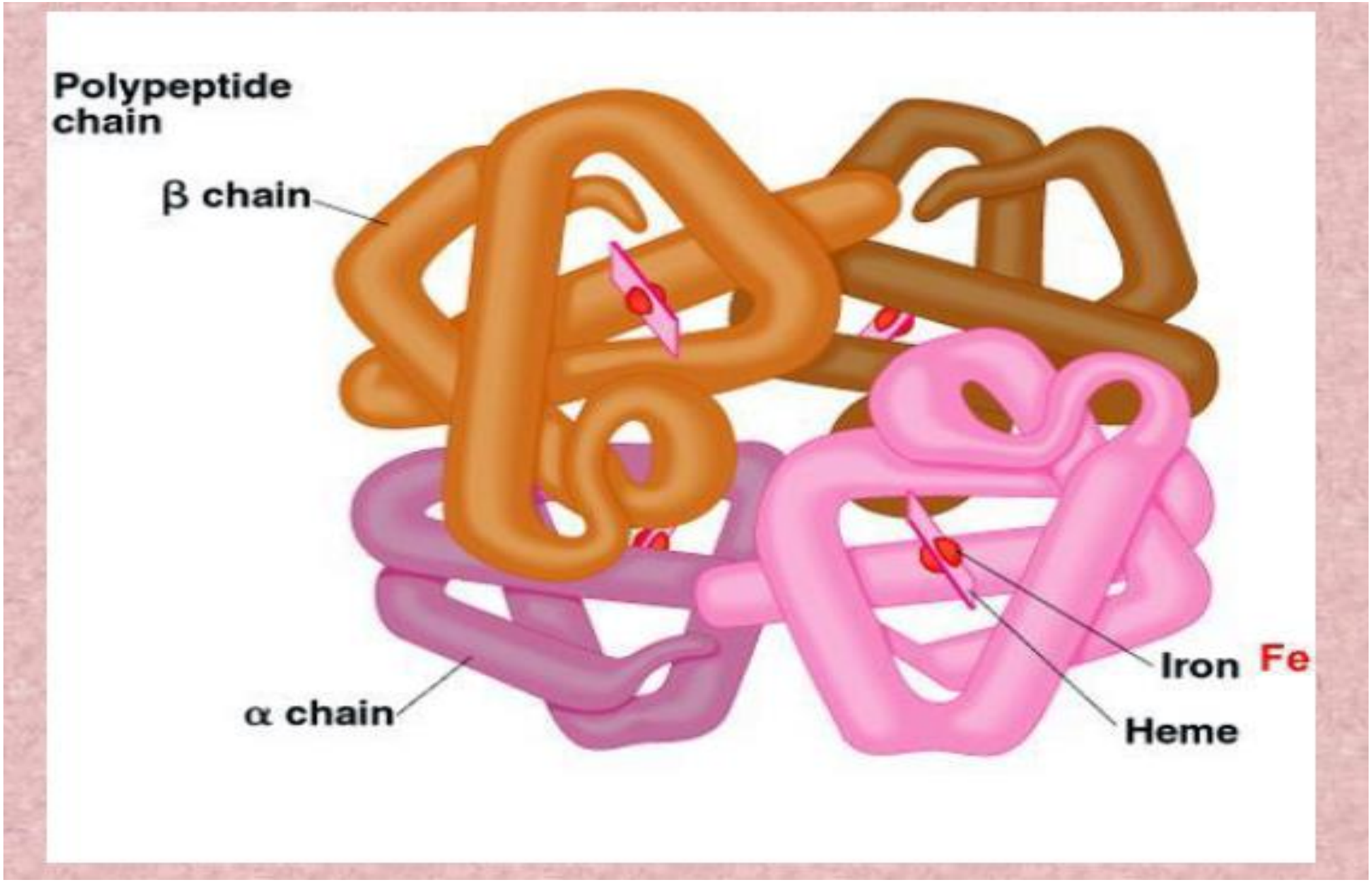
Hemoglobin : its protein of molecular weight 64,450 , in human beings it is enclose in the RBC .if it were in plasma, some of it leaks through the capillary membrane into the tissue space or through the glomerular membrane of the kidney into the glomerular filtrate each time the blood passes through the capillaries , high free plasma concentration of Hb increased blood viscosity and osmotic pressure. So for Hb to remain in the bloodstream , it must exist in the RBCs ,its major function is to carry O2 to the tissue and also it transport CO2 from the tissues to the lungs

Hemoglobin

Erythrocyte contains about 280 million hemoglobin molecules which give blood its red color. Hemoglobin forms 80% of the dry weight of RBC

Structure of hemoglobin.

Each hemoglobin molecule consists of 4 protein chains called globin, each one is bound to one heme. Heme is an iron-containing *porphyrin derivative*. The iron group of heme able to combine with oxygen in the lung and release oxygen in the tissues. Iron in the hemoglobin is in form of ferrous state "Fe^{++}"


Polypeptide chain
β chain
α chain
Iron Fe
Heme

- Because each chain has a heme so there are 4 iron atoms in each hemoglobin molecule each of these can bind with 1 Molecule of O_2 (or 8 oxygen atoms). Making a total of 4 molecules of O_2 (or 8 oxygen atoms)
- The nature of hemoglobin chain determines the binding affinity of Hb for oxygen. Abnormality of chain can alter the physical characteristics of Hb.

- **Synthesis of hemoglobin**

Hemoglobin synthesis is occur in the cytoplasm of the proerythroblast during erythropoiesis. Heme is synthesized in the mitochondria from succinyl CoA and glycine

I. 2 succinyl-CoA + 2glycine —› pyrole

II. 4 pyrole IX + Fe —› hems

Globin part of hemoglobin is synthesized in the ribosome from amino acids

III. Heme + polypeptide —› hemoglobin chain (α or β)

IV. 2 α Chain + 2β chain —› hemoglobin A

IRON METABOLISM

- when iron absorbed from small intestine it combine in blood plasma with beta globin (also called ***apotransferrin***) to form ***transferrin*** which then transported in the plasma. The iron is loosely combined with globin molecule and be released to any tissue cells, excess iron in the blood is deposited in all cells of the body but especially in liver and less in the reticuloendothelial cell of bone marrow. In the cell cytoplasm, it combine mainly with a protein ***apoferritin*** to form **ferritin**. This iron stored as ferritin is called storage iron.
- Smaller quantities of the iron in storage pool are stored in an insoluble form called ***hemosidrine***.

- When the quantity of iron in plasma decrease iron removed from ferritin. The iron is then transported in the form transferrin in the plasma to the proteins of the body where it is needed.
- When RBCs are destroyed, the hemoglobin released from the cell is ingested by the cell of monocyte –macrophage system (also called ***reticuloendothelial system***) especially spleen and free iron is liberated and stored in the ferritin pool or re-used for formation of hemoglobin.

Normal hemoglobin type:

Hb A: Its normal adult Hb . Its molecule consist of four polypeptide chains ,2 alpha (α) chains (each of which contains 141 amino acids) and 2 beta chains (each of which contains 146 amino acids).thus Hb A is designated α2 and β2. Hb A is predominant type of Hb in adult (95-97% of total Hb) .

Hb A2 : in the normal adult about 25% of the total Hb is Hb A2 in which chain are replaced by delta chains and is designated 2 α 2δ . Each δ chain also contain 146 amino acid but 10 amino acid differ from those in the β chain .

Hb F (Fetal Hb): it is the main Hb in fetus and new born . It is 2α 2γ,gamma(γ) chain also has 146 amino acid but 37 amino acid differ from those in β chain, Hb F is replaced gradually by adult Hb soon after birth, usually at about 6 months to one year of age, the normal adult Hb predominates . In normal adult Hb F may be found in a level of less than 2% of the total Hb . Hb F has greater affinity for O2 from Hb A, because of its lesser ability to bind 2,3-DPG.(D**iphosphoglycerate**) This facilitates movement of O2 from maternal to fetal circulation .

Embryonic hemoglobin's: Gower IHb containing 2 zeta chain and 2epsilon chains. Gower II containing 2 alpha chains and 2 epsilon chains. These are found in young embryos and persist until approximately 12 weeks of gestation .

Variant forms of normal Hb : Hb may be found in the blood in different forms :

Oxyhemoglobin: Hb combined with O2 each of the 4 iron atom in Hb molecule can bind reversibly one O2 molecule.

Carbaminohemoglobin : Hb combined with CO2 .

Carboxyhemoglobin: Hb combined with CO. Concentration of about 0.5%, Carboxyhemoglobin is produced by the normal degradation of Hb. Slightly increased levels can be found in blood of smokers and due to environmental pollution . Hb molecule becomes useless for O2 transport.

Sulfhemoglobin : Hb containing sulfur, and is incapable of transporting

Methemoglobin: Ferrous Fe++ is converted into ferric Fe+3 forming met hemoglobin.

this results in a decreased availability of oxygen to the tissues ,methemoglobin, a brown pigment incapable of transporting oxygen. The red cells contain enzymes capable of maintaining the iron in its normal state, but under abnormal conditions large amounts of methemoglobin may appear in the blood.

the enzyme system, NADH met hemoglobin reductase in the RBC converts methemoglobin back to Hb .

the congenital absence of this enzyme system is one cause of hereditary methemoglobinemia

Abnormalities of Hb chains can alter the physical characteristic of Hb molecule :

Sickle cell anemia, in which abnormal Hb (sickle cell Hb or Hb S) is produced Hb S has normal α chains but in each β chain glutamic acid at sixth position is replaced by valine . Hb S when deoxygenated becomes very insoluble and this causes the RBC to become sickle shaped and lose their deformability and hemolyzed easily .

In another type of inherited disorder of Hb ,the amino acid sequence is normal but polypeptide chain production is impaired or defined by decreased or absent . These are thalassemia. The α and β thalassemia are defined by decreased or absent α and β chains ,respectively

Destruction of RBC

R.B.C circulate in the blood for an average of 120 days, after that old RBCs are destroyed by macrophages in the mononuclear phagocyte system . in many parts of the body especially in the liver, spleen, and bone marrow. inside the mononuclear phagocyte system, the Hb is broken into its constituents (globin and heme). Globin is catabolized in the liver into its constituents amino acid and enters the circulating amino acid pool. The heme is converted into **biliverdin**. the iron from the heme is realized into the blood to be carried to the bone marrow for production of new RBC or to the liver and other tissues for storage .Biliverdin is converted into bilirubin which is released into the blood and later removed from the body by secretion through the liver into the bile.