HLS
Red Cell Disorders
Anemia-I.

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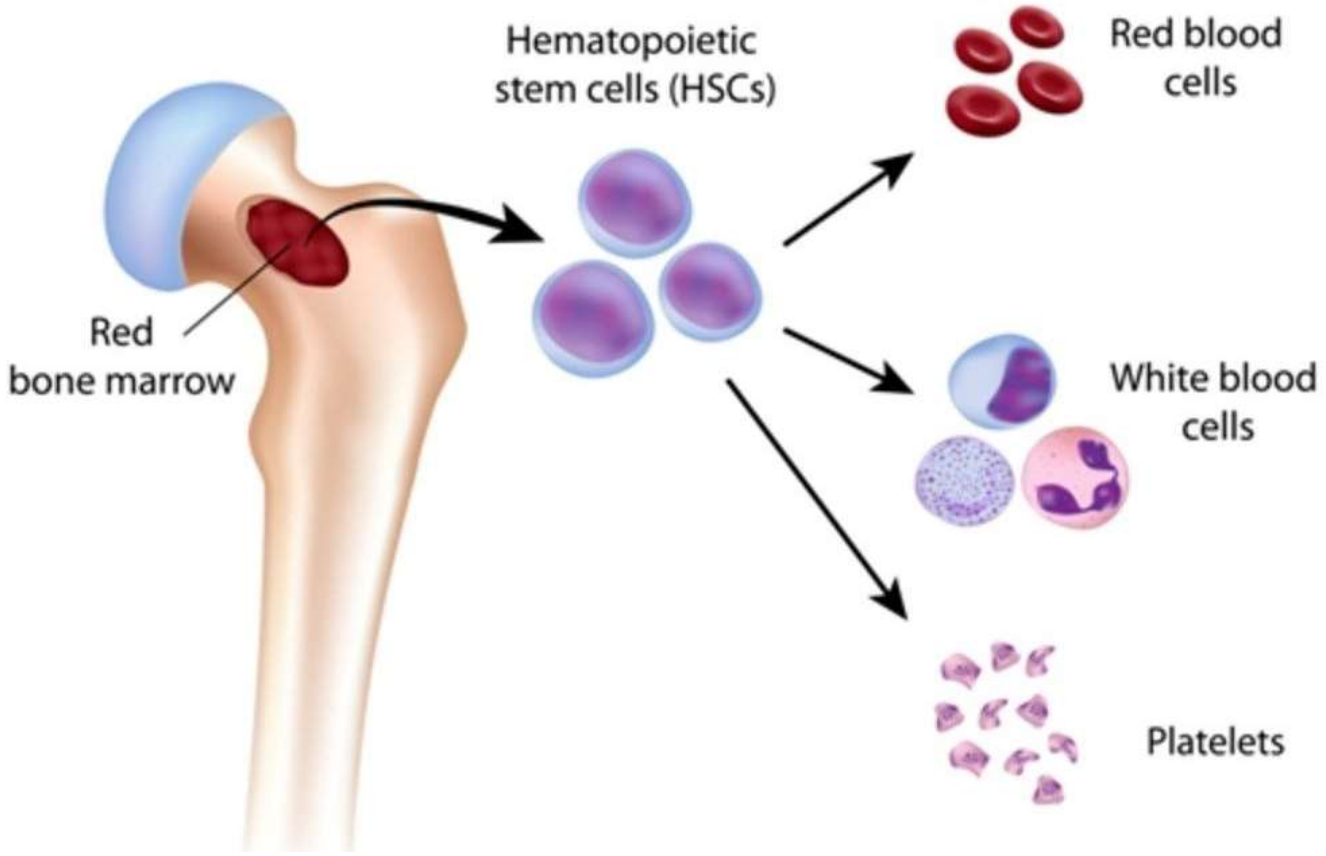
8-4-2026

Hematopoiesis



Lecture titles

1. Introduction to anemia, classification and strategies for diagnosis and nutritional anemias.
2. Introduction to anemia, classification and strategies for diagnosis and nutritional anemias II.
3. Thalassemia and hemoglobinopathies and hemolytic anemias.
4. Congenital bleeding disorders, DIC and thrombophilic disorders.
5. ITP, TTP and inherited disorders of platelets functions.
6. White blood cell and lymph node disorders. Non-neoplastic.
7. Lymphoid neoplasms I.
8. Lymphoid neoplasms II.
9. Plasma cell neoplasms and related entities.
10. Acute myeloid leukemia.
11. Myeloproliferative neoplasms I.
12. Myeloproliferative neoplasms II and MDS.
13. Histiocytic neoplasms.

CBC

White blood cells (WBC)	1.90	4.25	K/μL	4.5–11.5
Red blood cells (RBC)	3.75	2.47	M/μL	4–5.40
Hemoglobin (Hb)	11	8.8	g/dL	12–15
Hematocrit (Hct)	30.6	26.9	%	35–49
Mean cell volume (MCV)	81.6	108.9	fL	80–94
Mean cell hemoglobin (MCH)	29.3	35.6	pg	32–36
Platelets	12	51	K/μL	150–450
Reticulocyte absolute	0.020	0.128	%	0.5–2

Anemia

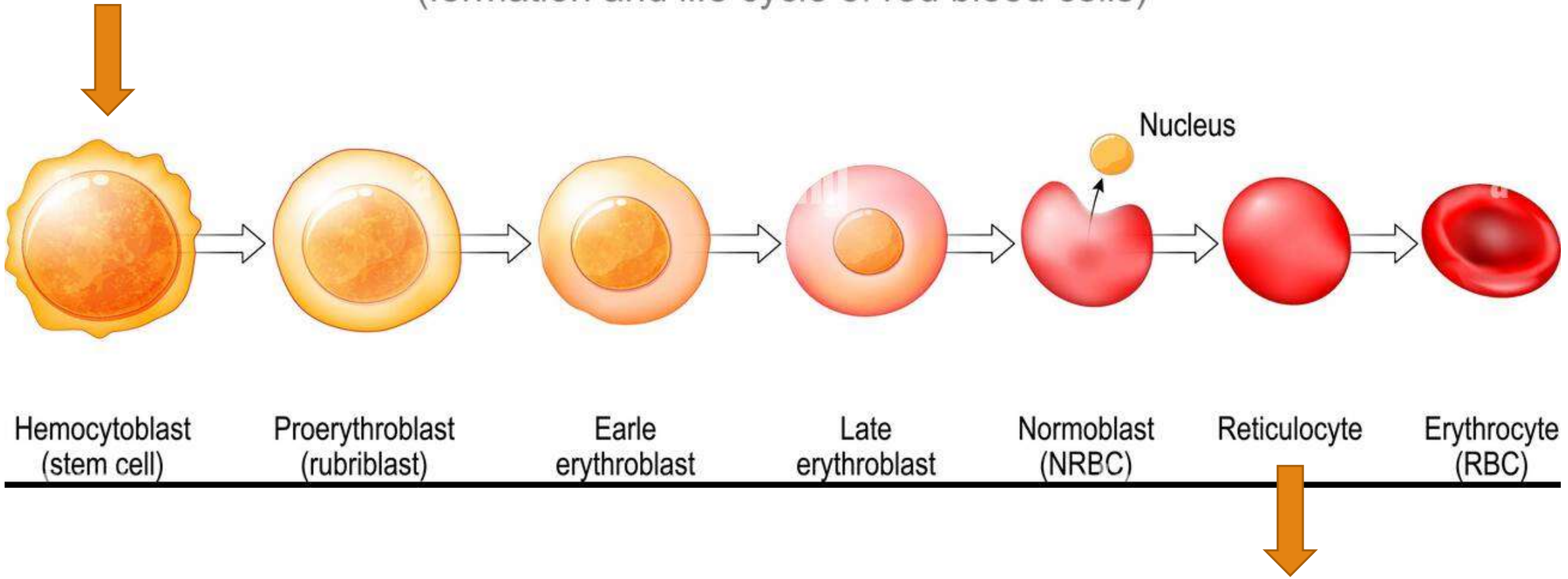
- Anemia is strictly defined as a decrease in red blood cell (RBC) mass.

The decrease may result from:

- ❖ blood loss.
- ❖ increased destruction of RBCs (hemolysis).
- ❖ decreased production of RBCs.

❖ The function of the RBC is to deliver oxygen from the lungs to the tissues and carbon dioxide from the tissues to the lungs. In anemia, a decrease in the number of RBCs transporting oxygen and carbon dioxide impairs the body's ability for gas exchange.

Erythropoietin :



erythroid precursors are released into circulation

Etiology

Genetic etiologies:

- Hemoglobinopathies
- Thalassemias

Nutritional etiologies :

- Iron deficiency.
- Vitamin B12 deficiency.
- Folate deficiency

Physical etiologies :

- Trauma.
- Burns.
- Frostbite

- Chronic disease and malignant etiologies.
- Infection.

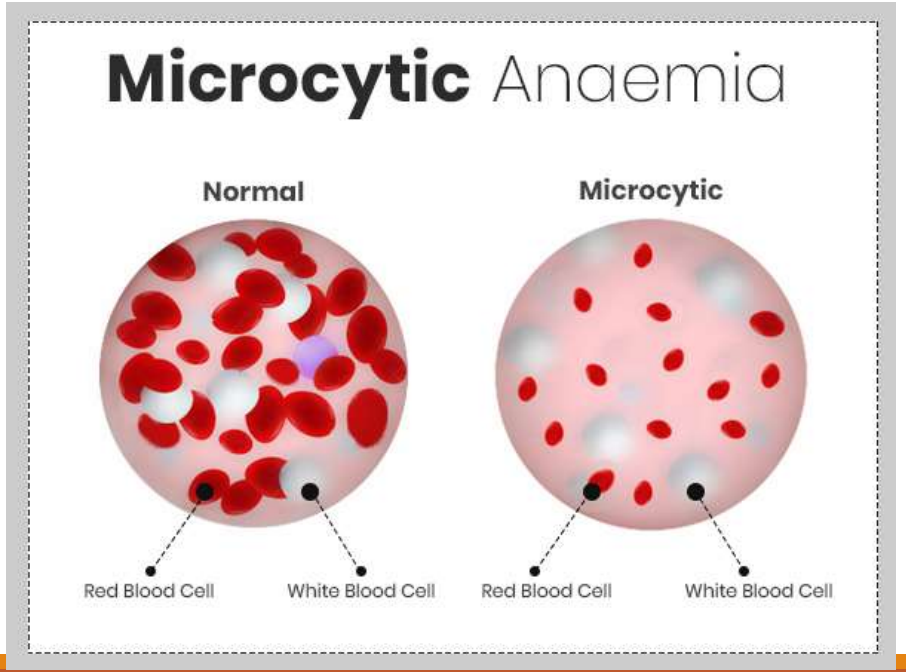
Morphological Classification of Anemia

Morphological-classification-of-anemia

Morphology	Microcytic	Normocytic	Macrocytic
MCV (fL)	<80	80 - 100	>100
Disorders	**T**halassemia **A**nemia of chronic disease **I**ron deficiency anemia **L**ead poisoning **S**ideroblastic anemia	**H**emolytic anemia **A**nemia of chronic disease **R**enal disease **A**cute blood loss **B**one marrow failure **A**plastic anemia	**M**egaloblastic anemia **A**lcoholism **L**iver disease **M**yelodysplasia

I. Microcytic anemia

- Small, often hypochromic, red blood cells in a peripheral blood smear and is usually characterized by a low MCV (< 80 fl).
  - Iron deficiency is the most common cause of microcytic anemia



A. Iron Deficiency Anemia

- The most common nutritional deficiency in the world
- 80% of functional body iron is present in hemoglobin, and 20% in the iron storage pool (hemosiderin and ferritin-bound iron in the cells in the liver, spleen, bone marrow, and skeletal muscle)

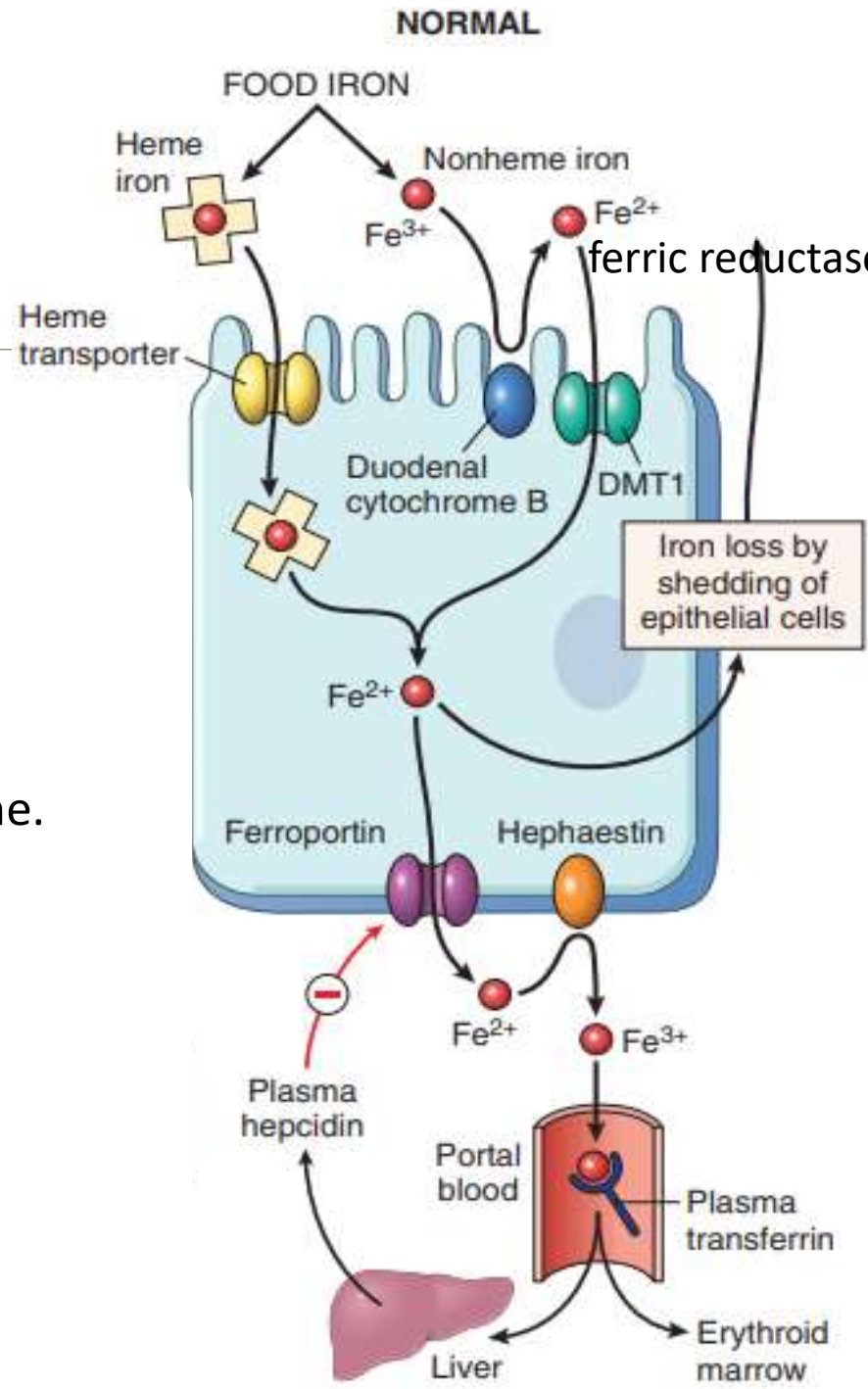
Regulation of iron absorption

- Regulation of iron absorption occurs within the duodenum.

- (Fe2+) is transported across the apical.
membrane by divalent metal transporter-1 (DMT1).

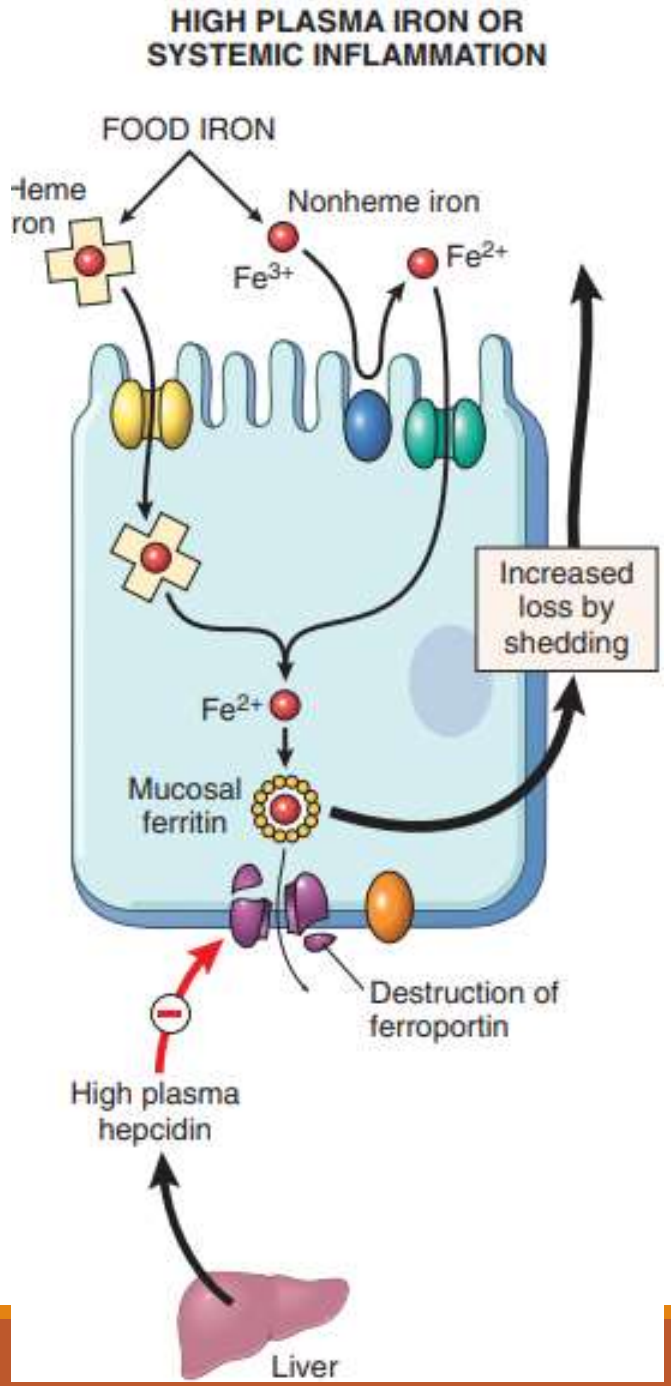
- A second transporter, ferroportin, then moves
iron from the cytoplasm to the plasma across the basolateral membrane.
In the form of (Fe3+).

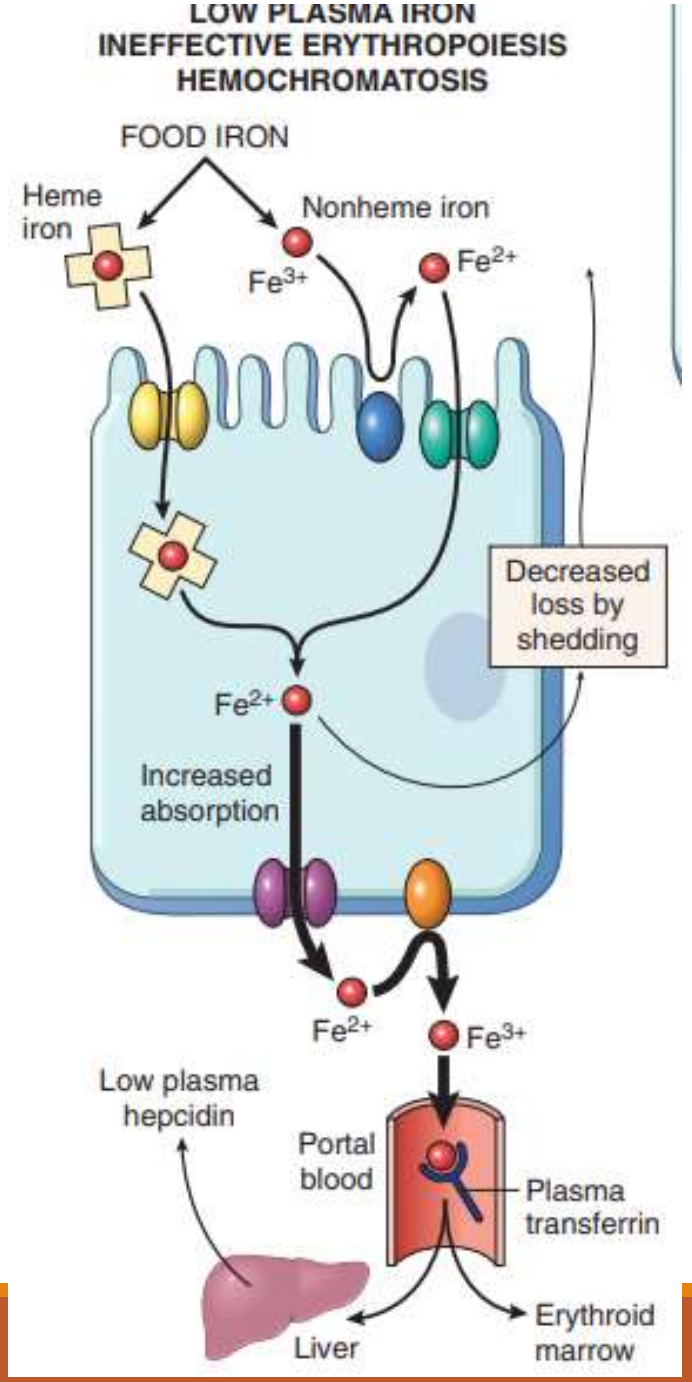
- The remainder is incorporated into cytoplasmic ferritin
and is lost through the exfoliation of mucosal cells



Hepcidin ??

- A small peptide that is synthesized and secreted from the liver in an iron-dependent fashion.
- high iron levels in the plasma enhance hepcidin production, whereas low iron levels suppress it.
- Hepcidin levels rise in the face of systemic inflammation because of the direct effects of inflammatory mediators such as IL-6 on hepatocytes


HIGH PLASMA IRON OR
SYSTEMIC INFLAMMATION
FOOD IRON
Heme iron
Nonheme iron
Fe3+
Fe2+
Increased loss by shedding
Fe2+
Mucosal ferritin
Destruction of ferroportin
High plasma hepcidin
Liver


LOW PLASMA IRON
INEFFECTIVE ERYTHROPOIESIS
HEMOCHROMATOSIS
FOOD IRON
Heme iron
Nonheme iron
Fe3+
Fe2+
Decreased loss by shedding
Fe2+
Increased absorption
Fe2+
Fe3+
Low plasma hepcidin
Portal blood
Plasma transferrin
Liver
Erythroid marrow

ETIOLOGY

- Chronic blood loss: GI bleeding (e.g., peptic ulcers, colon cancer, hemorrhoids) and the female genital tract (e.g., menorrhagia, endometrial cancer).

- Low intake and poor bioavailability (predominantly vegetarian diets) .

- Increased demands not met by normal dietary intake: pregnancy and infancy.

- Malabsorption: e.g.; celiac disease or after gastrectomy

Clinical manifestation

- Fatigue and diminished capability to perform hard works.
- Leg cramps on climbing stairs.
- Cold intolerance.
- abnormalities of the fingernails (thinning, flattening, and “spooning,”) and pica

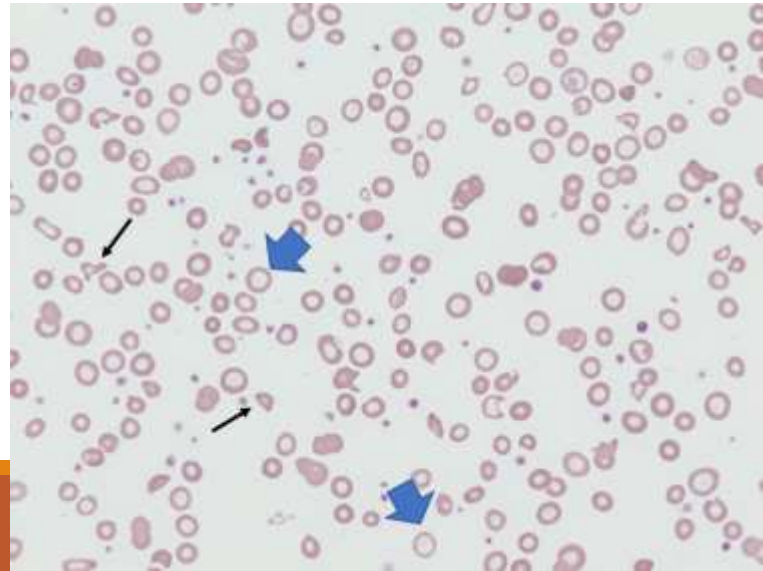
Laboratory manifestation

- Complete blood count (CBC):

microcytic and hypochromic erythropoiesis, decrease in both mean corpuscular volume (MCV) and the mean corpuscular hemoglobin concentration (MCHC).

- Low serum iron and ferritin levels

- Peripheral Smear: microcytic and hypochromic red blood cells



B. Anemia of chronic inflammation

Arises from the suppression of erythropoiesis by systemic inflammation:

1. Chronic microbial infection (osteomyelitis, endocarditis).
2. Chronic immune disorders (RA).
3. Neoplasms (Carcinoma or lymphoma)

Anemia of chronic inflammation stems from:

1- High levels of plasma hepcidin, which blocks the transfer of iron to erythroid precursors by downregulating ferroportin in macrophages and duodenum.

**The elevated hepcidin levels are caused by proinflammatory cytokines such as IL-6 (increase hepatic hepcidin synthesis) .

2-Chronic inflammation blunts erythropoietin synthesis by the kidney

II. Normocytic anemia

- Normocytic normochromic anemia is a type of anemia in which the circulating red blood cells (RBCs) are the same size (normocytic) and have a normal red color (normochromic).

- Normocytic anemia is further divided into 2 broad categories:

* anemia with primary bone marrow involvement, include:

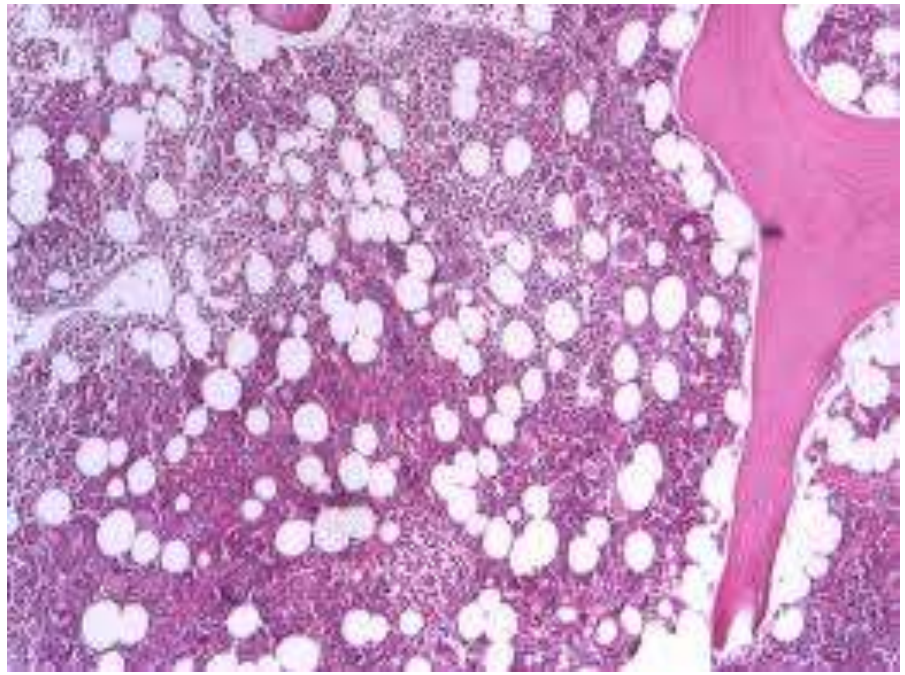
  - Aplastic anemia.

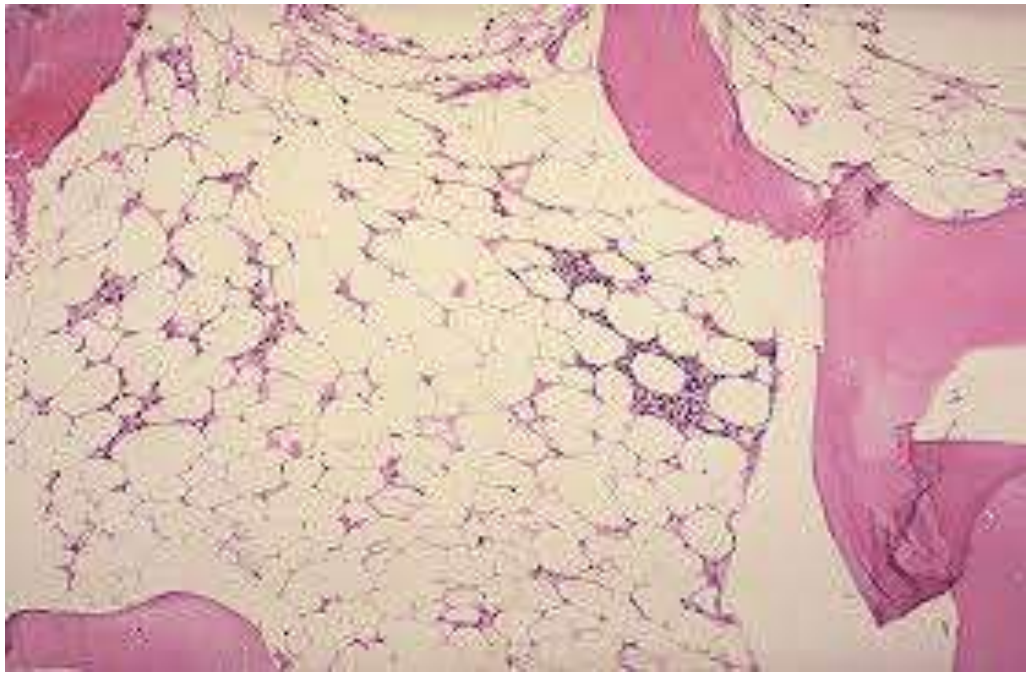
  - Myelophthisic anemia.

* anemia secondary to underlying disease.

Aplastic anemia

Aplastic anemia is a syndrome of bone marrow failure characterized by peripheral pancytopenia and marrow hypoplasia





Aplastic anemia

- Characterized by marrow failure due to primary defects or damage to the stem cell or the marrow microenvironment.

- Mostly (more than 80% of cases) are acquired.

- The clinical presentation includes signs and symptoms related to the decrease in bone marrow production of hematopoietic cells:

❖ Anemia.

❖ Bleeding.

❖ Fever or infections

Myelophthisic anemia

- Myelophthisis is a form of bone marrow failure that results from the destruction of bone marrow precursor cells and their stroma.

- Generally, in myelophthisic anemia, a form of fibrosis, occurs secondary to injury by nonhematopoietic cells or pathogens, which destroys the normal hematopoietic cells and their supportive stromal cells