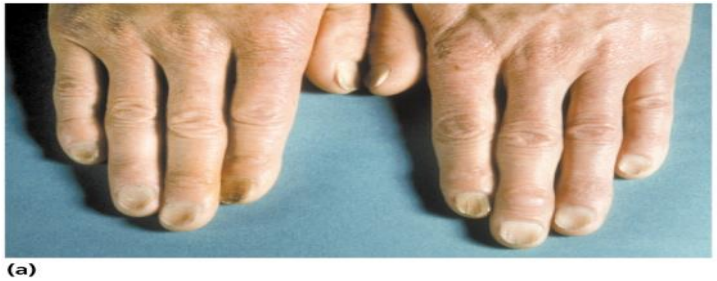
Signs and symptoms of IDA:

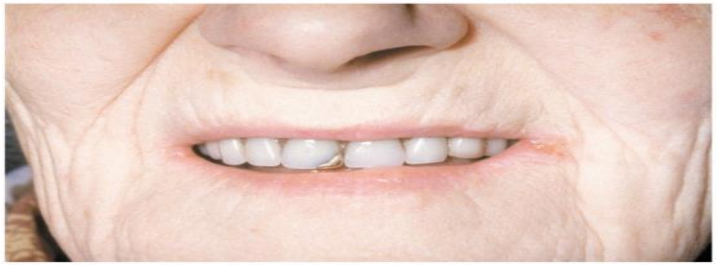
Beside symptoms and signs of anaemia +/- bleeding patients present with:

(a): Koilonychia (spoon-shaped nails)

(b): Angular stomatitis and/or glossitis

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


(a)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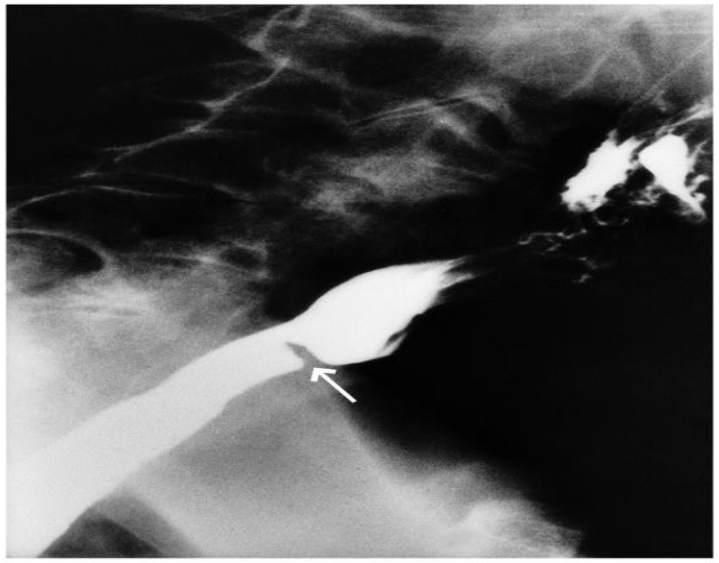
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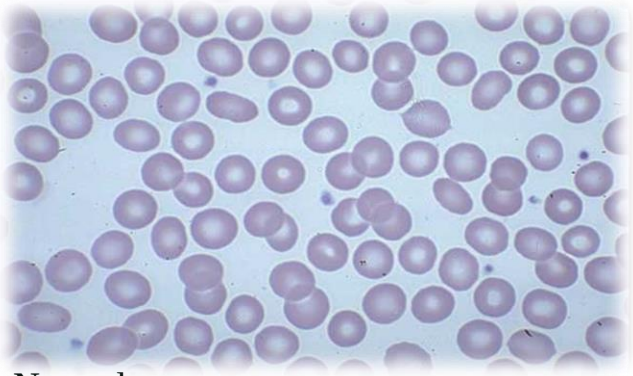
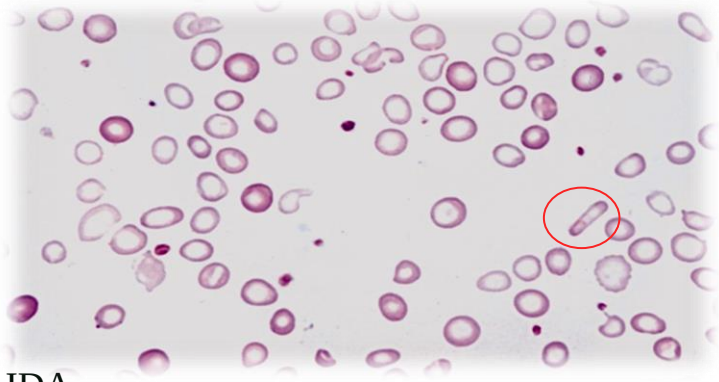
Investigation:



Normal



IDA

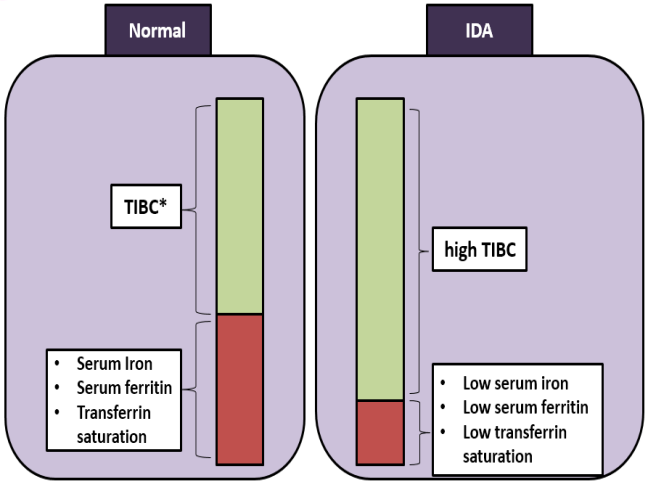
Microcytic hypochromic anemia with:

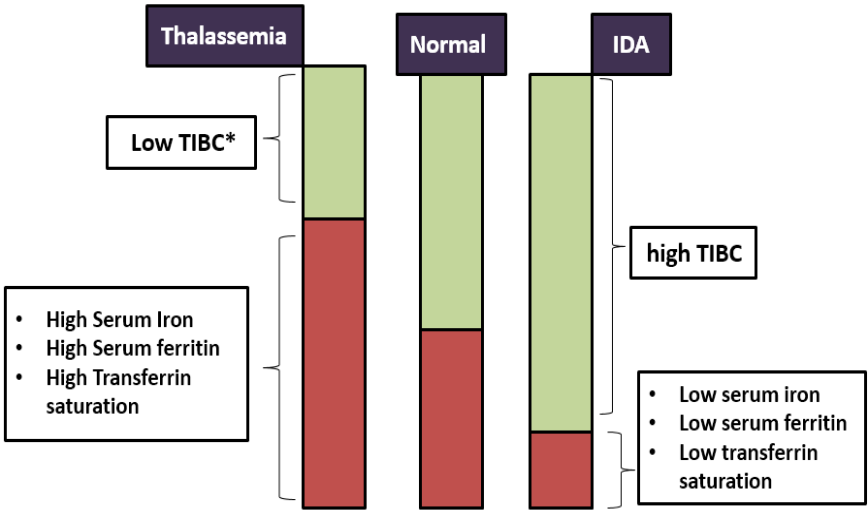
-Anisocytosis (variation in size) and Pokiliocytosis (variation in shape)

-pencil-shaped cells (the circled one)

- target cells .

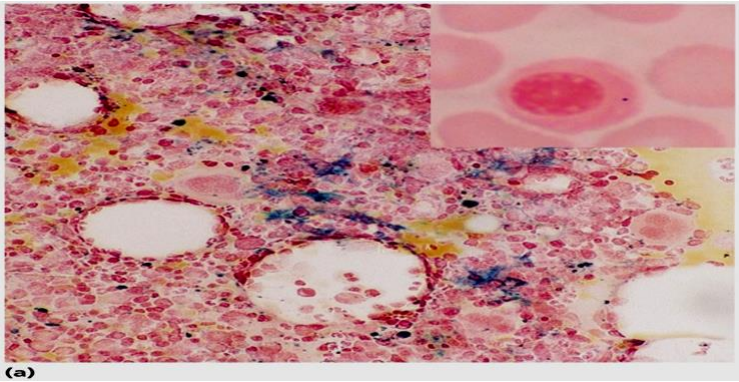
Iron studies :

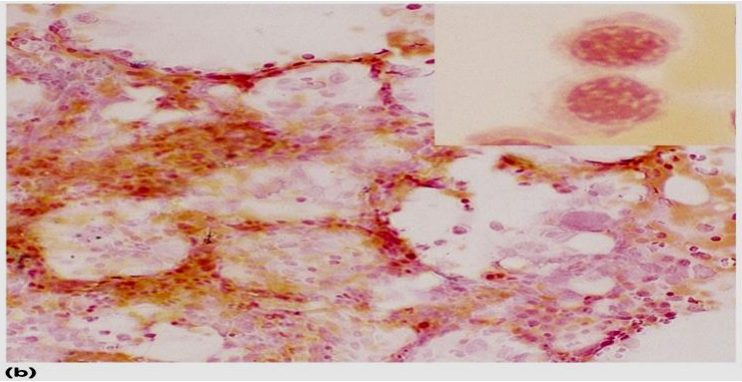




Investigation:

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





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).

  Intravenous:(Ferric sucrose OD for 6 months).In case of malabsorption

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

Prevention of IDA:

- ✓ **Dietary modification:**

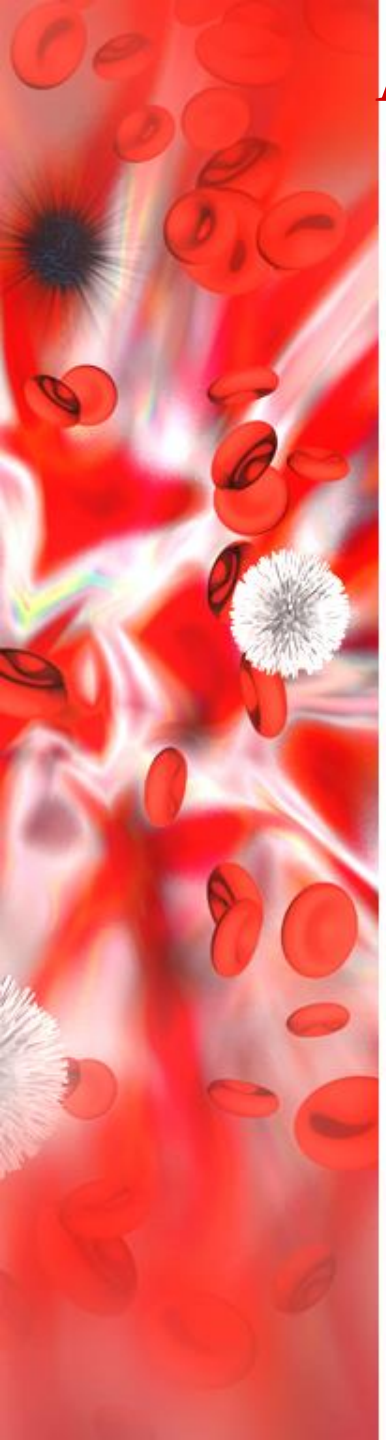
Meat is better source than vegetables.

- ✓ **Food fortification (with ferrous sulphate):**

It has side effects: GIT disturbances, staining of teeth and 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 (by increasing IL-6, IL-1and TNF)

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 (Total iron-binding capacity).
-Normal or high serum ferritin (acute phase reactant).
-High haemosiderin in macrophages but low in normoblasts.

-Manegement:

treat the underlying cause and iron replacement +/- EPO (erythropoietin).

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Good luck …