BLOOD PHYSIOLOGY

Lecture 2

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Objectives

At the end of this lecture you 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 haemaglobin structure and its functions.**
4. **Discuss iron metabolism (absorption, storage and transport)**

Objectives – cont.

5. Describe the fate of old RBC.
6. Describe anemia and its causes.
7. Recognize causes of polycythemia.

Topics:

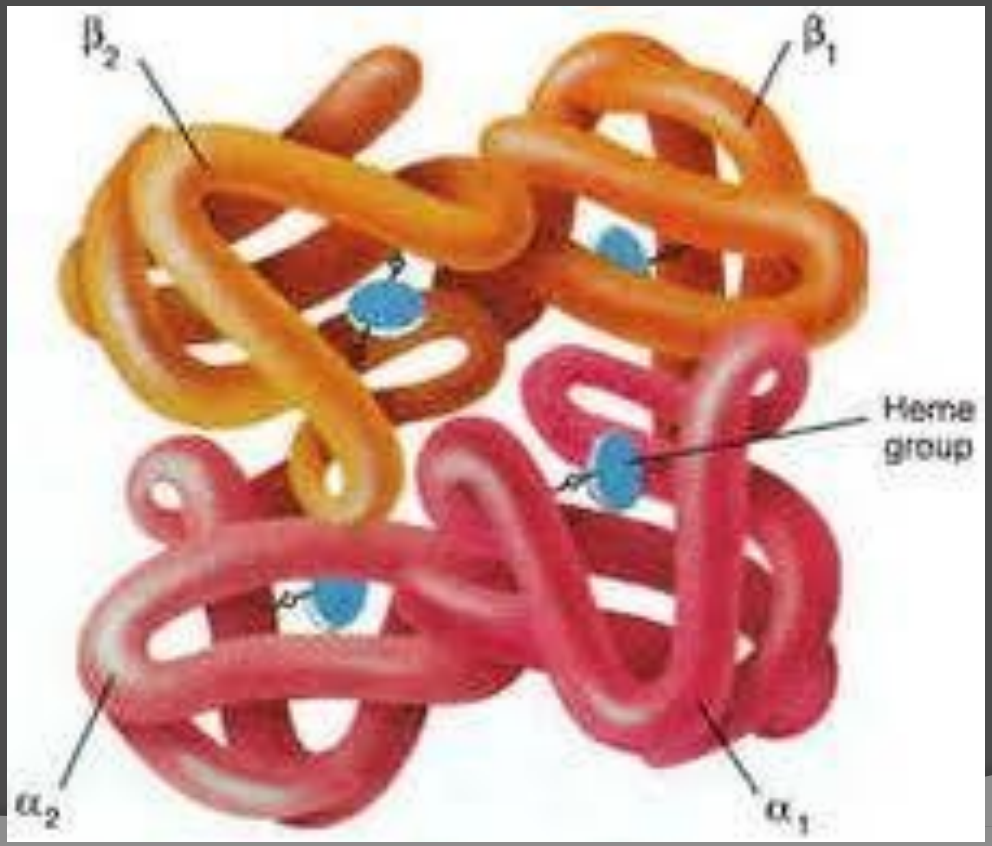
1. Essential elements for RBC formation
   - Proteins
   - Vitamins: B12, Folic acid, Vit C …)
   - Iron Metabolism.
2. Anemia
3. Polycythemia
4. Structure & functions of Hb

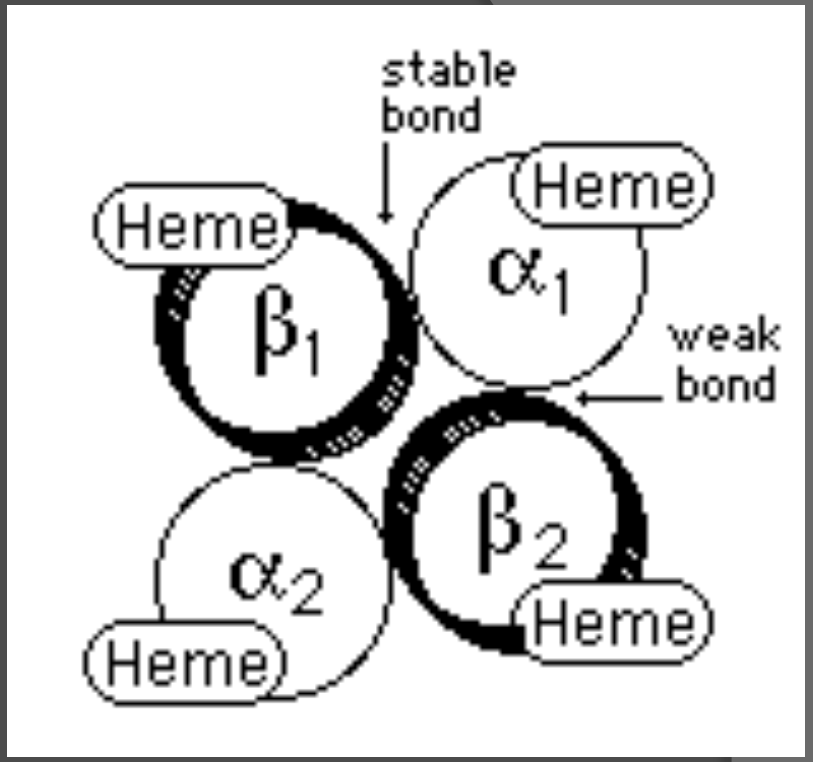
Essential elements for RBCs formation and Maturation

Certain elements are essential for RBC formation and maturation:

1. **Amino acids**: formation of **globin** in haem**o**globin
   - sever protein deficiency → anaemia

2. **Iron**: formation of haemoglobin
   - Deficiency → anaemia


β2
β1
Heme group
α2
α1


stable bond
Heme
Heme
α1
β1
weak bond
β2
α2
Heme
Heme

Essential elements for RBCs formation and Maturation *cont.*

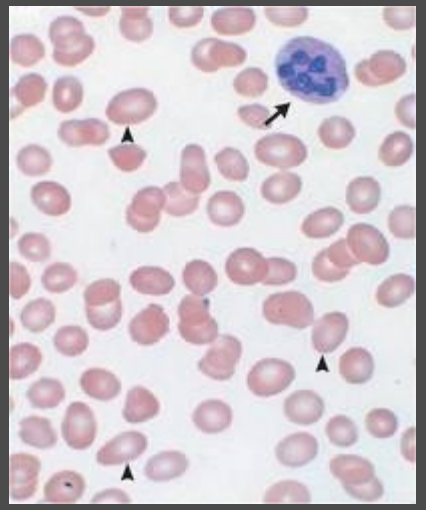
3. **Vitamins:**
   - **Vit B12 and Folic acid**
     - Synthesis of nucleoprotein
     - Deficiency → anemia
   - **Other :Vit B6, Riboflavin, nicotinic acid, biotin, Vit C, Vit E**

4. **Essential elements**
   - Copper, Cobalt, zinc, manganese

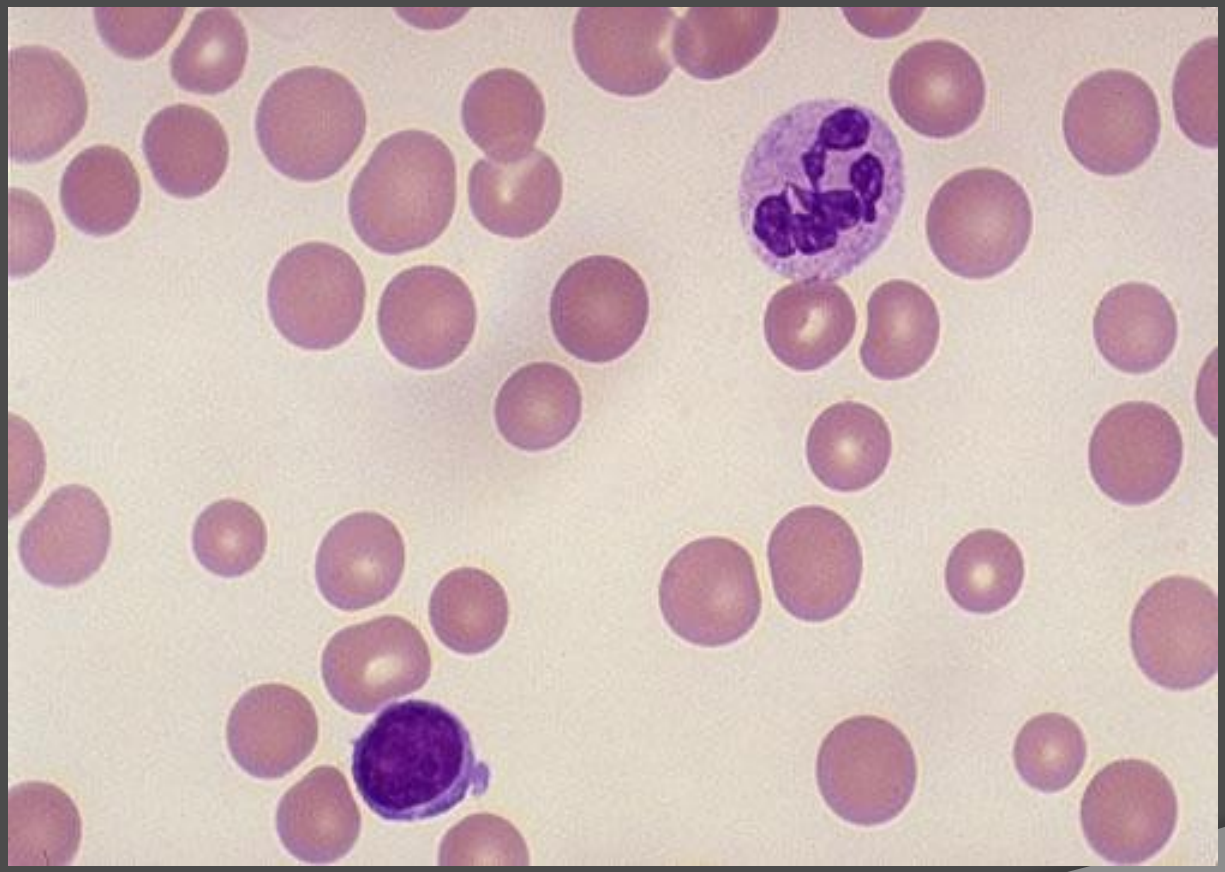
5. **Hormones**
   - Androgens, Thyroid, cortisol & growth hormones
     Deficiencies of any one results in anaemia
   -

Vitamin B12 & Folic acid

- Important for DNA synthesis and final maturation of RBC.
- Dietary source: meat, milk, liver, fat, 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

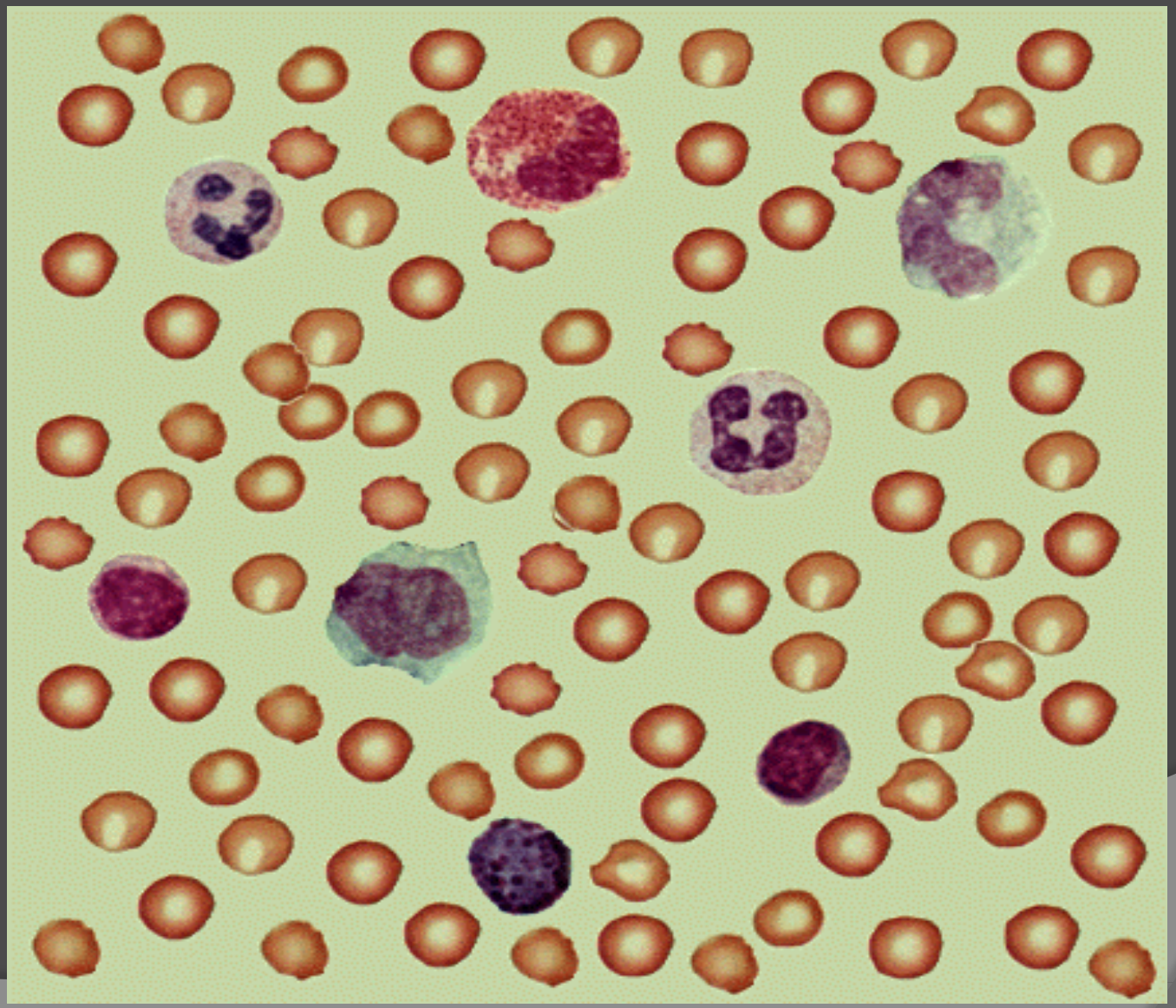


Macrocytic anemia

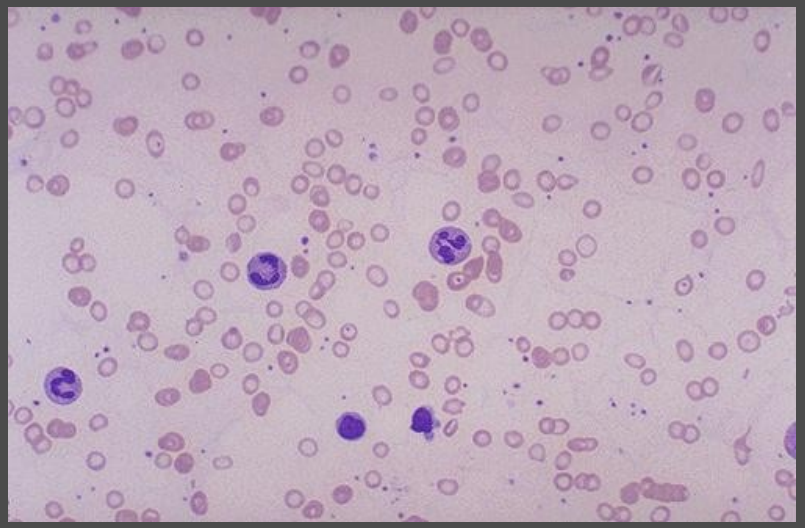


Note the hypersegmented neurotrophil and also that the RBC are almost as large as the lymphocyte. Finally, note that there are fewer RBCs.

Blood Film



Microcytic hypochromic anemia



- The RBC's are smaller than normal and have an increased zone of central pallor.

- This is indicative of a **microcytic** (smaller size of each RBC) and **hypochromic** (less hemoglobin in each RBC) anemia.
- There is also increased anisocytosis (variation in size) and poikilocytosis (variation in shape).

ANAEMIAS

- **Definiation**
  - Decrease number of RBC
  - Decrease Hb
  -
- **Symptoms**: Tired, Fatigue, short of breath, heart failure.

Causes of anaemia

1.Blood Loss

–acute ➡ accident (RBC return to normal 3-6w)

–Chronic ➡ microcytic hypochromic anaema (ulcer, worms)

2.Decrease RBC production

➢ Nutritional causes:

•Iron ➡ microcytic hypochromic anaemia.

•Vit B12 & Folic acid ➡ megaloblastic anaemia .

➢Bone marrow failure: destruction by cancer, radiation, drugs Aplastic anaemia.

3.Haemolytic ➡ excessive destruction

➢ Abnormal cells or Hb

•Spherocytosis

•sickle cells

➢ Incompatible blood transfusion.

➢ Erythroblastosis fetalis .

Polycythemia

Increased number of RBC

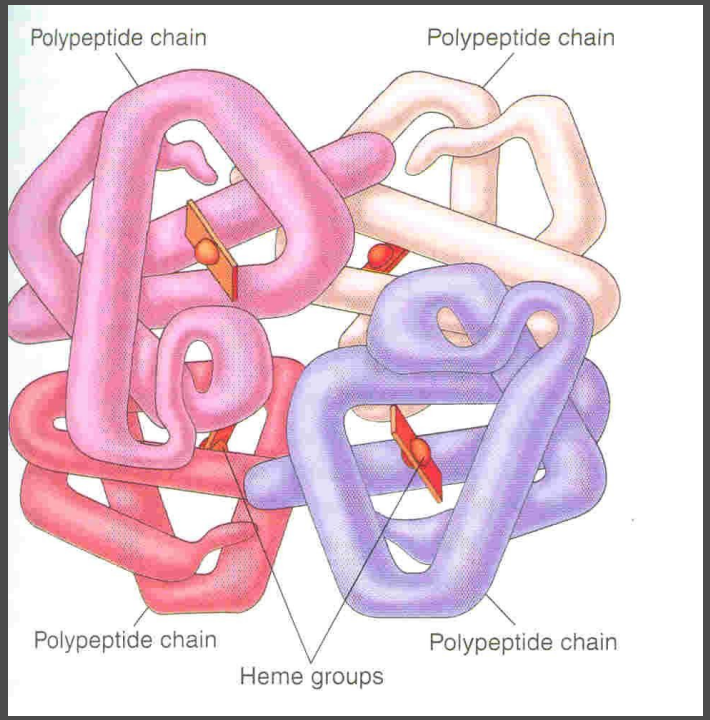
Types:

1. Primary (Polycythemia Rubra Vera - PRV): uncontrolled RBC production.
2. Secondary to hypoxia: high altitude (physiological), chronic respiratory or cardiac disease

HAEMOGLOBIN

- Hb molecules consist **4** chains each formed of **heme** & polypeptide chain (**globin**)

- **Heme** consist of **protoporphyrin ring** + **iron (F^{2+})**



Types of normal Hb.:

-Hb A (2 α & 2 beta chains) (adult Hb) (98%).

- Hb A2 (2 α & 2 delta chains) (2%)

-Hb F (2 α & 2 γ 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 bind O_2 to form oxyhemoglobin, affect by pH, temperatre, H^+
- Carriage of CO2
  - Hb bind CO_2 = carboxyhemaglobin
- Buffer

Malabsorption of Vit. B12

Pernicious Anemia

- VB12 absorption needs **intrinsic factor** secreted by **parietal cells** of stomach.
- VB12 + intrinsic factor is absorbed in the **terminal Ileum.**
- Deficiency arise from (Causes of deficiencies):
  - **Inadequate** intake
  - **Poor absorption** due to Intestinal disease

Iron metabolism (Fe)

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

- **Total Iron in the body = 4-5g**
  - **65% ….. Haemoglobin**
  - **5% …….. other hems**
  - **1% ……. bound to transferrin** (betaglobulin) **in blood**
  - **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 transport in plasma in the form of Transferrin (apotransferrin + iron).**

- **Iron is stored in two forms:**
  - **Ferritin (apoferritin + iron)**
  - **Haemosiderin (insoluble complex molecule,** in liver, spleen, bone marrow)

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

Destruction of RBC

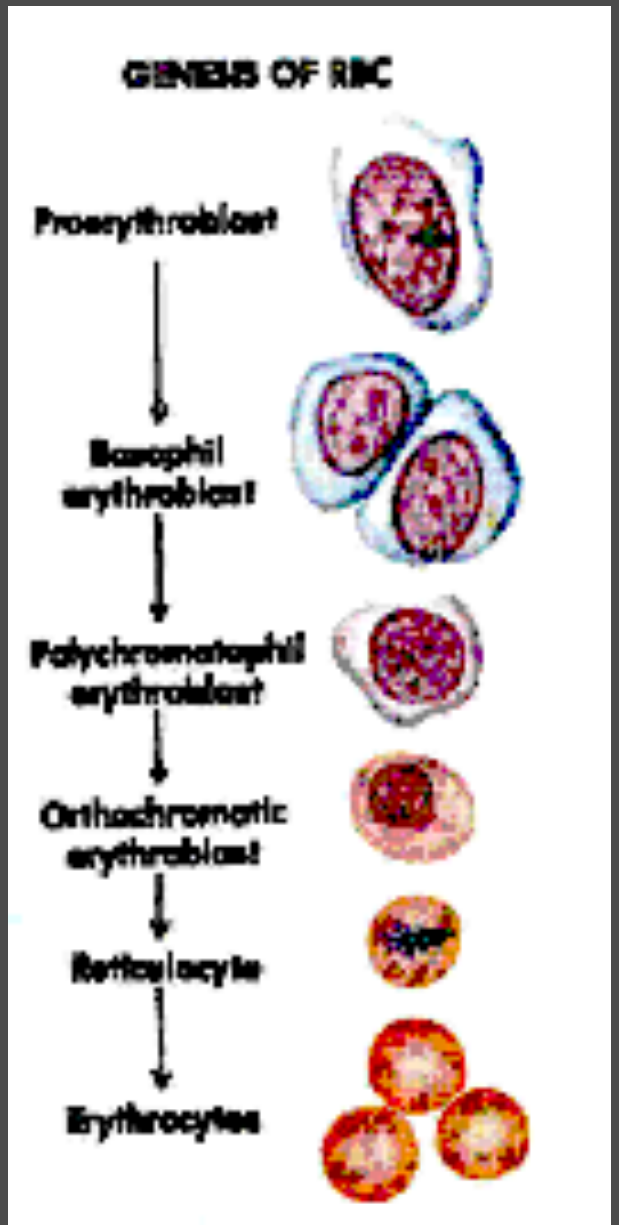
- RBC life span in circulation = 120 days.

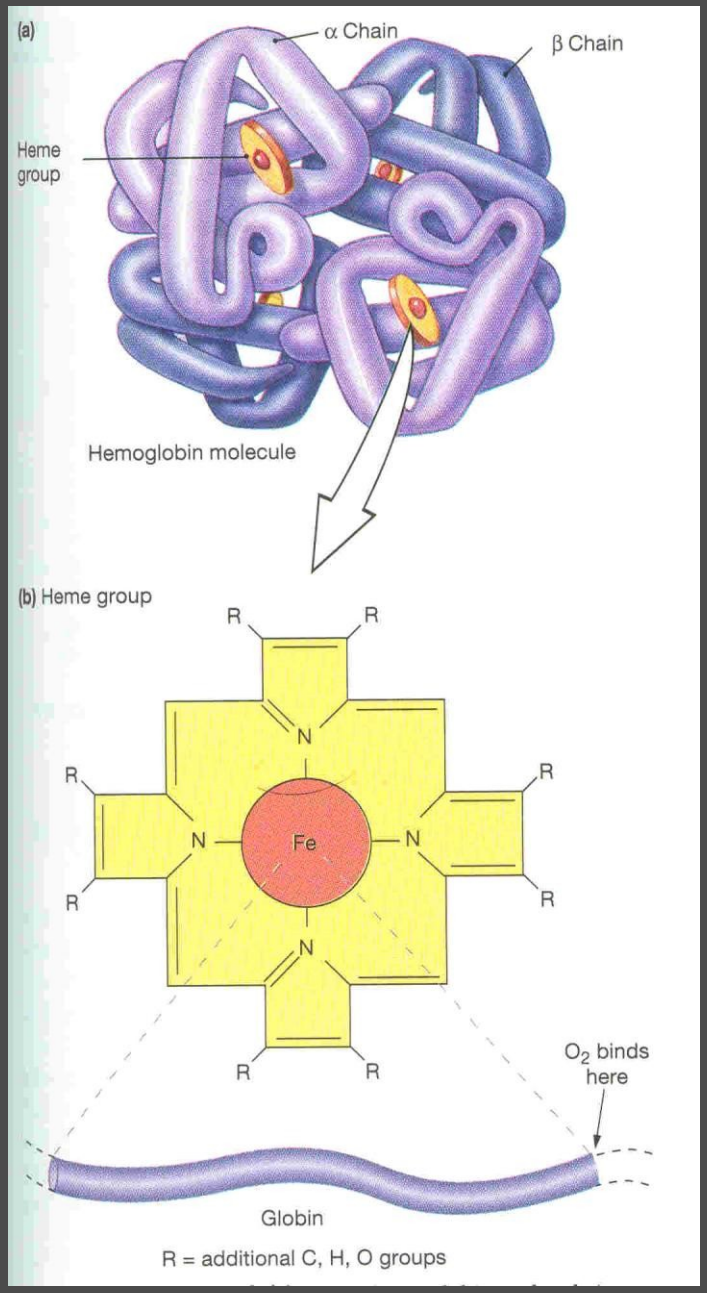
- Metabolic active cells.
- Old cell has a fragile cell membrane, cell will rupture as it passes in narrow capillaries (and spleen).

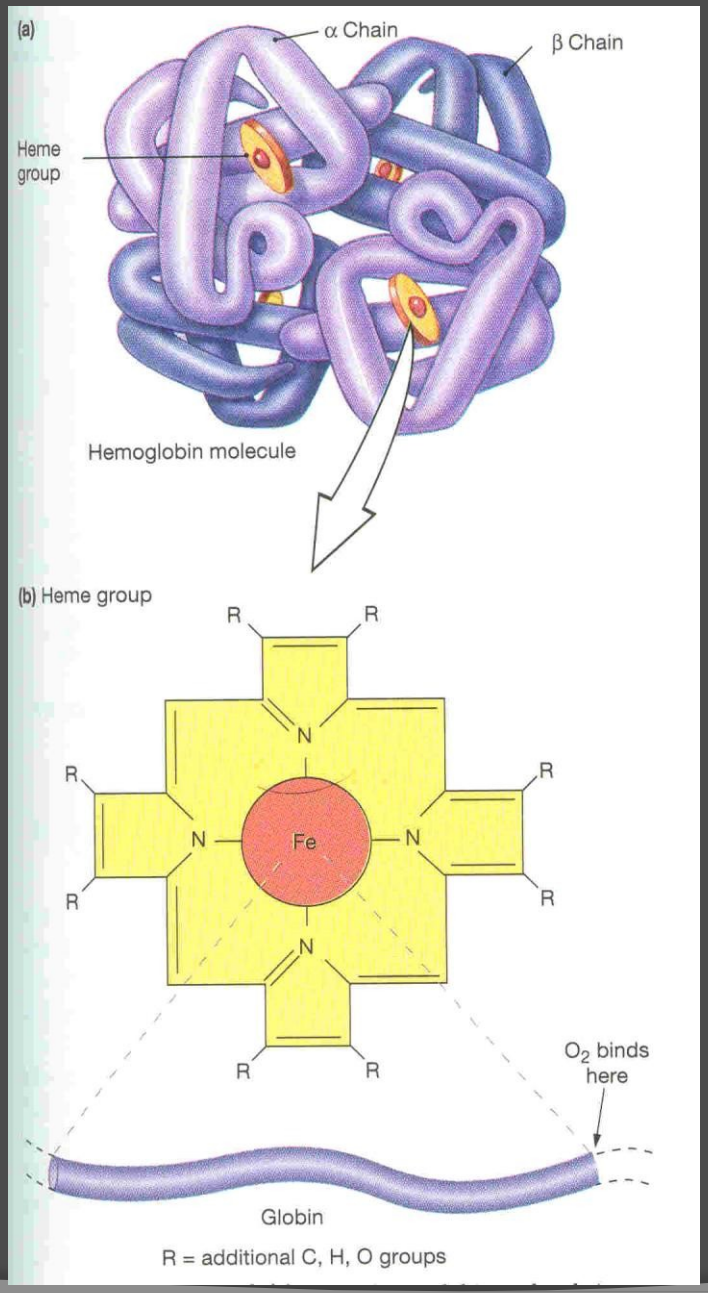
- Released Hb is taken up by macrophages in liver, spleen & bone marrow:
  - Hb is broken into its component:

    - Polypeptide—amino acids (protein pool = storage)
    - Iron ---- ferrtin
    - Haem (Porphyrin)>>—bilirubin>>—secreted by the liver into bile. [excess destruction of RBC → Jaundice]

Stages of differentiation of RBC




(a)
α Chain
β Chain
Heme group
Hemoglobin molecule
(b) Heme group
R
N
Fe
O_2 binds here
Globin
R = additional C, H, O groups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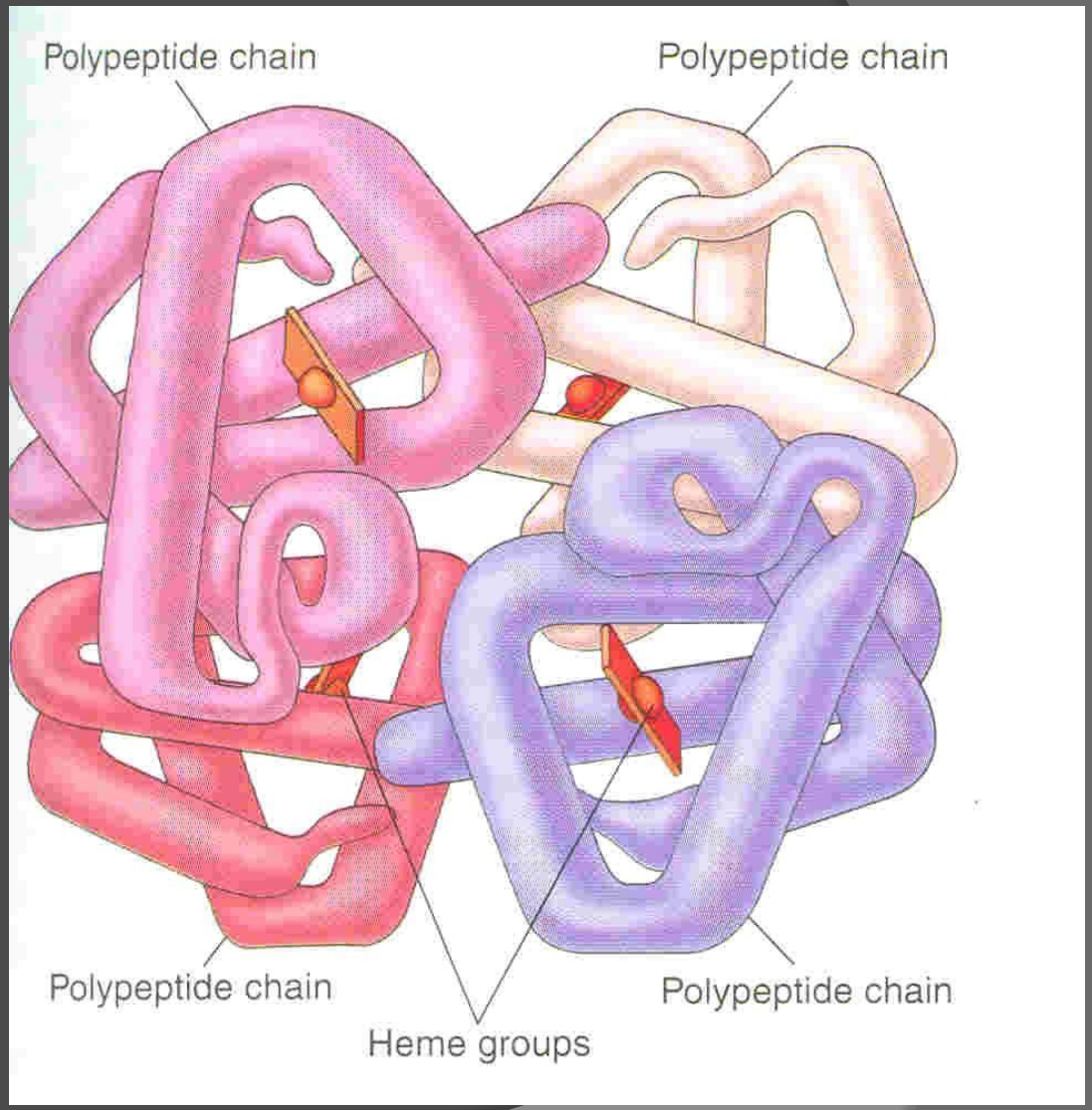
Polypeptide chain
Polypeptide chain
Polypeptide chain
Polypeptide chain
Heme groups