
بسم الله الرحمن الرحيم

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

صدق الله العظيم

3 - Erythropoiesis

Objectives;

Intended learning outcomes (ILOs)

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

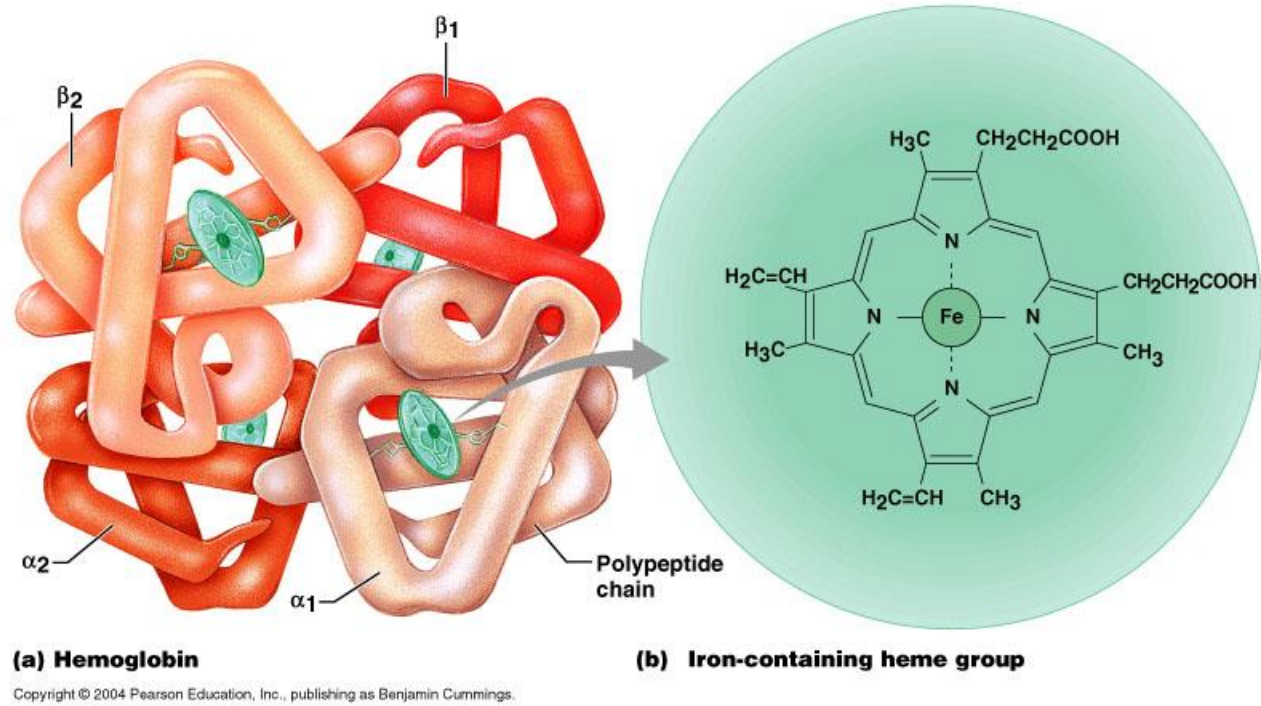
- Describe the normal structure of Hemoglobin.
- Recognize the abnormal types of Hemoglobin.
- Know the definition, sites and stages of erythropoiesis.
- Enumerate the factors affecting erythropoiesis.
- Summarize the role of hypoxia & erythropoietin hormone in the process of erythropoiesis.
- Discuss the importance of vitamin B12 & folic acid as maturation factors for the RBCs.
- Discuss the mechanism of Vitamin B12 & folic acid absorption.

- Globular protein
- Heme + Globin

Hemoglobin (Hb)

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

N.B: Concentration of plasma proteins = 7 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.

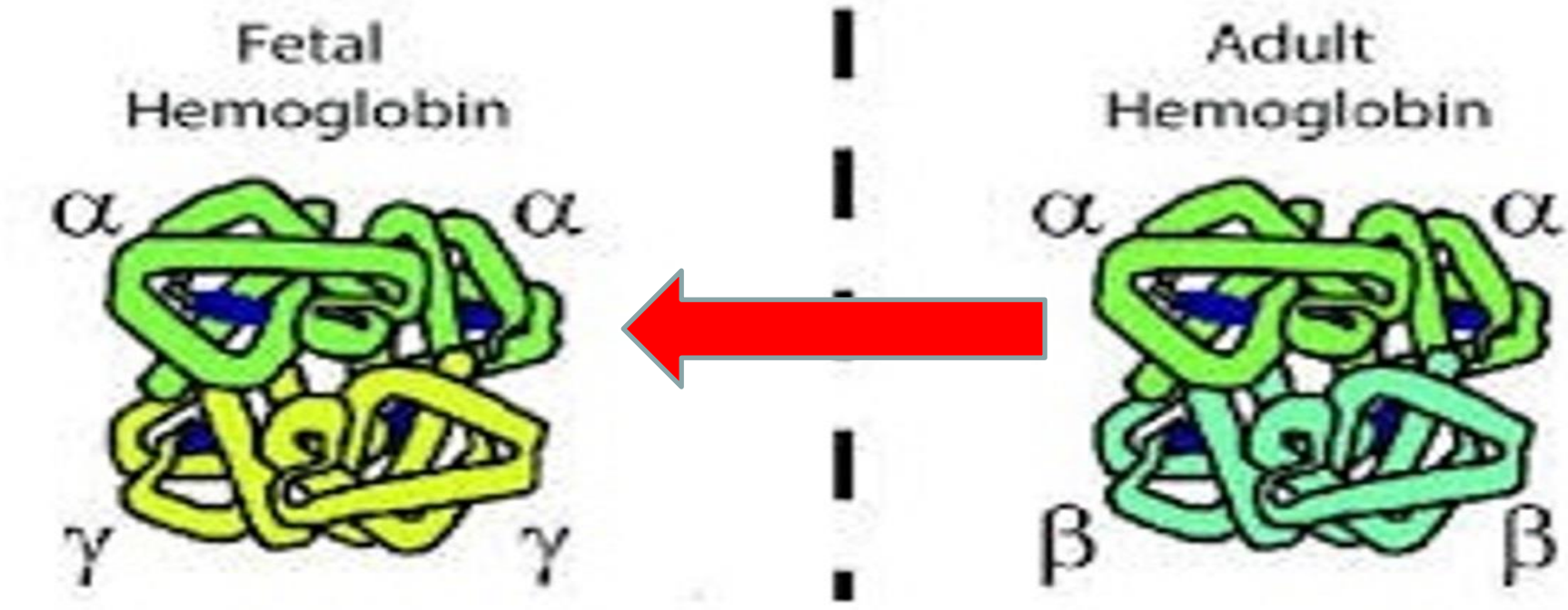
Hb – F = Fetal hemoglobin (Hemoglobin of intrauterine life)

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

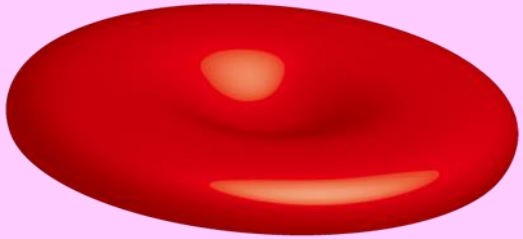
Abnormal types of Hemoglobin

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.

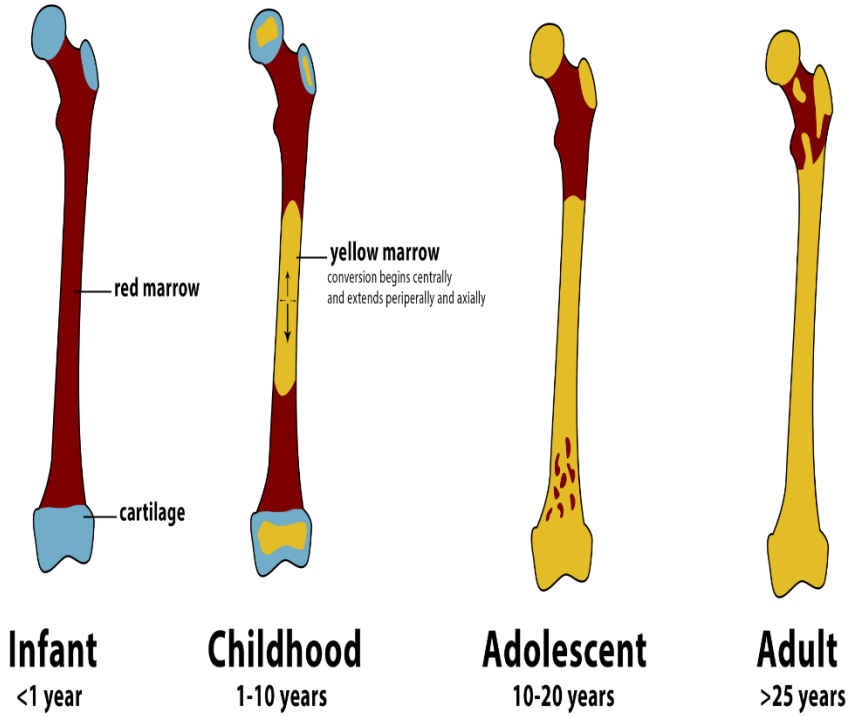
During intrauterine life: Liver – Spleen – Lymph nodes.

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

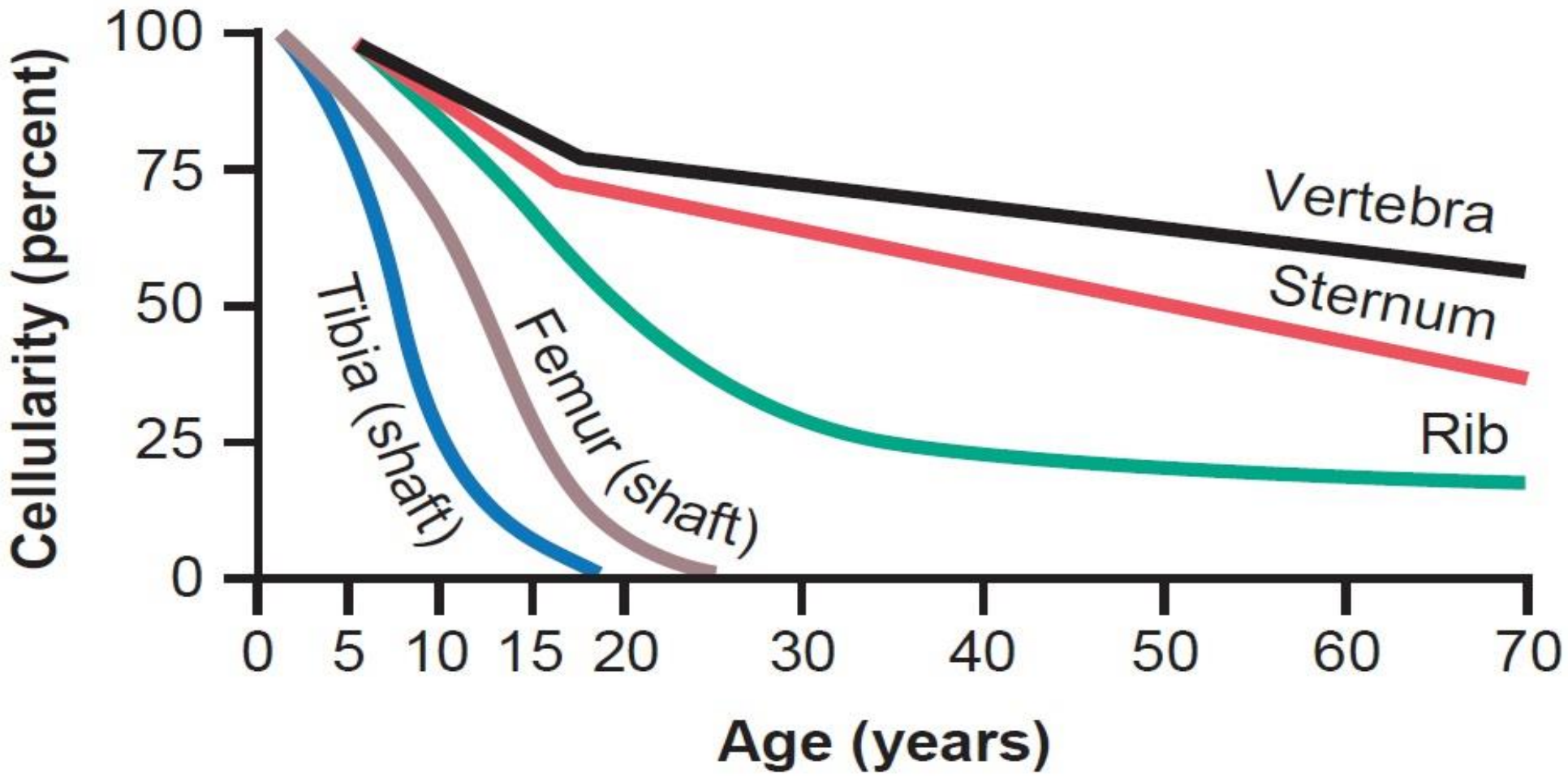
After the age of 20 years: Bone marrow of membranous bones only.

RBCs Erythropoiesis Sites

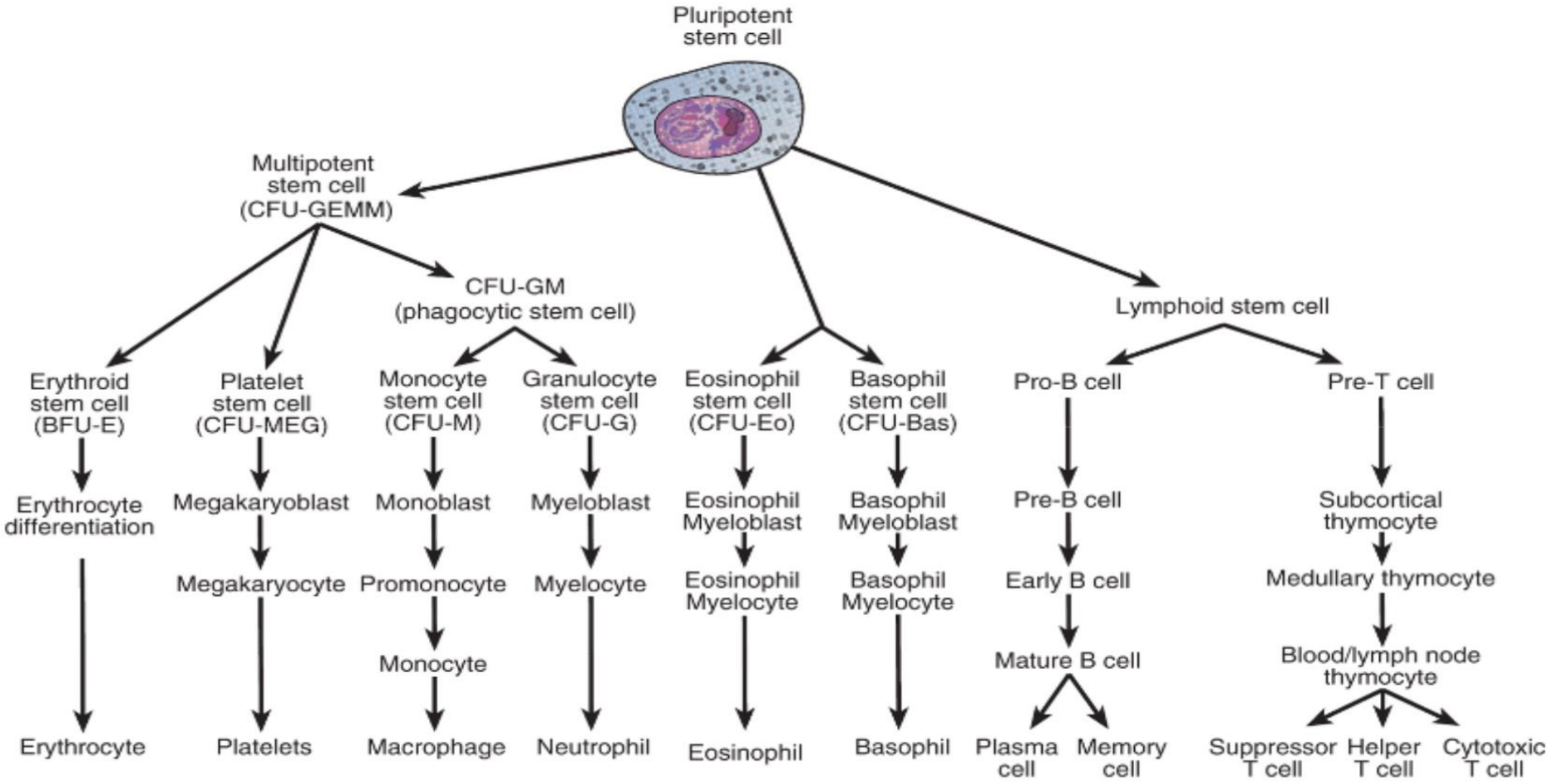
Normal bone marrow conversion



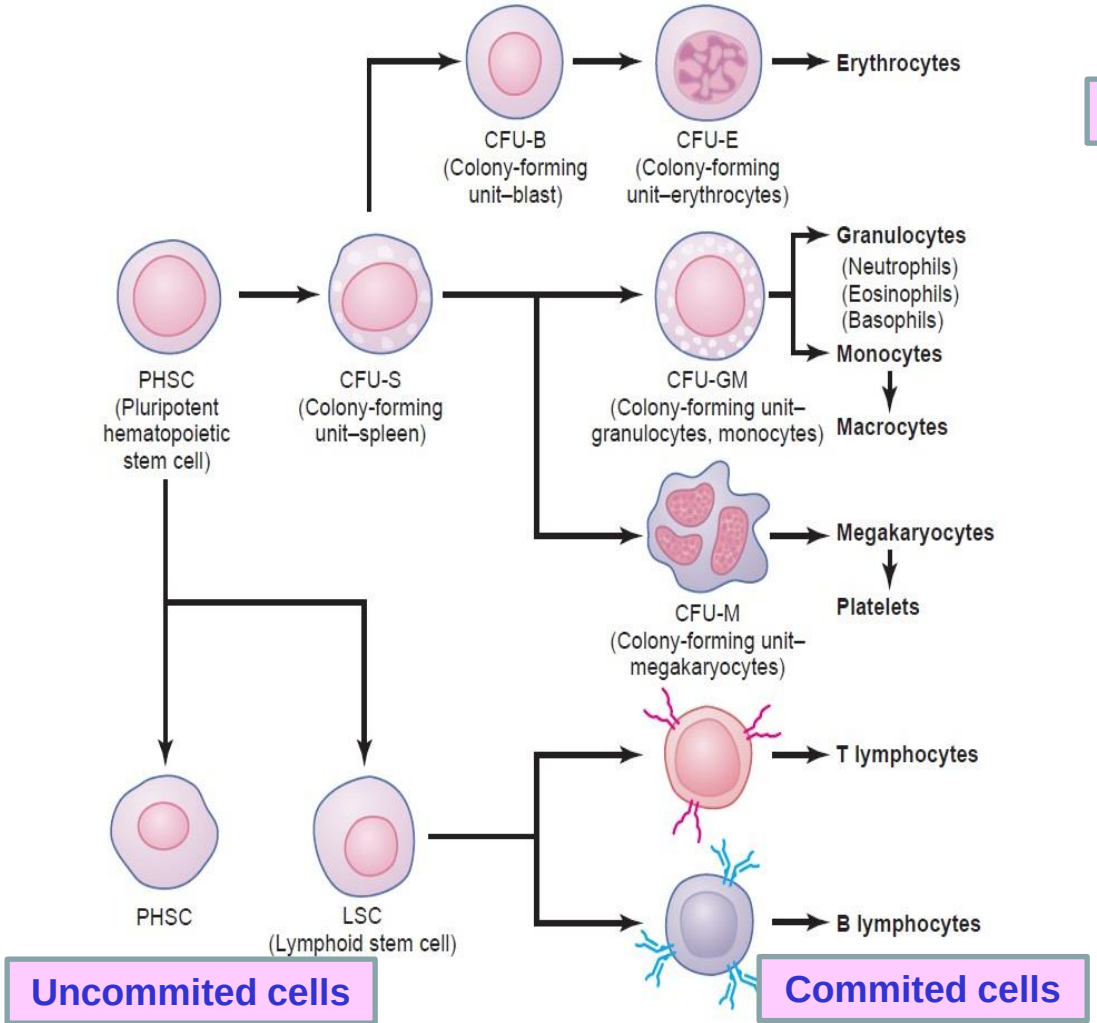
RBCs
Erythropoiesis
Sites

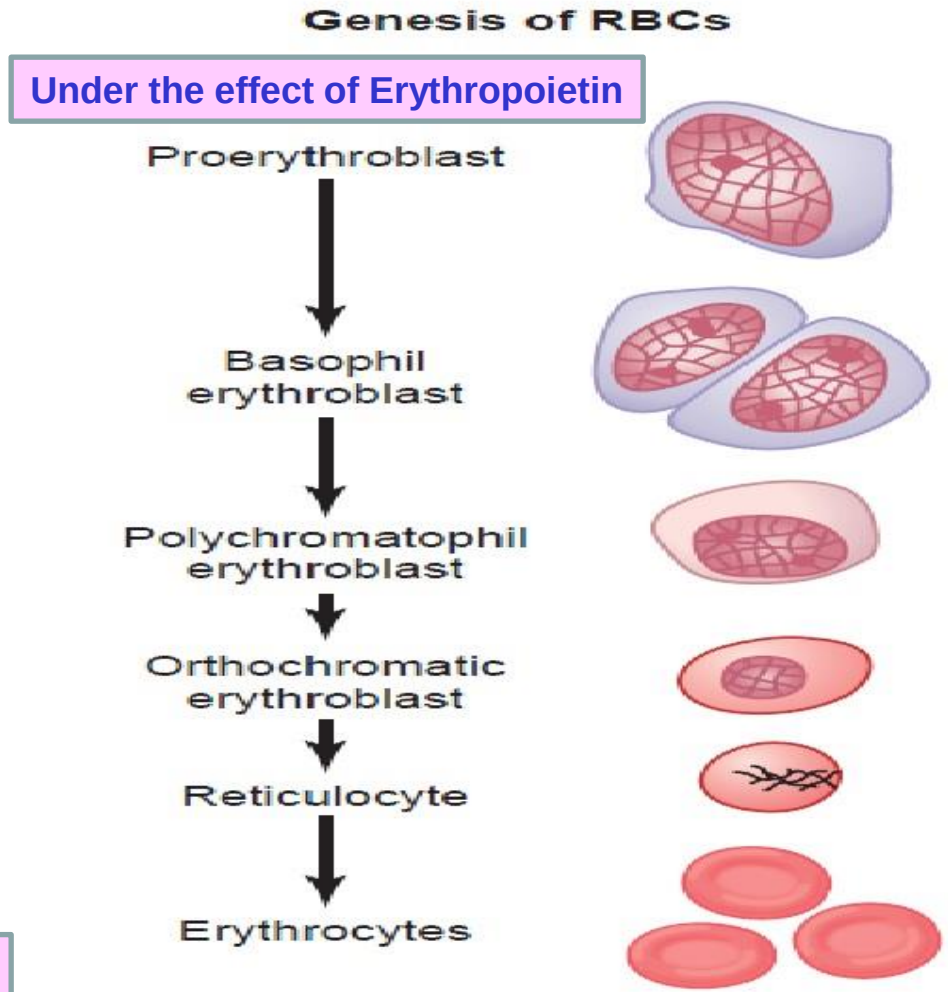


RBCs
Erythropoiesis
Stages



RBCs
Erythropoiesis
Stages





RBCs
Erythropoiesis
Factors

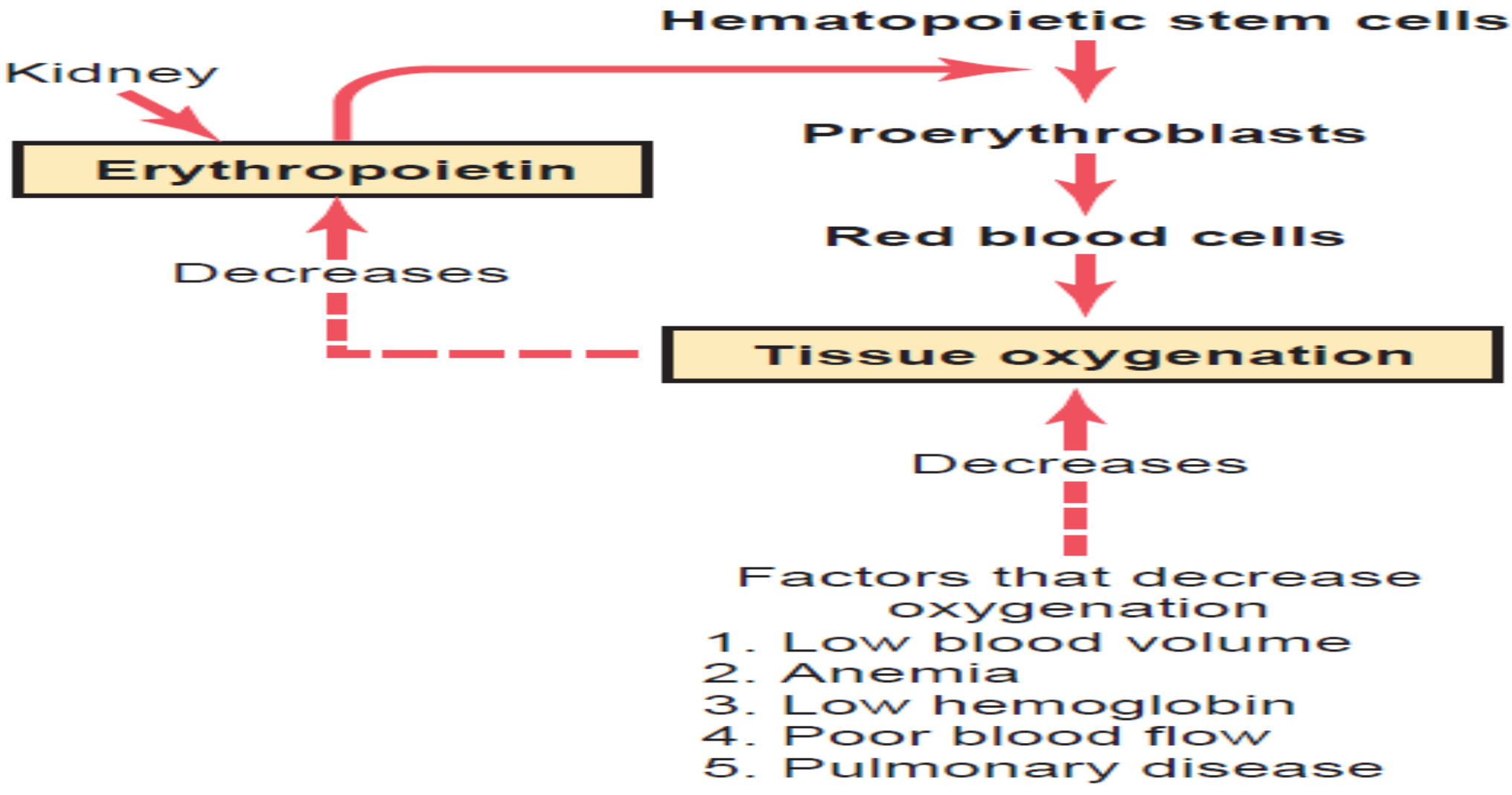
Oxygen supply to the tissues (Hypoxia).

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)



Causes of decreased Oxygen supply to the tissues (Hypoxia)

- High Altitudes.
- Cardiac or respiratory diseases.
- Hematological disorders.
- Relative deficiency (increased demands as in athletes).
- Stagnation of blood flow (Thrombosis or Embolism).
- Defective tissue utilization (e.g. Druga & Toxins).

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

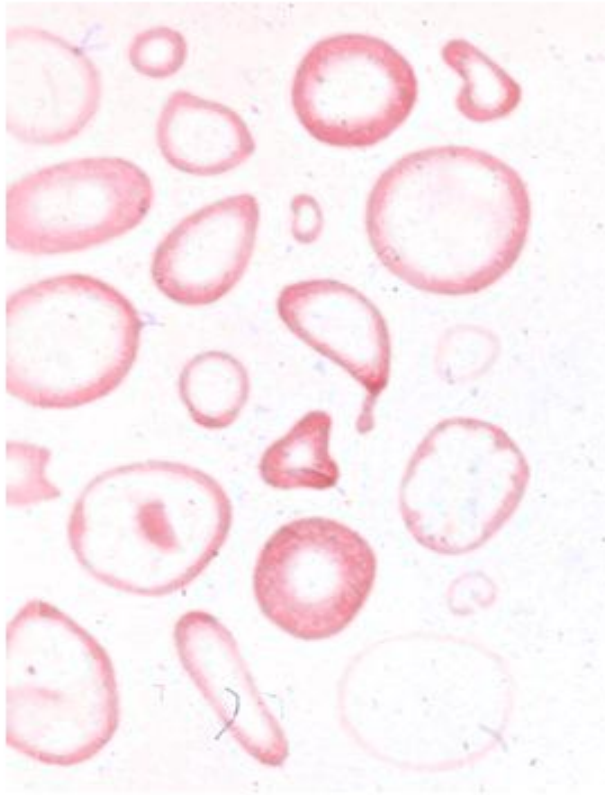
Clinical correlation

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.

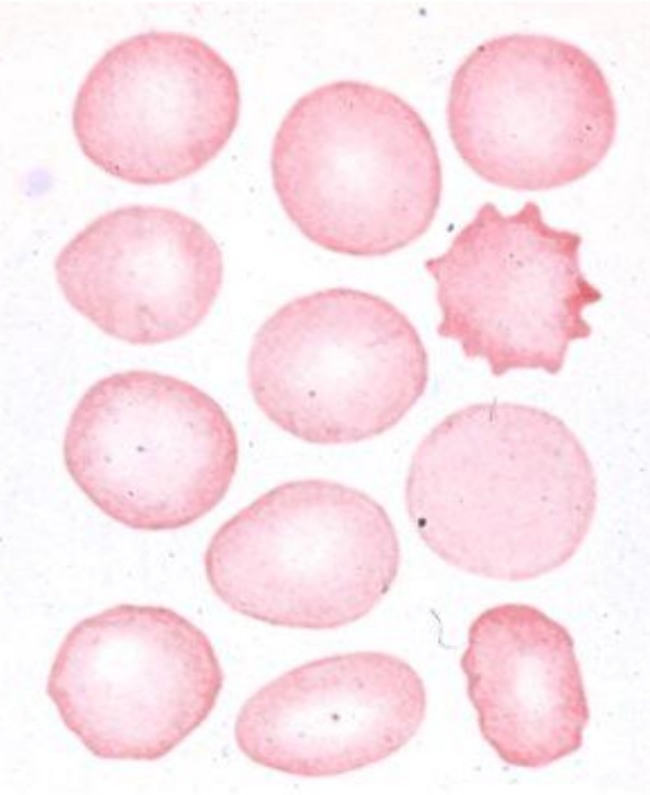
Anemia of renal disease is treated with erythropoietin

Normocytic normochromic	Microcytic hypochromic	Macrocytic hyperchromic
		
Other causes Aplastic Hemolytic Acute hge	Iron deficiency anemia	Folate or vitamin B_{12} deficiency
– MCV – MCH	↓ MCV ↓ MCH	↑ MCV ↑ MCHC

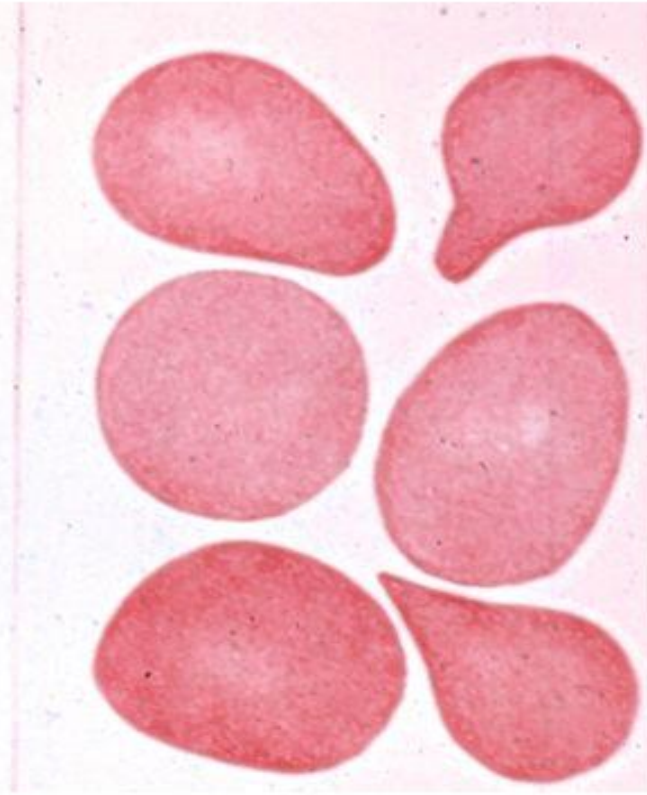
Hypochromic/Microcytic



Normochromic/Normocytic



Macrocytic(/Normochromic)



Vitamin B12 and folic acid (Maturation factors)

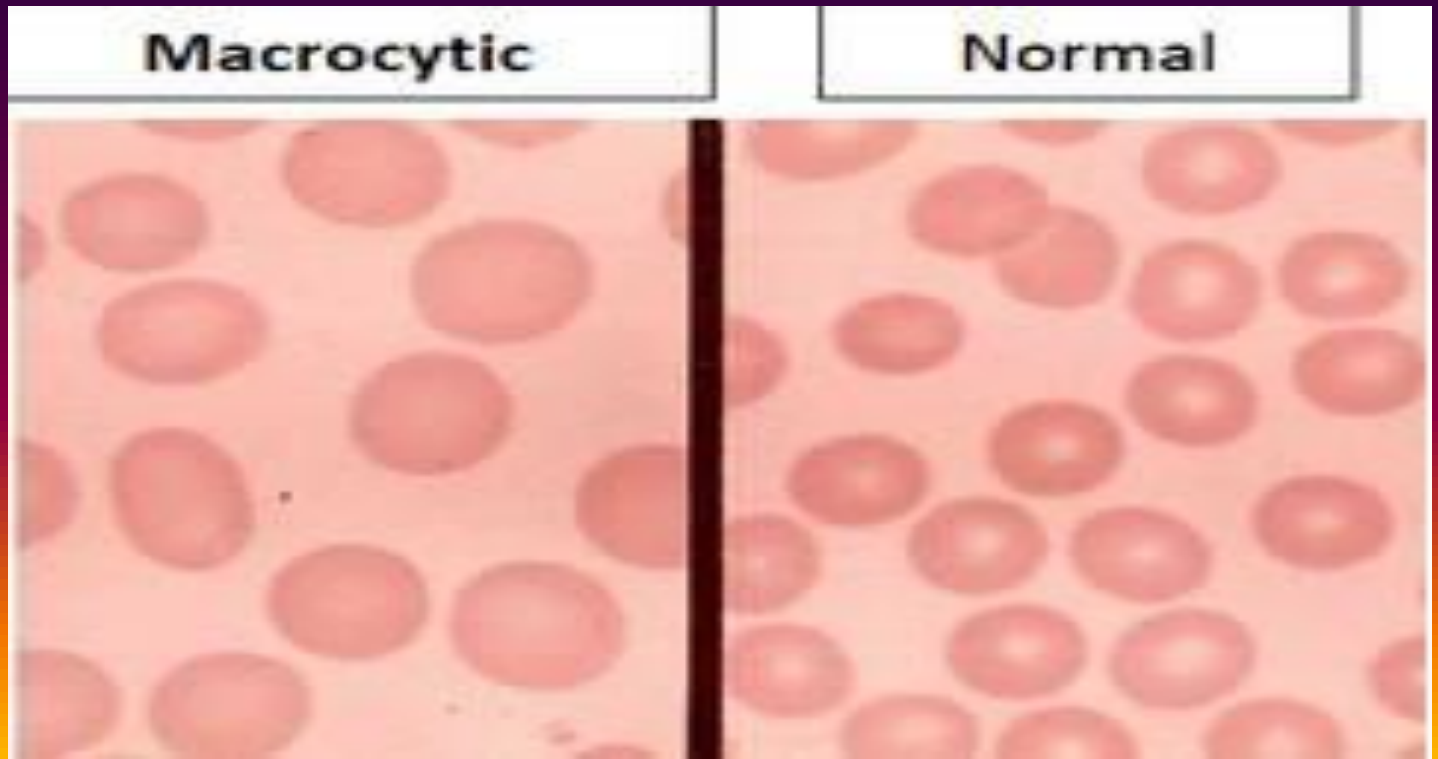
importance

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

Manifestations of Deficiency

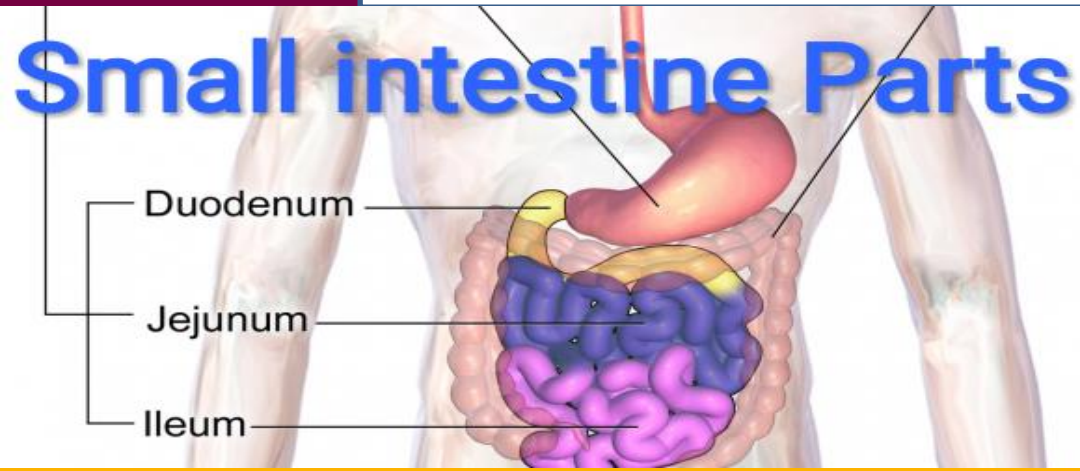
Macrocytic (megaloblastic anemia).
Abnormal large & fragile cells.

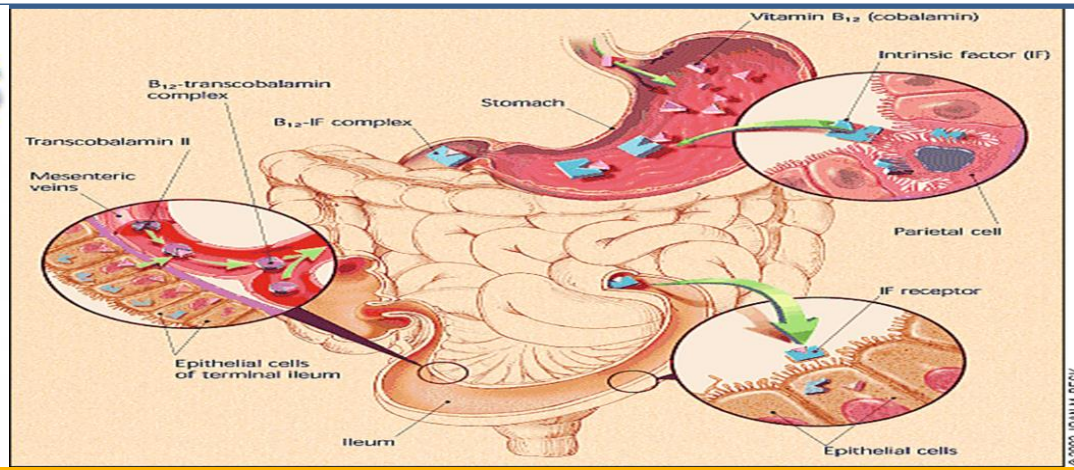
Blood film



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 – Autoimmune deficiency of intrinsic factor (Pernicious anemia)





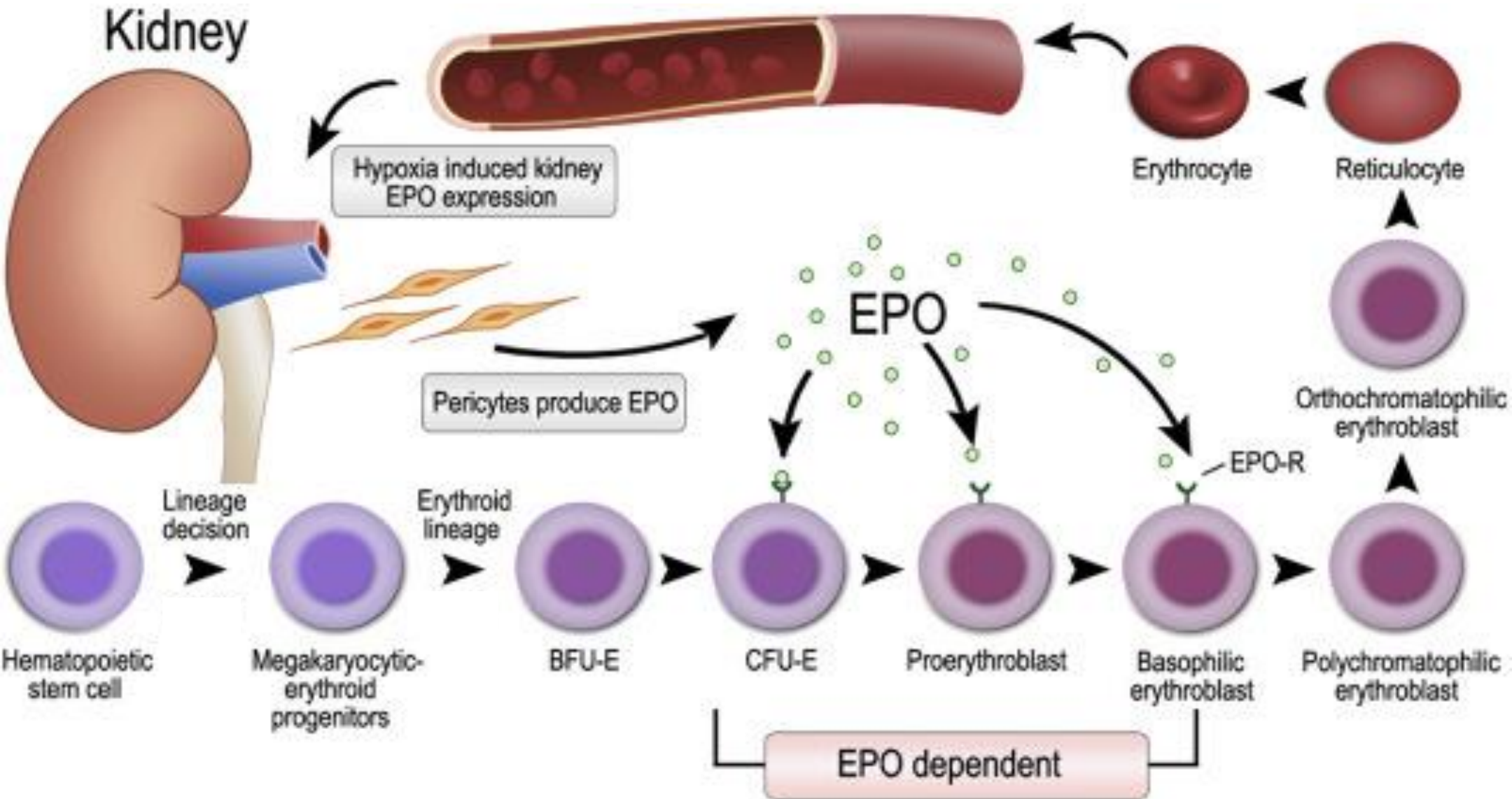
Folic acid

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.

Role of different organs in Erythropoiesis

- Role of Kidney
- Role of bone marrow
- Role of liver

Role of different organs in Erythropoiesis
Role of Kidney (Release of erythropoietin)

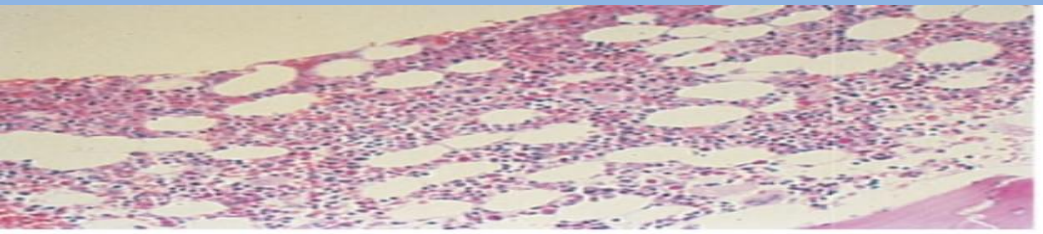
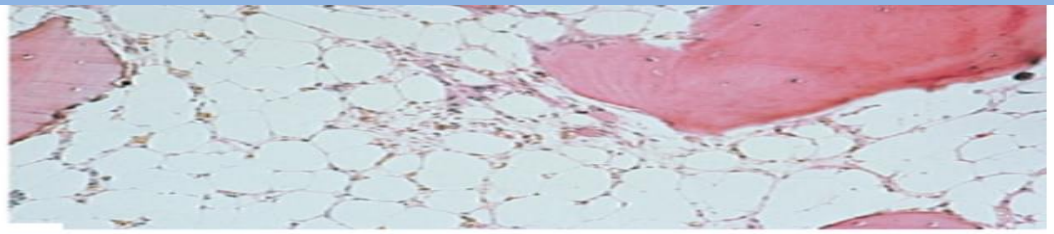
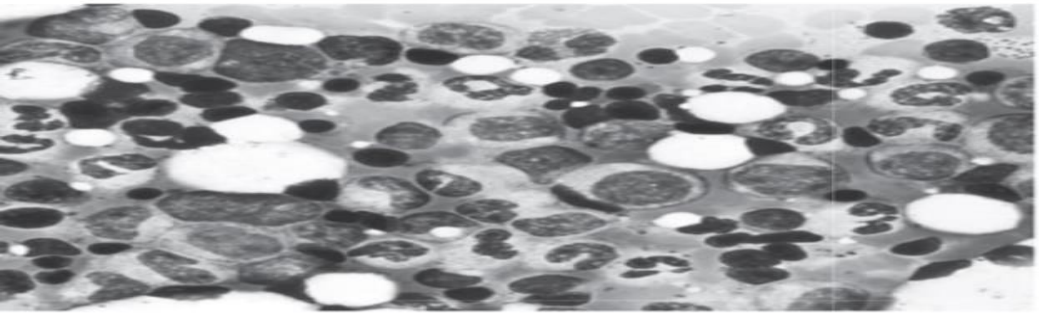
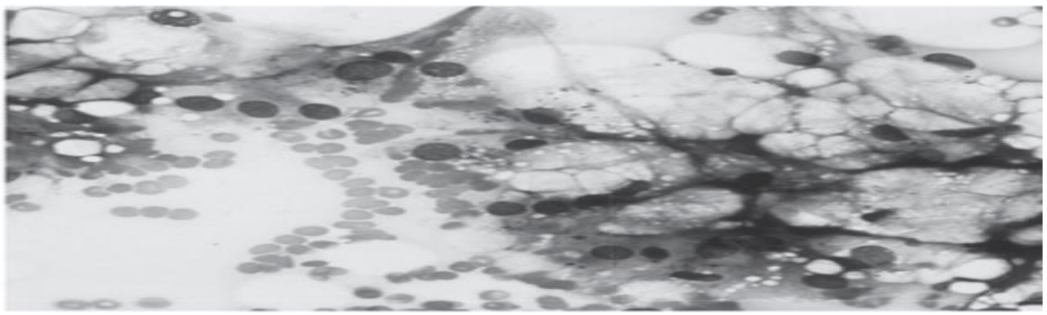


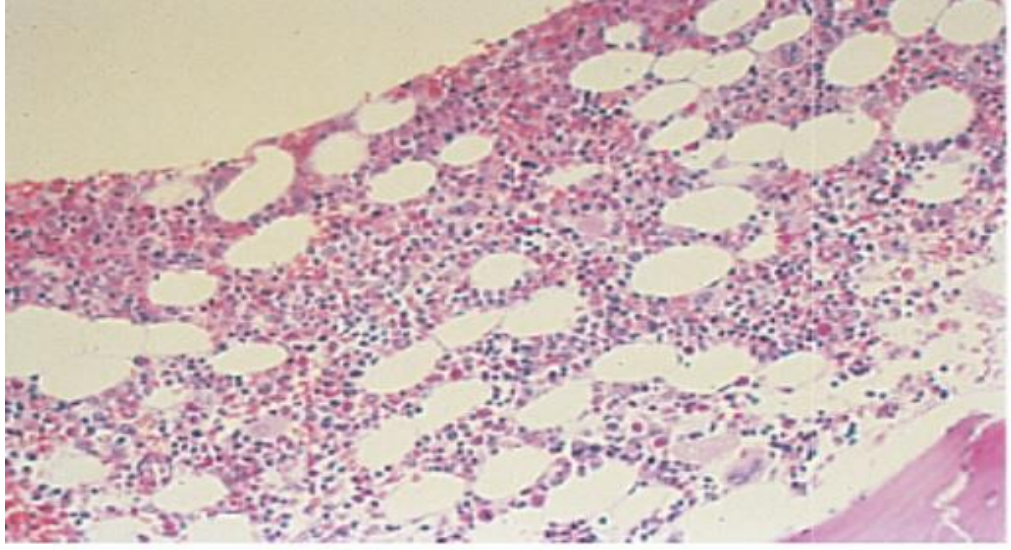
Role of different organs in Erythropoiesis
Role of Bone marrow (Site of formation)

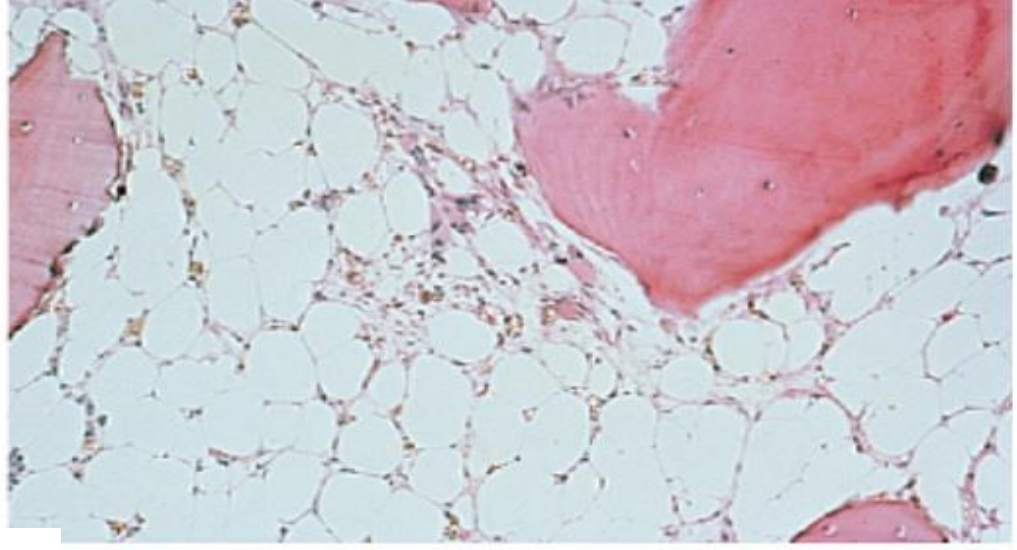
Failure of the bone marrow to produce RBCs is known as Aplastic anemia.

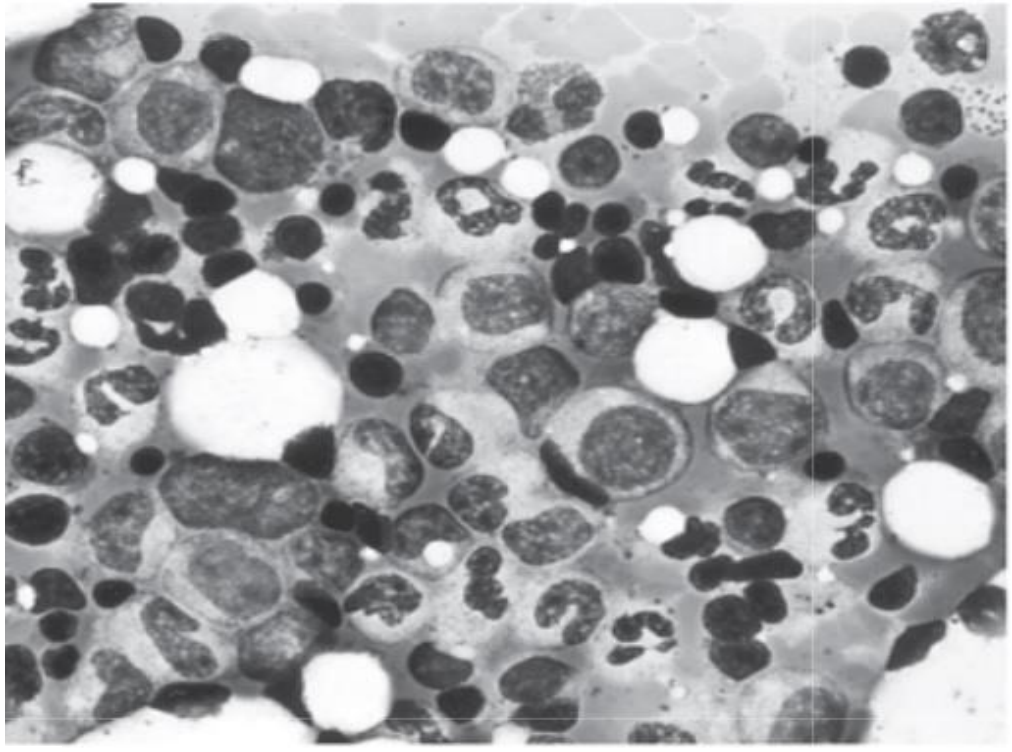
Commonly associated with pancytopenia (decreased production of all types of blood cells.

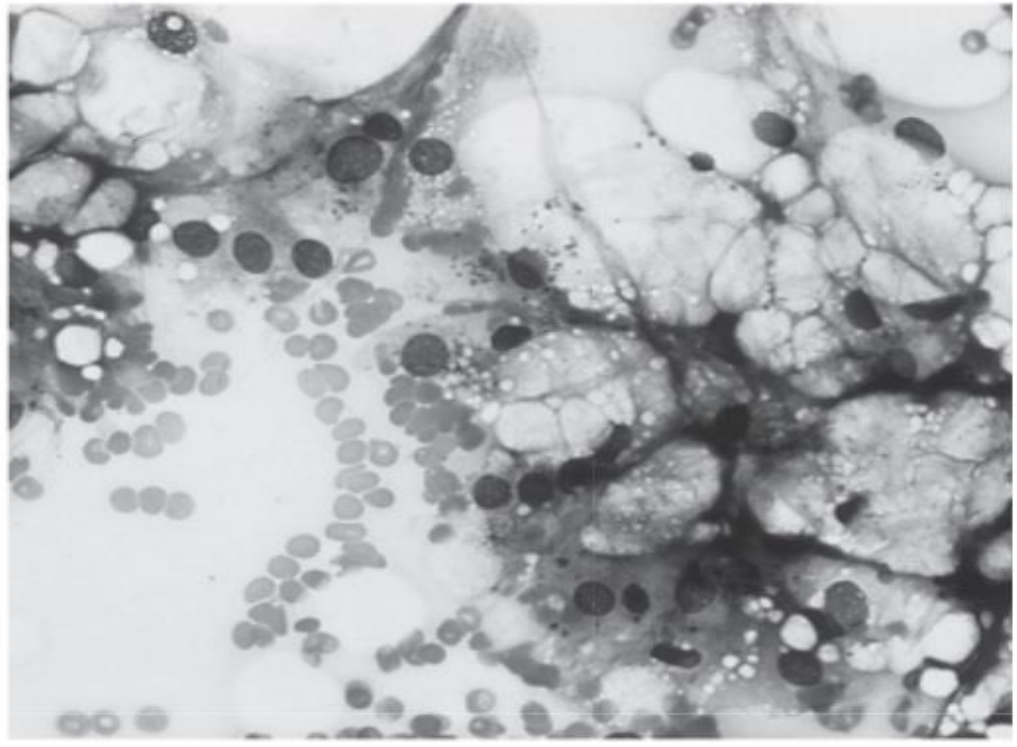
Treatment depends on the cause.









Role of different organs in Erythropoiesis
Role of liver (Site of storage or synthesis of different substances)

Storage of	Synthesis of
Vitamin B12	Globin (protein part of the hemoglobin)
Ferritin (Storage form of Iron)	15% of Erythropoietin

Thank You