
بسم الله الرحمن الرحيم

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”قالوا سبحانك لا علم لنا إلا ما علمتنا إنك أنت العليم الحكيم“

صدق الله العظيم

2 - erythropoiesis

Objectives;

Intended learning outcomes (ILOs)

After reviewing the PowerPoint presentation and the associated learning resources, the student should be able to:

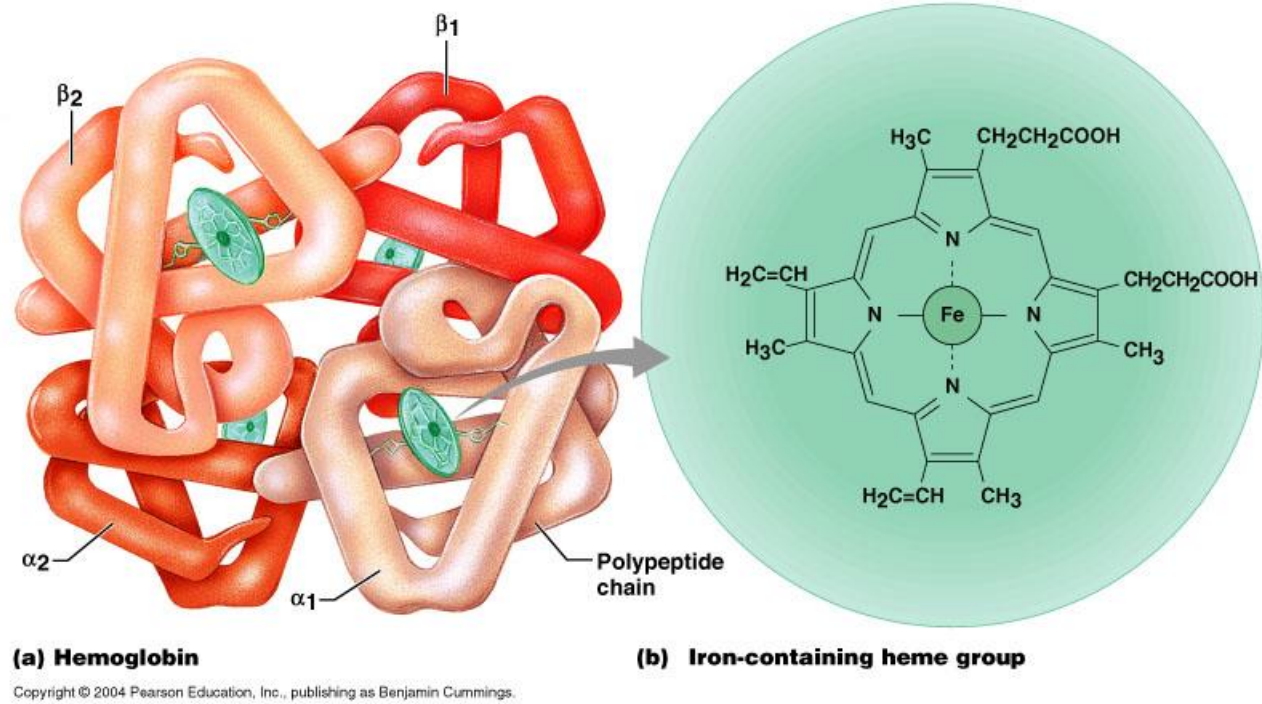
- **Enumerate the factors affecting erythropoiesis.**
- **Describe the normal structure of Hemoglobin.**
- **Summarize the role of hypoxia & erythropoietin hormone in the process of erythropoiesis.**
- **Discuss the importance of vitamin B12 & folic acid as maturation factors for the RBCs.**
- **Discuss the mechanism of Vitamin B12 & folic acid absorption.**
- **Describe the importance of iron in the process of erythropoiesis & hemoglobin synthesis.**
- **Discuss the mechanism of iron absorption.**

Hemoglobin (Hb)

- Globular protein
- Heme + Globin

Accounts for > 95% of protein in RBC

Main functions: transportation of respiratory gases. It carries ~ 98.5% of all O_2 ??



Hb Content of Blood

Concentration of Hb in the Blood

Measured as g/dl (grams per deciliter, or per 100 ml)

Average values:

Male: 13.5 – 17.5 g/dl (16 g/dl)

Female: 12.0 – 15.5 g/dl (14 g/dl)

Infants: 14.0 – 19.0 g/dl

- Each gram of pure hemoglobin is capable of combining with 1.34 ml of oxygen.
- Therefore, in a normal man a maximum of about 20 milliliters of oxygen can be carried in combination with hemoglobin in each 100 milliliters of blood, and in a normal woman 19 milliliters of oxygen can be carried.

Types of Hemoglobin

Hb – A = Adult hemoglobin (98%)

2 alpha + 2 beta chains.

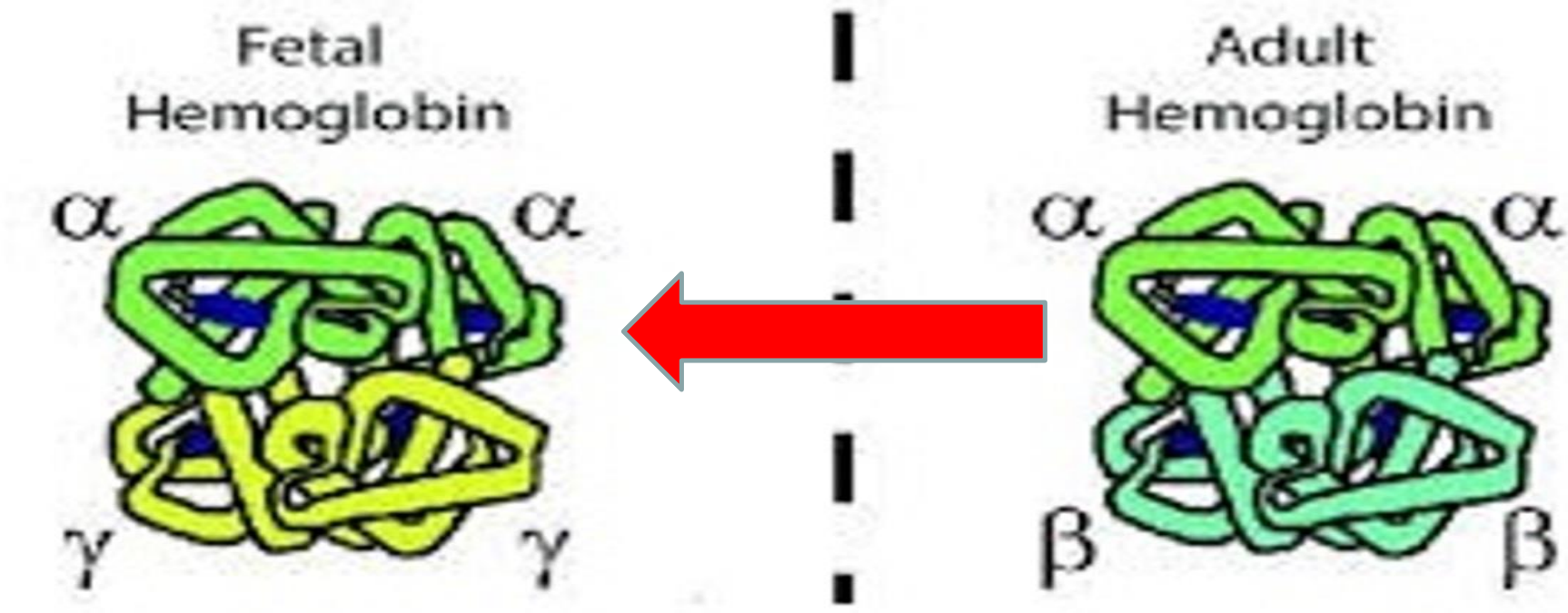
Hb – F = Fetal hemoglobin (Hemoglobin of intrauterine life)

2 alpha + 2 gamma chains.

Hb – A2 (2%)

2 alpha + 2 delta chains.

Types of Hemoglobin



Hb – F
2 alpha + 2 Gamma chains
Has higher afininty for Oxyhen than Hb - A

Hb - A
2 alpha + 2 beta chains

Abnormal types of Hemoglobin

Several types.

Examples:

Thalassemia: Decreased synthesis of the globin polypeptide chains.

Sickle cell anemia: Abnormal sequence of the amino acids in the globin polypeptide chains.

RBCs
Erythropoiesis

Definition Sites Stages Factors

Definition: Formation of new RBCs.

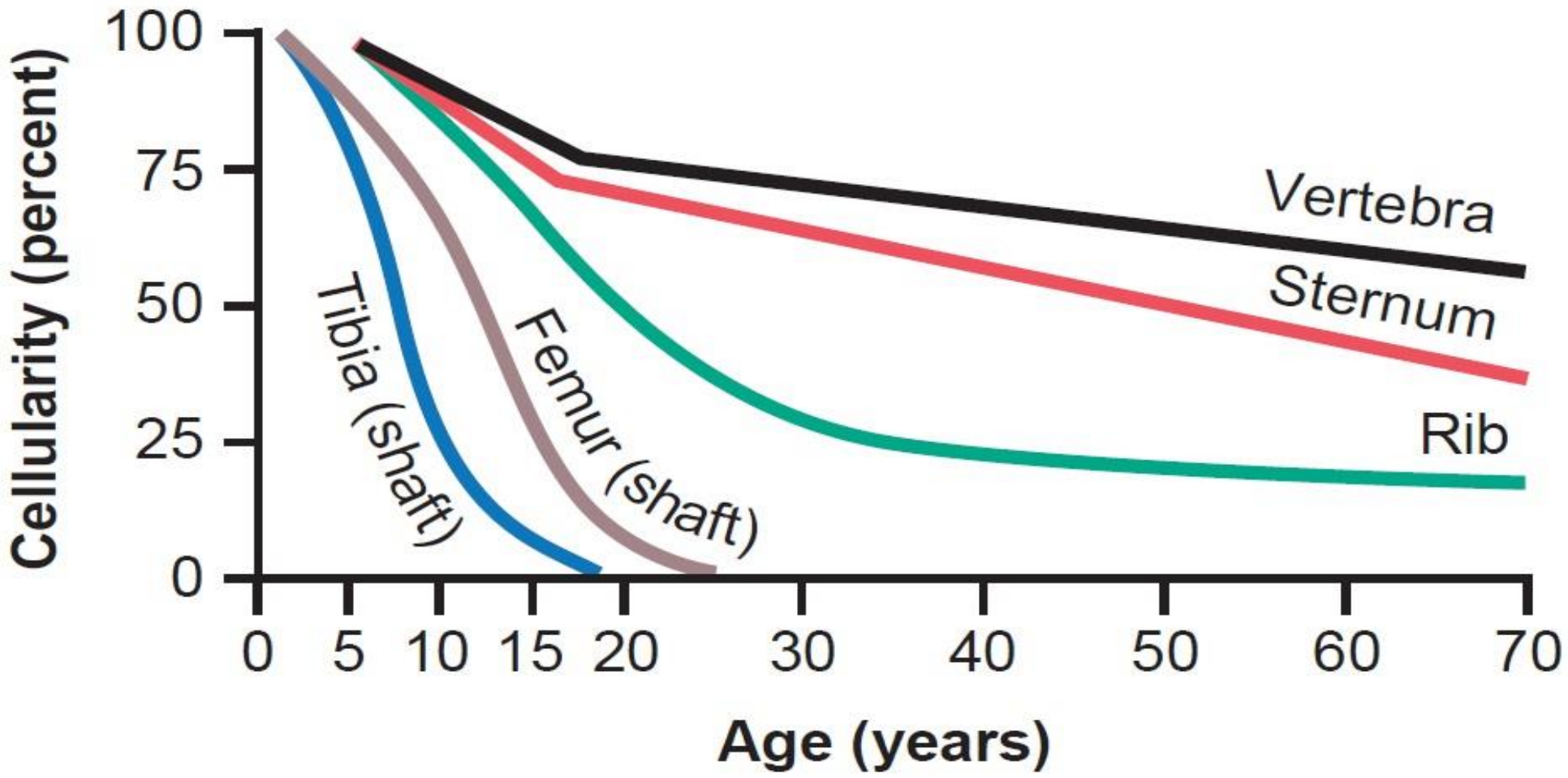
Sites: Bone marrow.

During intrauterine life: Liver – Spleen – Lymph nodes.

Before the age of 20 years: Bone marrow of all bones.

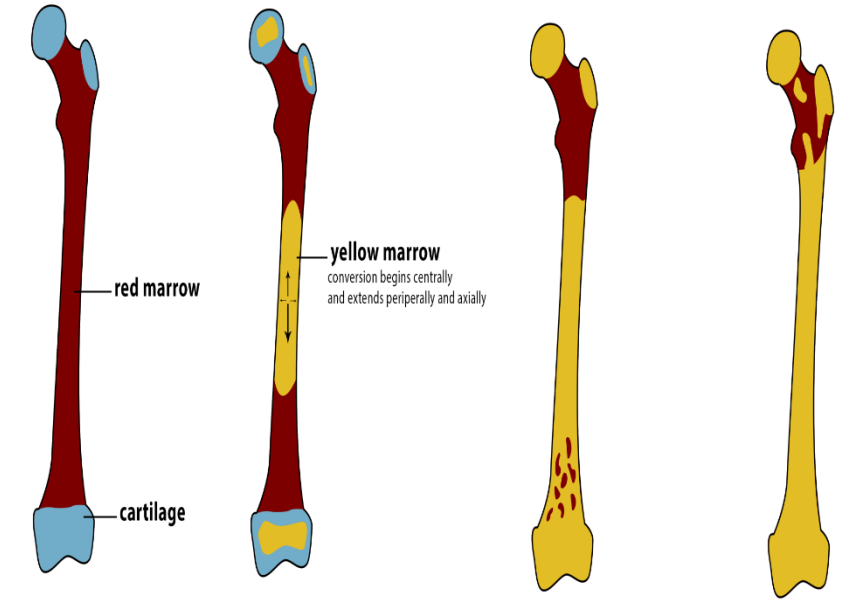
After the age of 20 years: Bone marrow of membranous bones only.

RBCs
Erythropoiesis
Sites

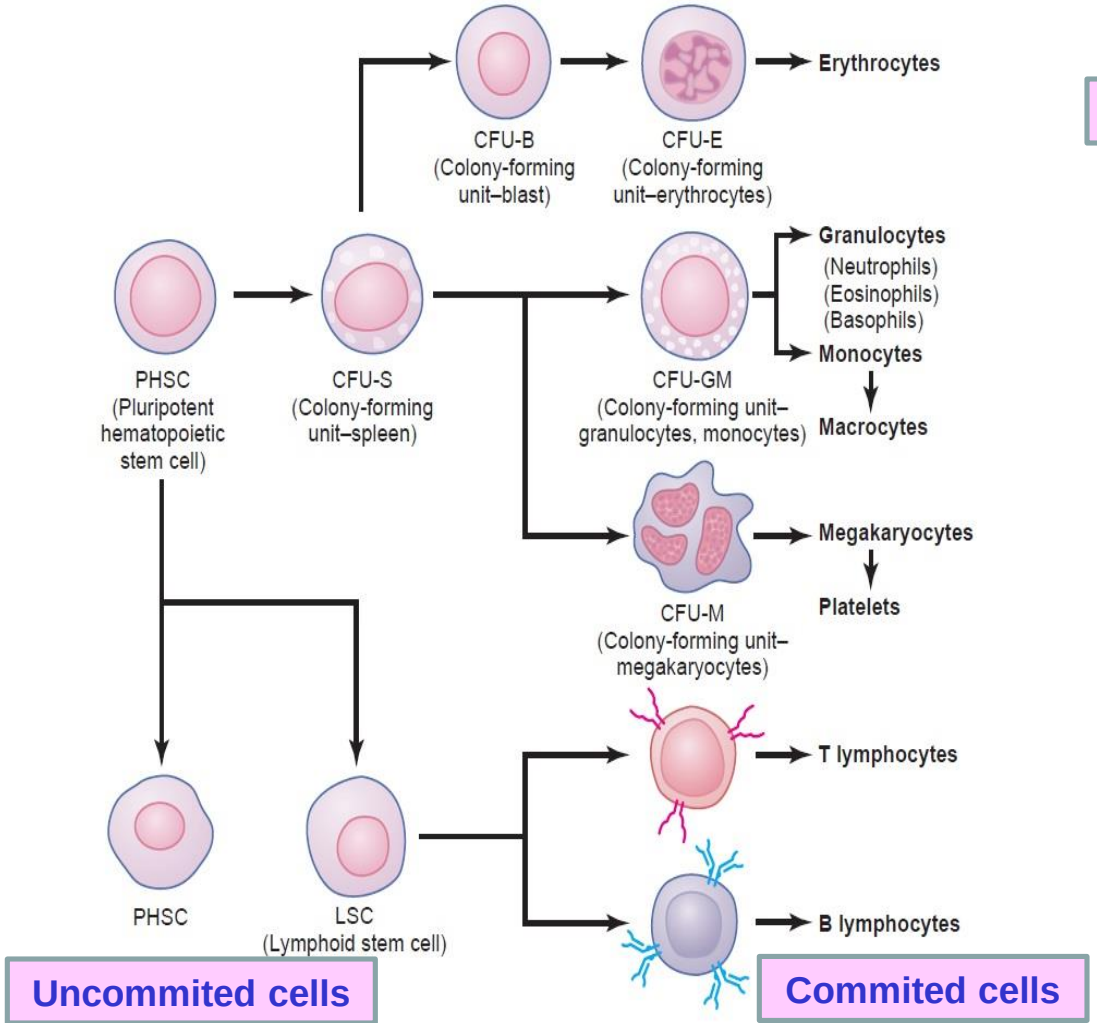


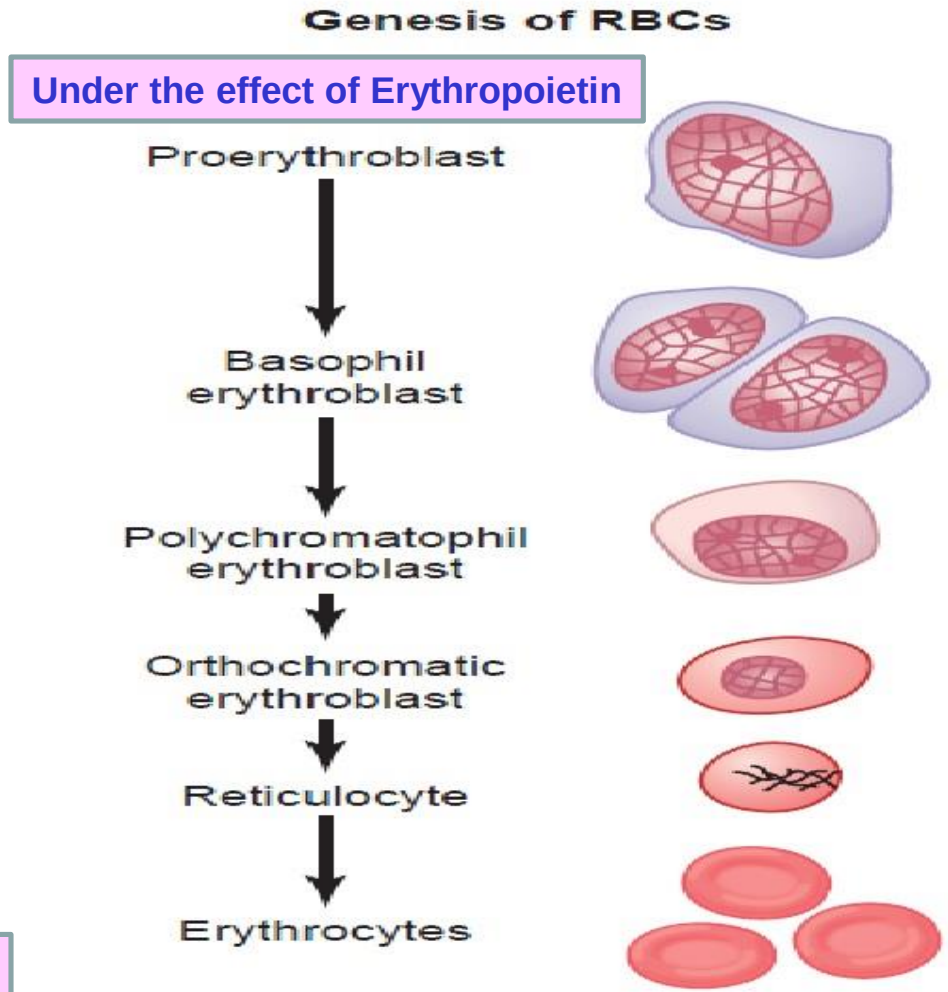
RBCs Erythropoiesis Sites

Normal bone marrow conversion



RBCs
Erythropoiesis
Stages





RBCs
Erythropoiesis
Factors

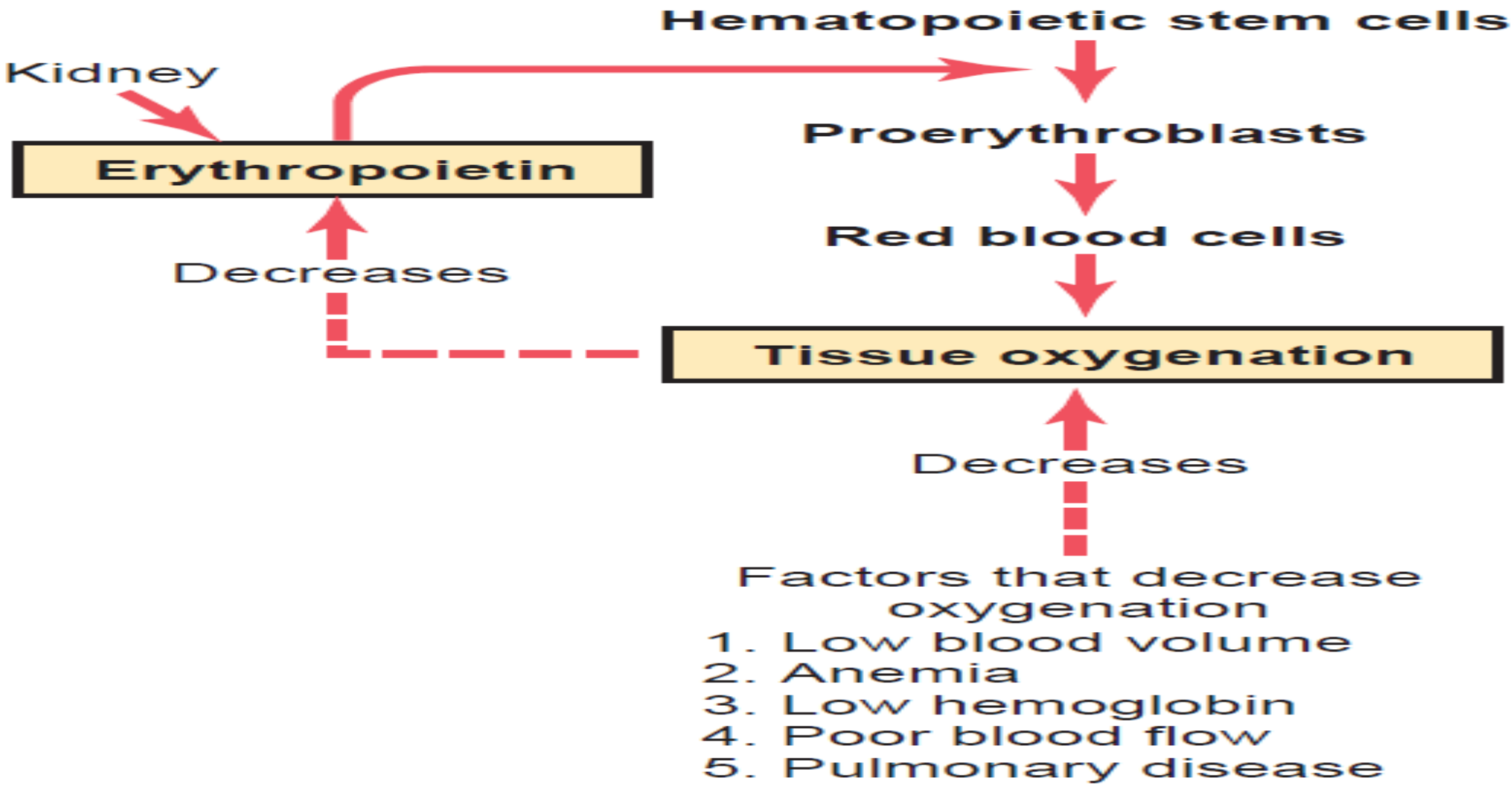
Oxygen supply to the tissues (Hypoxia).

Dietary requirements (**Vitamins – Iron** – Copper – Cobalt – Zinc – Other elements).

Healthy organs (Bone marrow – Liver – Kidney).

Hormones (Erythropoietin – Androgens – Thyroxin – Cortisol)

RBCs
Erythropoiesis
Factors
Oxygen supply to the tissues (Hypoxia)



RBCs – Erythropoiesis -Factors
Oxygen supply to the tissues (Hypoxia) = Effect of erythropoietin

importance	Tissue oxygenation is the most essential regulator of RBCs production. The mechanism is via the stimulatory effect of hypoxia on the release of erythropoietin hormone.
Nature	Glycoprotein with a molecular weight = 34,000
Site of release	Mainly from the kidney (90%). Small amount from the liver.
Site of action	Bone marrow.
Action	Stimulate the growth and differentiation of early hematopoietic stem cells

Clinical correlation

In severe renal diseases, the person becomes invariably very anemic as the liver cannot compensate for the role of kidneys in the release of erythropoietin.

Anemia of renal disease is treated with erythropoietin

Vitamin B12 and folic acid (Maturation factors)

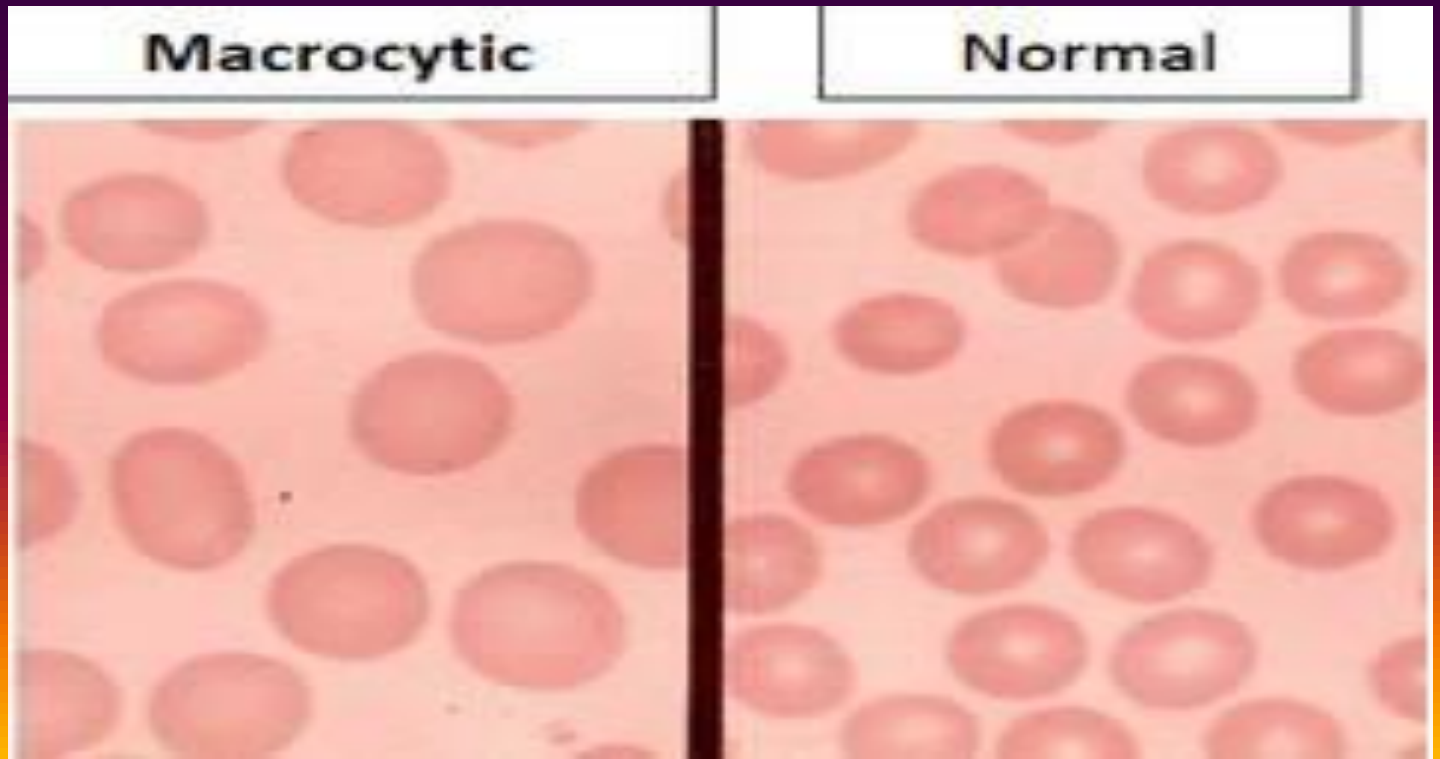
importance

Maturation factors for the RBCs.
Essential for DNA synthesis and maturation.

Manifestations of Deficiency

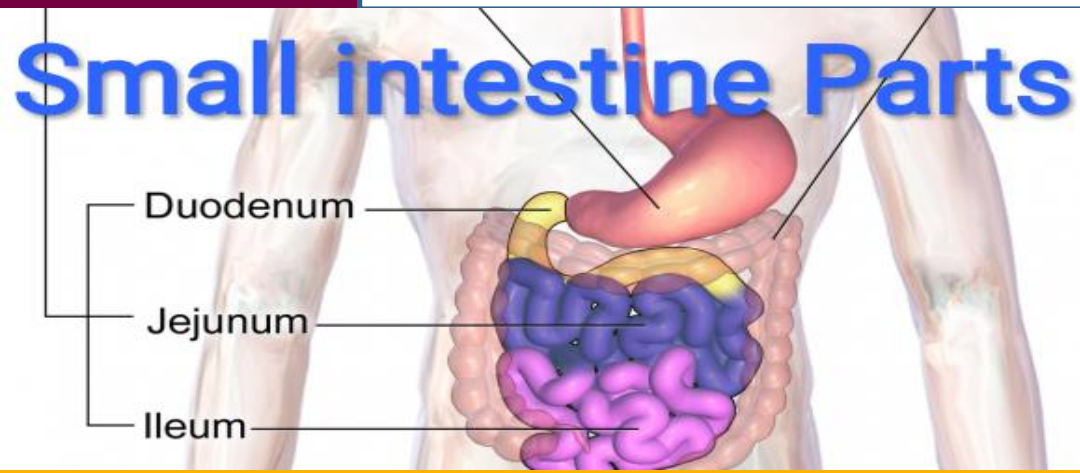
Macrocytic (megaloblastic anemia).
Abnormal large & fragile cells.

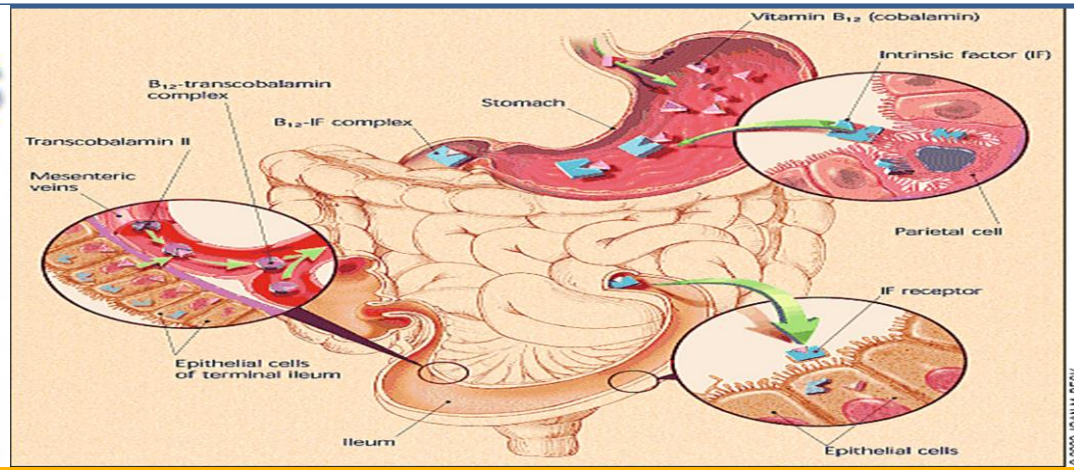
Blood film



Vitamin B12

Origin	Animal sources only (meat, liver,,, etc)
Storage	In the liver in large amounts, enough for around 3 -4 years
Causes of Deficiency	1 – Defective absorption (pernicious anemia). 2 – Defective storage (liver diseases). 3 – dietary deficiency (very rare).
Absorption	Intrinsic factor is secreted from the stomach to bind vitamin B12 and helps its absorption. Absorption occurs in the terminal ileum. So macrocytic anemia occurs in: 1 – Distal small intestinal diseases. 2 – deficiency of intrinsic factor (Pernicious anemia)



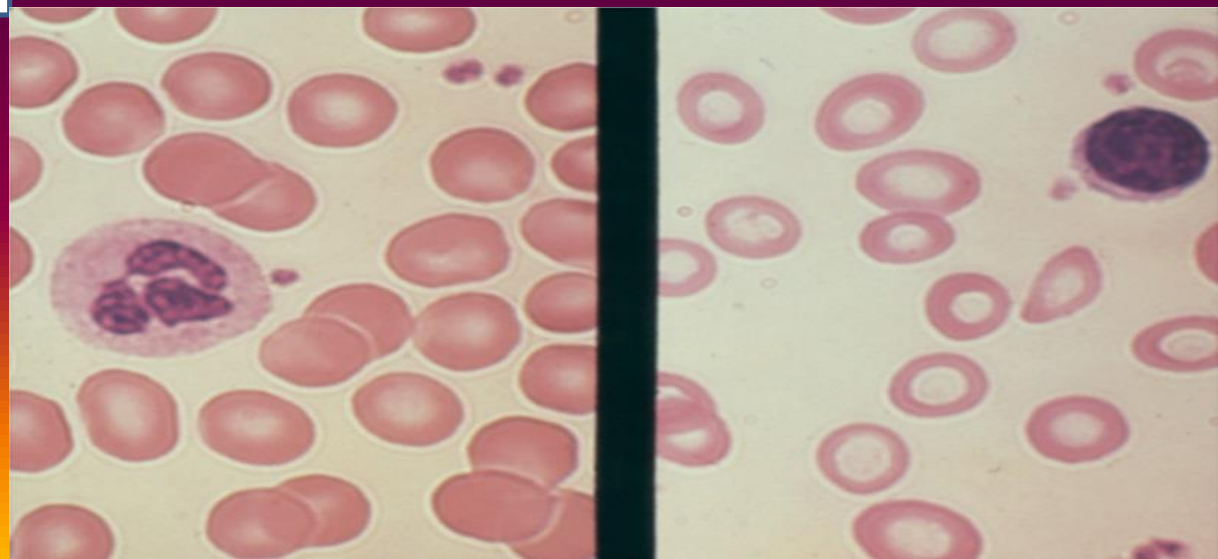


Folic acid

Origin	Animal and plant sources (meat, liver, fruits, vegetables). Easily destroyed by cooking.
Storage	In the liver in very small amounts.
Causes of Deficiency	1 – dietary deficiency (Important cause). 2 – Defective absorption. 2 – Defective storage (liver diseases).
Absorption	Mainly in the jejunum.

Iron

Origin	Animal and plan sources (meat, liver, fruits, vegetables).
Storage	In the liver in the form of ferritin.
Causes of Deficiency	1 – Blood loss (the most important cause). 2 – Dietary deficiency. 3 – Defective absorption. 4 – Defective storage (liver diseases).
Absorption	Mainly in the duoedunum.
Blood film	Microcytic anemia.

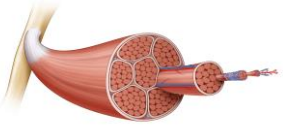


Mechanism of iron absorption

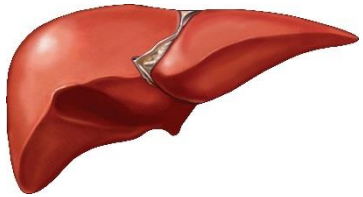
Forms of iron

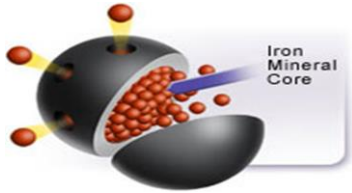
Hemoglobin: 65%

Myoglobin: 4%



Ferritin (The storage form): 30%





Intracellular oxidative enzymes: 1%

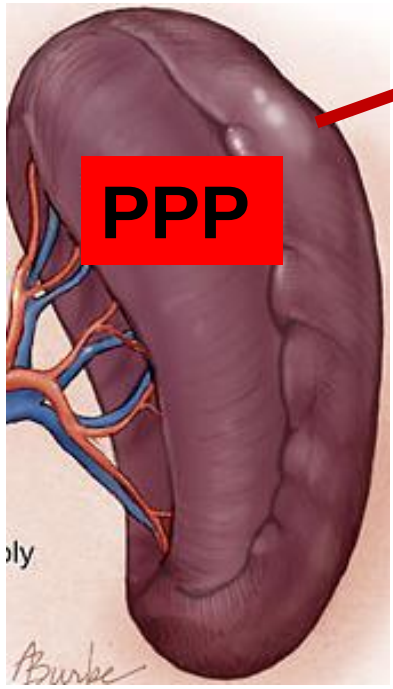
Steps of iron absorption

Iron must be absorbed in the ferrous (reduced of Fe^{++}) state.
Conversion from the ferric (oxidized state or Fe^{+++}) is helped by the presence of gastric HCL & Ascorbic acid (vitamin C) in the diet.
Rate of absorption is determined by the rate of iron loss from the body.
And is regulated by the hepatic protein (Hepcidin).
Then Iron is transported in the bloodstream carried on the carrier protein: Transferrin.
To be transferred to the functions or storage sites.

RBC Life Cycle & fate

- RBCs live only 120 days (cells need to be continually replaced)
- Cells rupture during passage into tight capillaries due to loss of membrane flexibility.
- Repair is not possible due to lack of organelles
- damaged cells are removed by macrophages in the spleen and liver
- Breakdown products (Iron & vitamins) are recycled
- Hemoglobin is released then converted into biliverdin.
- Biliverdin is then converted to bilirubin.
- Bilirubin is secreted by liver into bile.

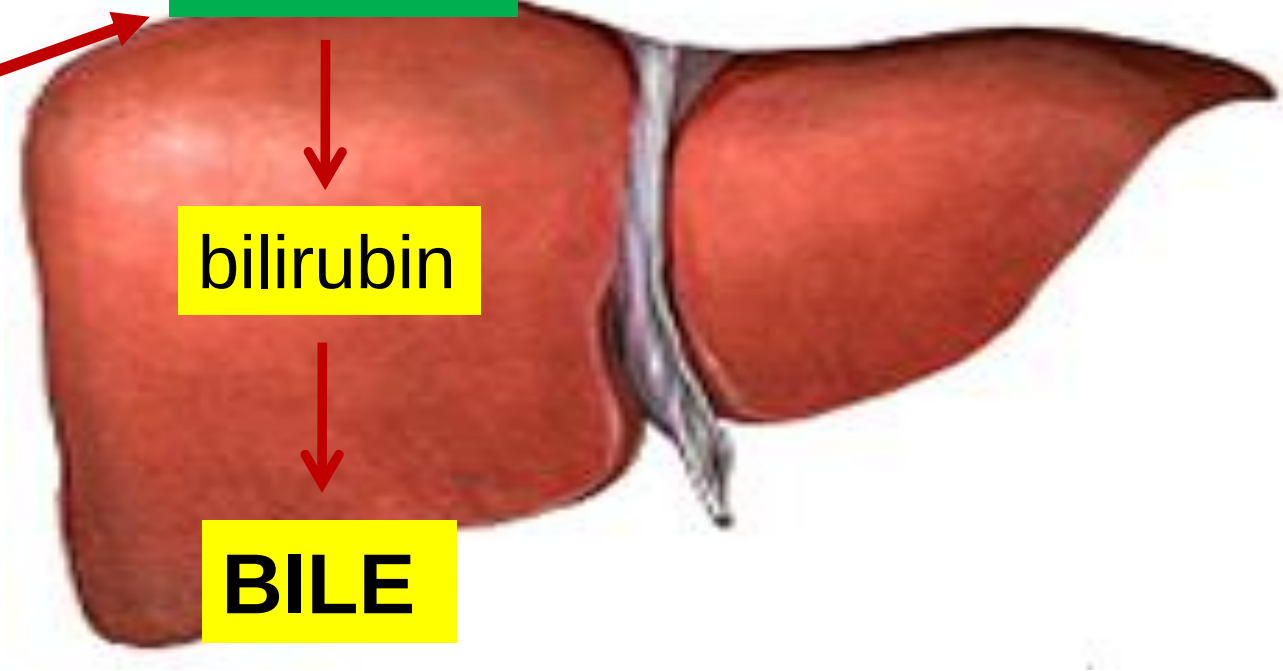
RBCs Fate



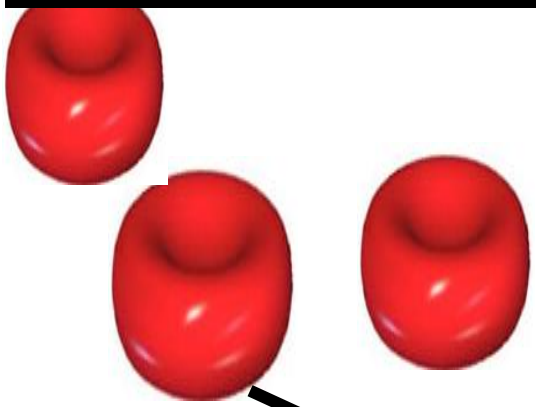
biliverdin

bilirubin

BILE



Excessive destruction → Hemolytic Jaundice



Thank You