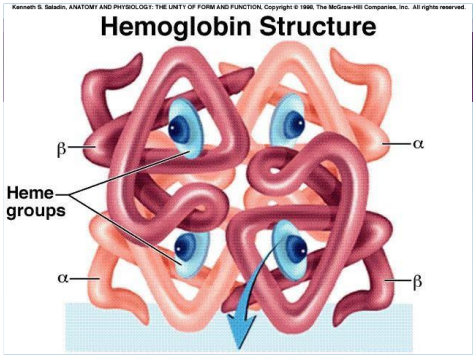
Hemoglobin

Hb is a pigment in R.B.C., it is a protein with molecular weights (64,458). The normal value of Hb is 14-16 gm/100ml blood, every 1 gm of Hb can combine with 1.39 ml O2 . Synthesis of Hb begins in the erythroblasts and continues through the normoblast and reticulocyte stage. Heme portion of Hb is synthesized mainly from acetic acid and glycine and that most of this synthesis occur in mitochondria. The chemical steps in formation of Hb. First, succinyl-CoA binds with glycine to form pyrrole. In turn, four pyrrole combine to form protoporphyrin 1x, which then combine with iron to form heme molecule. Finally, each heme molecule combine with long polypeptide chain, called globin, synthesized by the ribosomes, forming a subunit called Hb chain. Each chain has a molecular weight about 16.000, four of them turn, bind together loosely to form Hb.

1. 2 succinyl-coA+2 glycine → pyrrole
2. 4 pyrrole → protoporphyrin 1x
3. protoporphyrin 1x + Fe → heme
4. heme+polypeptide→hemoglobin chain(α or β)
5. 2 α chains + 2 β chains → hemoglobin A



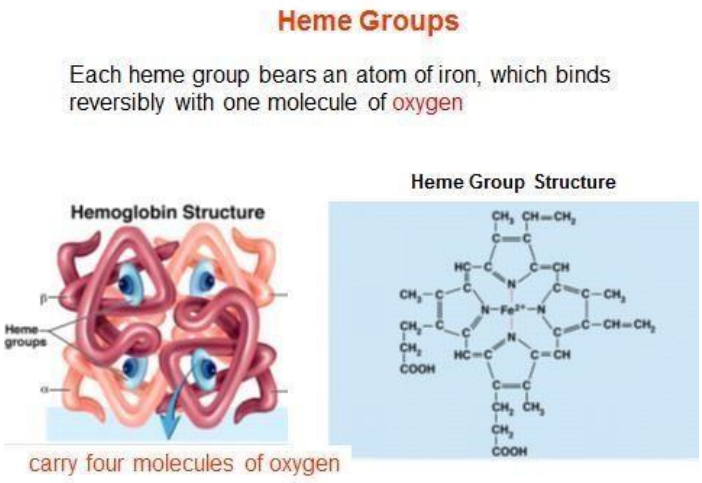
Formation of Hemoglobin

• Each erythrocyte contains about 280

million molecules of Hb. Hemoglobin consists of four protein chain called globins, two of these, the alpha chain (α), are 141 amino acids long, and other two, the beta (β) chains are 146 amino acids long. Each chain is conjugated with a nonprotein moiety called the heme group. Each heme can carry one molecule of O2, the Hb molecule as a whole can transport up to 4 O2 . About 20% of carbon dioxide in the bloodstream is also transported by Hb.

- Hemoglobin exists in several forms that display slight differences in the globin chains, the form adult Hb (HbA).

- About 2.5% of (HbA), however, is of a form called HbA2, which has a two delta (δ) chains in place of the β chains. The fetus produces a form called fetal Hb or (HbF), which has two Gamma (γ) chains in the place of the adult β chains. HbF has a higher oxygen-binding capacity than adult HbA and enables the fetus to extract oxygen from the mother's bloodstream. The delta (δ) and gamma (γ) chains are the same length as the (β) chains, but differs in amino acid sequence. HbF is converted into HbA, but in some cases is not converted.



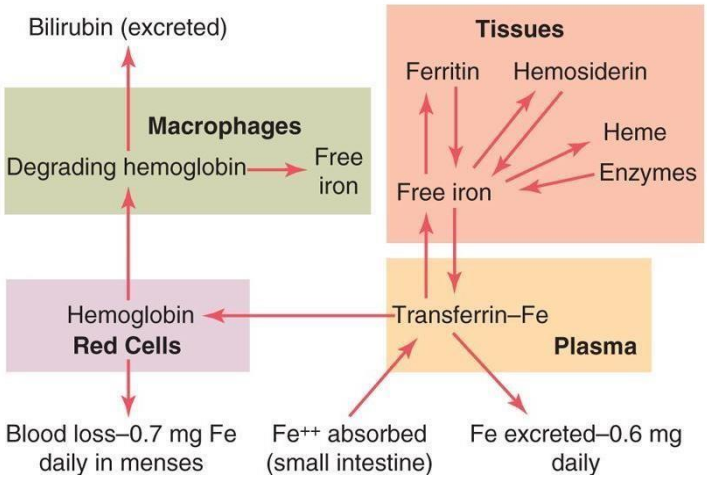
Iron Metabolism

- Because iron is important for formation of Hb, myoglobin and other substances such as cytochromes, cytochrome oxidase, peroxidase, and catalase, it is essential to understand the means by which iron is utilized in the body.
- The total quantity of iron in the body average 4-5 grams, about 65% of which is in the form of Hb.
- About 4% is in the form of myoglobin, 1% is in the form of the various heme compounds that promote intracellular oxidation, 0.1% is combined with the protein transferrin in the blood plasma, and 15-30% is stored mainly in the reticuloendothelial system and liver parenchymal cells, principally in the form of ferritin. A man excretes about 1 mg of iron each day, mainly into the feces

When iron is absorbed from the small intestine, it immediately combines in the blood plasma with beta globulin, apotransferria to form transferrin, which is then transported in the plasma.

The iron is loosely combined with the globulin molecule and consequently, can be released to any of tissue cells at any point in the body. Excess iron in the blood is deposited in all cells of the body, but especially in liver hepatocytes. In the cell cytoplasm, it combines mainly with a protein, apoferritin to form ferritin. The iron stored as ferritin is called ***storage iron***. Smaller quantities of the iron in the storage pool are stored, insoluble form called ***hemosiderin***. When the quantity of iron in plasma falls

very low, iron is removed from ferritin quite easily, but much less easily from hemosiderin. When red blood cells have lived their life span and are destroyed, the Hb released from the cells is ingested by the cells of the monocytesmacrophage system. There free iron is liberated, and it is mainly stored in the ferritin pool or formation of new Hb.



Hb Compounds

There are different compounds of Hb:

1. ***Oxyhemoglobin:*** this results from combination of O2 with Hb.

$$Hb + O2 \rightarrow HbO2$$

2. ***Carboxy Hb:*** this results from union of Co gas with Hb, Co gas is a very poisonous gas even if it is present in very small amount it displaces O2 in OxyHb so that carboxy Hb is produced, this is because of Co gas is about 250 times greater than O2 to Hb.

3. ***Sulfa Hb:*** this compound results from the combination of Hb with sulpher compounds.

4. ***Carbamino Hb:*** this results from the combination of CO2 gas with Hb.

$$Hb + CO2 \rightarrow HbCO2$$

5. ***Methemoglobin:*** if Hb subjected to O2 in the presence of an oxidizing agent, oxidation occurs and a new compound is produced is called Meth Hb.

$$Met\ Hb\ Fe \rightarrow Fe + Hb \rightarrow HbFe$$

Destruction of Hb

The Hb released from the cells when they burst is phagocytosed almost immediately by macrophages in many parts of the body, but especially in liver (Kupffer cells), spleen and bone marrow. During the next few hours to days, the macrophage release the iron from the Hb back into the blood to be carried by transferrin either to bone marrow for production of new R.B.C. or to the liver and other tissues for storage in the form of ferritin. The porphyrin portion of the Hb molecule is converted by the macrophages, through a series of stages, into bile pigment bilirubin, which released into the blood and later secreted by the

liver into the bile. A high level of bilirubin in the blood causes Jaundice, a yellowish cast in light-colored skin and the whites of eyes. Jaundice may be a sign of rapid hemolysis or a liver diseases. The normal plasma concentration of bilirubin is 0.5 mg/dl. The skin begins to appear jaundiced when concentration rise 1.5 mg/dl .

<u>The common causes of jaundice are:</u>

1. Increased destruction of R.B.C. with rapid release of bilirubin into blood.
2. Obstruction of the bile duct or damage to the liver cells.

