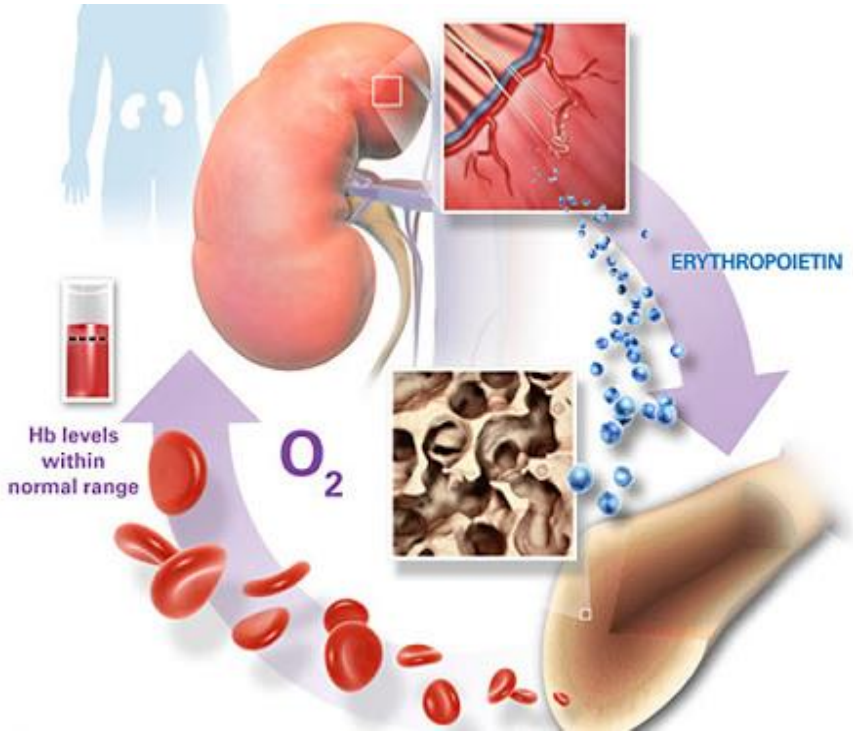
Control of erythropoiesis, iron metabolism, and hemoglobin

TEXTBOOK OF MEDICAL PHYSIOLOGY

GUYTON & HALL 11TH EDITION

UNIT VI CHAPTERS 32



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Objectives of the today's lecture

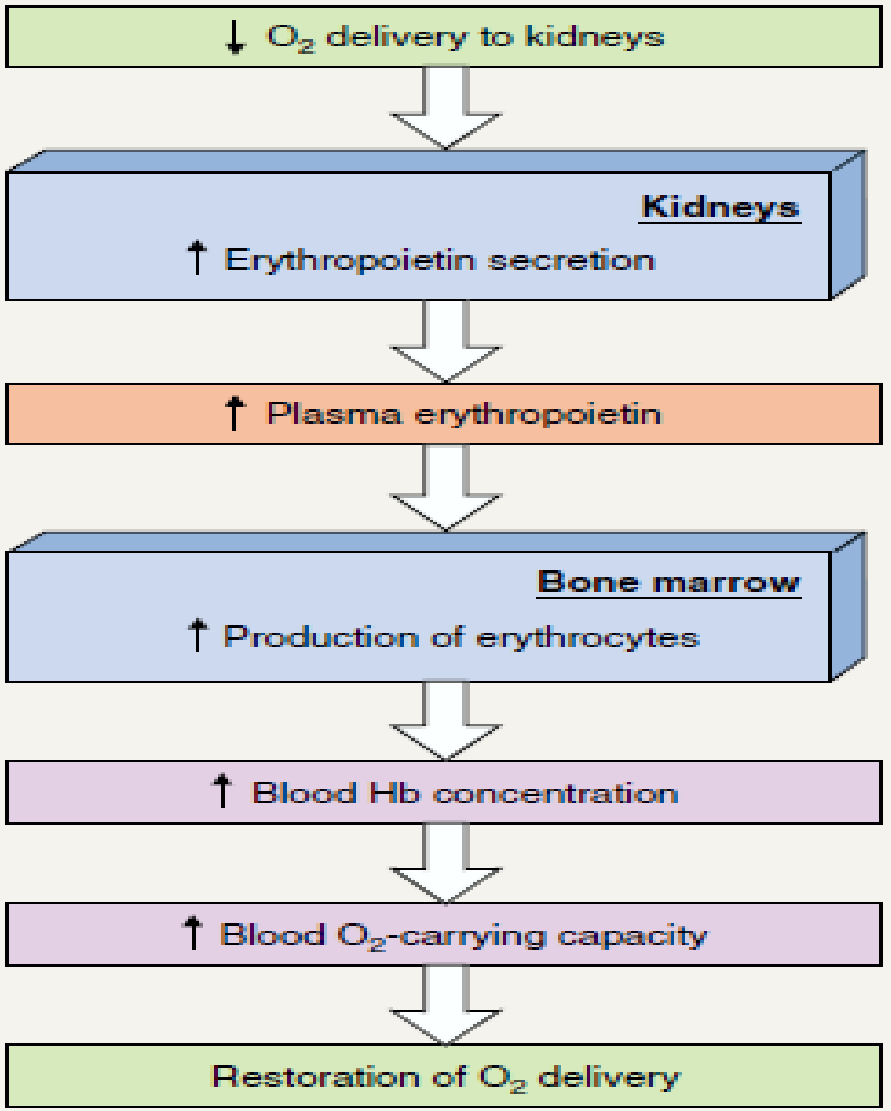
At the end of this lecture student should be able to:

1. Describe **essential elements** needed for RBC formation.
2. Describe the process of **Vit B12** absorption and its malabsorption.
3. Recognize the structure and the function of **hemoglobin.**
4. Understand the metabolism of **iron** (absorption, storage and transport).
5. Recognize the causes of anemia and polycythemia.

Regulation of Erythropoiesis

- **Importance**
- **Factors affecting Erythropoiesis**
  - **Tissue Oxygenation**
    - Anemia, High Altitudes, heart and lung problems.
    - **ERYTHROPOITEN (EPO)**

The regulation of RBC production and erythropoietin hormone secretion in response to hypoxia



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- **Factors affecting Erythropoiesis**
  - **Tissue Oxygenation**
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    - **ERYTHROPOITEN**
  - **Vitamins**
  - **Metals**
  - **Proteins**
  - **Hormones**
  - **Other factors/Conditions**

Vitamins

- **Vit B_{12} & Folic acid**
- Essential for formation of **thymidine triphosphate**
- Essential **building block of DNA**
- **Diminished DNA**
  - **Failure of nuclear maturation**
  - **Inadequate Erythropoiesis**
- **Other vitamins : Vit B6, Riboflavin, nicotinic acid, biotin, Vit C, Vit E**

Minerals

- **Iron**
  - Formation of hemoglobin
  - Deficiency can lead to anaemia

- **Copper**
  - Necessary for Iron metabolism
- **Cobalt**
  - Forms a part of Vitamin $\mathbf{B_{12}}$
- **Zinc and Manganese**

Amino acids and hormones

- **Proteins & Amino acids:** formation of globin in hemoglobin

–sever protein deficiency results in anaemia

- **Hormones:**

- Testosterone
- Growth hormone
- Thyroid hormone
- Cortisol
- Adrenocorticotrophic hormone (ACTH)

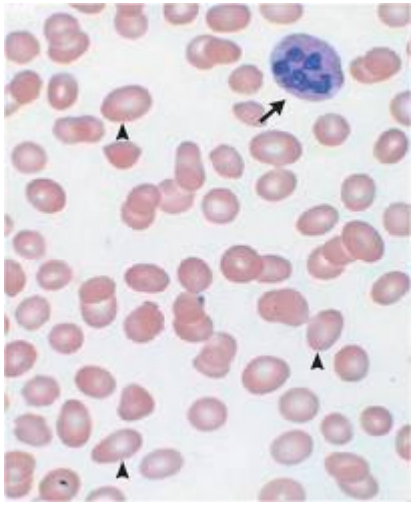
Vitamin B12 & Folic acid

Important for DNA synthesis and final maturation of RBC.

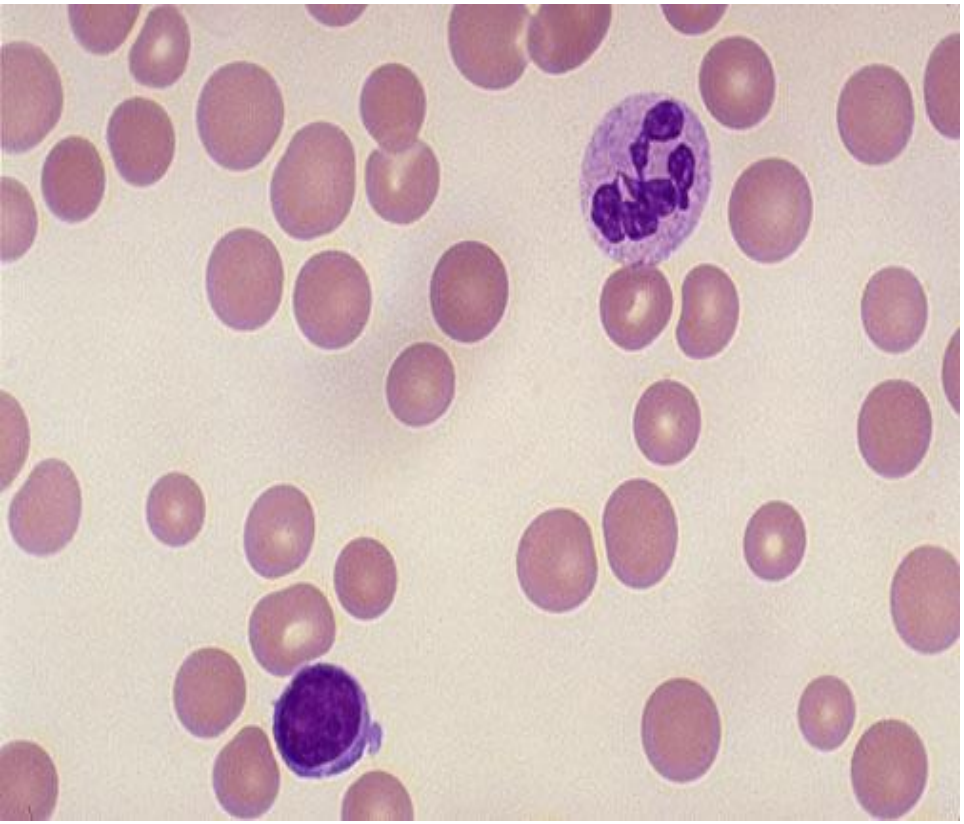
Dietary source: meat, milk, liver, green vegetables.

Deficiency leads to:

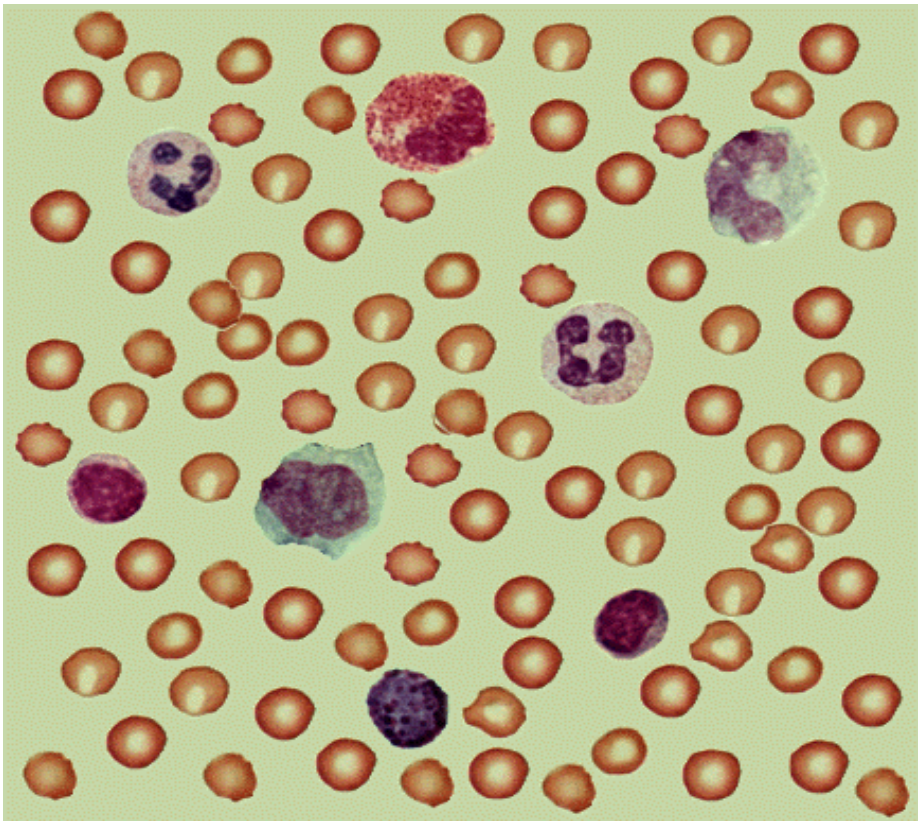
- **Failure of nuclear maturation & division**
- **Abnormally large & oval shape RBC**
- **Short life span**
- **Reduced RBC count & Hb**
- **Macrocytic (megaloblastic) anemia**



Macrocytic anemia



Normal blood film



Note the hypersegmented neurotrophil and also that the RBC are almost as large as the lymphocyte. Finally, note that there are fewer RBCs.

Malabsorption of Vit. B12

- Pernicious Anemia

- VB12 absorption needs intrinsic factor secreted by parietal cells of stomach.

- VB12 + intrinsic factor are absorbed in the terminal Ileum.

- Causes of deficiencies:
- Inadequate intake
- Poor absorption due to Intestinal disease

Iron metabolism (Fe)

✓ Iron is needed for the synthesis of haemoglobin, myoglobin, cytochrome oxidase, peroxidase & catalase

✓ Total Iron in the body = 4-5g

- 65% ….. Hemoglobin
- 4% …….. In the form of myoglobin
- 1% ……. other heme-containg proteins
- 0.1% …….. Is combined with transferrin in the bood plasma
- 15-30% …… stored iron in the form of ferritin in the liver, spleen and bone marrow.

Iron absorption

✓ Iron in food mostly in oxidized form (Ferric, F^{3+})

✓ Better absorbed in reduced form (Ferrous, F^{2+})

✓ Iron in stomach is reduced by gastric acid, Vitamin C.

✓ Rate of iron absorption depend on the amount of iron stored

Transport and storage of iron

❖ Iron is transported in the plasma in the form of Transferrin (apotransferrin + iron).

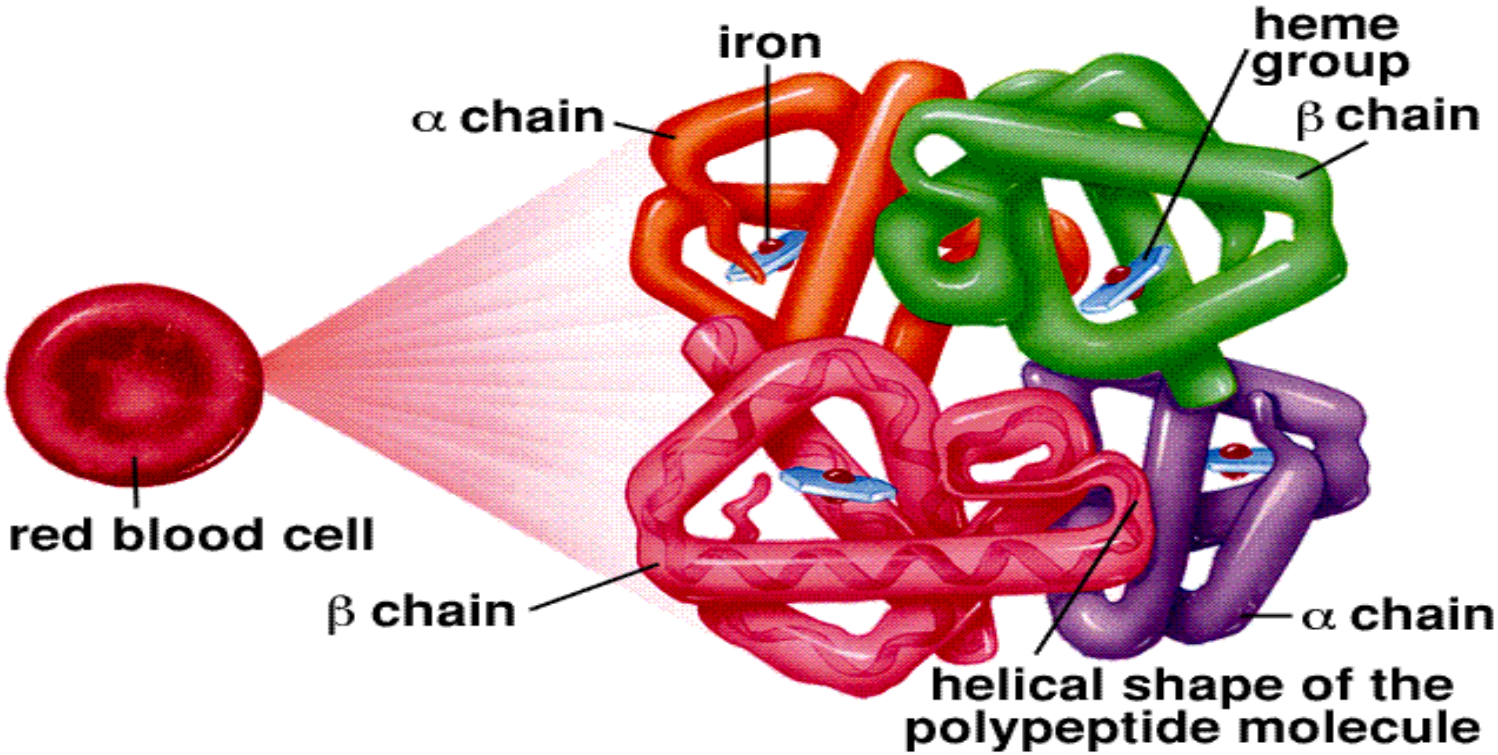
❖ Iron is stored in two forms:

- ✓ Ferritin (apoferritin + iron)
- ✓Hemosiderin (insoluble complex molecule, in liver, spleen, bone marrow)

❖ Daily loss of iron is 0.6 mg in male & 1.3mg/ day in females.

HEMOGLOBIN (Hb)

- Each RBC contains 280 million Hb molecules.
- Hb molecules consist 4 chains each formed of heme & polypeptide chain (globin).
- Heme consist of porphyrin ring + iron (F^{2+}).



Types of normal Hb:

-Hb A (2 alpha and 2 beta chains) (adult Hb) (98%).
- Hb A2 (2 alpha and 2 delta chains) (2%)
-Hb F (2 alpha and 2 gamma chains) (Hb of intrauterine life).

-**Abnormality in the polypeptide chain - abnormal Hb (hemoglobinopathies) e.g thalassemias, sickle cell (HbS).**

Functions of Hemoglobin

- **Carriage of O2**
  - Hb reversibly binds O2 to form Oxyhemoglobin, affect by pH, temperatre, H+

- **Carriage of CO2**
  - Hb binds CO2 = Carboxyhemaglobin

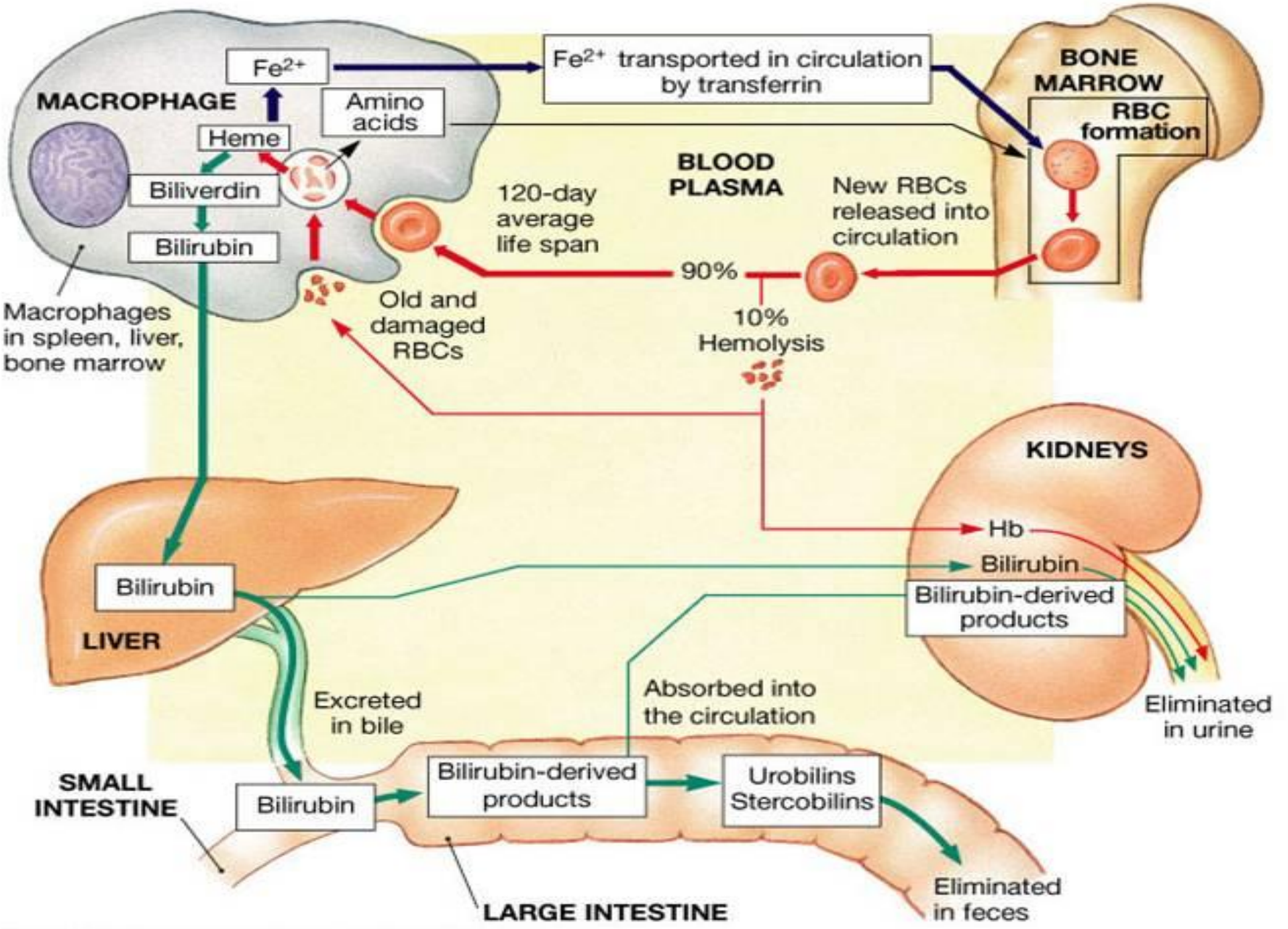
- **Buffer**

Destruction of RBC

- RBC life span in circulation = 120 days.
- Metabolic active cells.
- Old cell has a fragile cell membrane, cell will rupture as it passes in narrow capillaries (and spleen).
- Released Hb is taken up by macrophages in liver, spleen & bone marrow:

- Hb is broken into its component:

  - Polypeptide—amino acids (protein pool = storage)
  - Iron ---- stored in liver and bone marrow as ferrtin
  - Heme (Porphyrin)>>—bilirubin>>—secreted by the liver into bile. [excess destruction of RBC ---Jaundice]


MACROPHAGE
Fe2+
Amino acids
Heme
Biliverdin
Bilirubin
Macrophages in spleen, liver, bone marrow
Fe2+ transported in circulation by transferrin
BONE MARROW
RBC formation
BLOOD PLASMA
120-day average life span
New RBCs released into circulation
90%
10% Hemolysis
Old and damaged RBCs
KIDNEYS
Hb
Bilirubin
Bilirubin-derived products
Eliminated in urine
Bilirubin
LIVER
Excreted in bile
Absorbed into the circulation
SMALL INTESTINE
Bilirubin
Bilirubin-derived products
Urobilins Stercobilins
Eliminated in feces
LARGE INTESTINE

ANAEMIAS

- **Definition:**
  - Decrease number of RBC
  - Decrease Hb

- **Symptoms:** Tired, Fatigue, short of breath, heart failure.

Physiological Causes of anaemia

1.Blood Loss

-Rapid hemorrhage caused by accident (RBC return to normal 3-6w)

-Chronic blood loss caused by microcytic hypochromic anaemia (iron)

2.Decrease RBC production

✓ Nutritional causes:

- Iron deficiency results in microcytic hypochromic anaemia.
- Vit B12 & Folic acid deficiencies result in megaloblastic anaemia.

✓ Bone marrow failure: destruction by cancer, radiation, and drugs result in Aplastic anaemia.

3.Haemolytic leading to excessive destruction of RBCs

❖ Abnormal cells or Hb

- Hereditary Spherocytosis anemia
- sickle cells anemia

❖Erythroblastosis fetalis.

Polycythemia

(Increased number of RBC)

Types:

1.Primary polycythemia (Polycythemia Vera - (Erythremia):

- Uncontrolled RBC production (genetic).
- The RBC count can reach 7-8 millions/ mm^3 and the hematocrit may be 60 to 70%

2.Secondary polycythemia: secondary to hypoxia caused by high altitude (physiological), chronic respiratory or cardiac disease