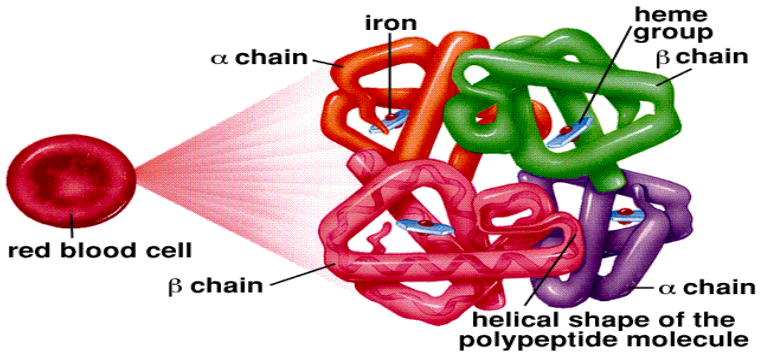
Hemoglobin

Hemoglobin (Hb) is the iron containing coloring pigment of RBC. It forms 95% of dry weight of RBC and 30 to 34% of wet weight. The molecular weight of Hb is 68,000.

STRUCTURE OF HEMOGLOBIN

Hb is a conjugated protein. It consists of a protein called globin and an iron containing pigment called heme. Iron is present in an unstable ferrous (Fe++) form. Heme part is called porphyrin. It is formed by four pyrole rings (tetrapyrole). The iron is attached to each pyrole ring and globin molecule. Globin is made up of four polypeptide chains. Among the four polypeptide chains, two are α chains and two are β chains



NORMAL HEMOGLOBIN CONTENT

Average Hb content in blood is 14 to 16 g/dL. However, it varies depending upon age and sex of the individual and the number of RBCs.

Age

At birth: 25 g/dL
After 3rd month: 20 g/dL
After 1 year: 17 g/dL
From puberty onwards: 14-16 g/d
At the time of birth and in infants and growing children, Hb content is high because of increased number of RBCs

Sex

In adult males: 15 g/dL
In adult females: 14.5 g/dL

TYPES OF NORMAL HEMOGLOBIN

Hb is of two types:
1. Adult Hb (Hb A)
2. Fetal Hb (Hb F)

Both the types of Hb differ from each other structurally and functionally.
Structural Difference In adult Hb, the globin contains two α chains and two β chains. In fetal Hb, there are two α chains and two γ chains instead of β chains.
Functional Difference
Functionally, fetal Hb has more affinity for oxygen than adult Hb. And, the oxygen hemoglobin dissociation curve of fetal blood is shifted to left.

Abnormal hemoglobin derivatives

-Carboxyhemoglobin

Carboxyhemoglobin or carbon monoxyhemoglobin is the abnormal Hb derivative formed by the combination of carbon monoxide with Hb.

-Methemoglobin

Methemoglobin is the abnormal Hb derivative formed when iron molecule of Hb is oxidized from normal ferrous state to ferric state

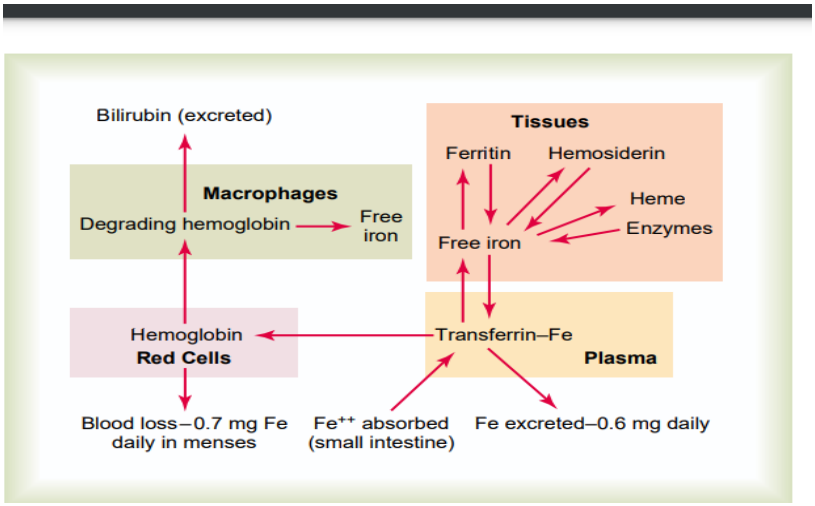
-Sulfhemoglobin

Sulfhemoglobin is the abnormal Hb derivative formed by the combination of hemoglobin with hydrogen sulfide.

Formation of Hemoglobin

Synthesis of hemoglobin begins in the proerythroblasts and continues even into the reticulocyte stage of the red blood cells. Therefore, when reticulocytes leave the bone marrow and pass into the blood stream, they continue to form minute quantities of hemoglobin for another day or so until they become mature erythrocytes. First, succinyl-CoA, formed in the Krebs metabolic cycle , binds with glycine to form a pyrrole molecule. In turn, four pyrroles combine to form protoporphyrin IX, which then combines with iron to form the heme molecule. Finally, each heme molecule combines with a long polypeptide chain, a globin synthesized by ribosomes, forming a subunit of hemoglobin called a hemoglobin chain. Each chain has a molecular weight of about 16,000; four of these in turn bind together loosely to form the whole hemoglobin molecule. There are several slight variations in the different subunit hemoglobin chains, depending on the amino acid composition of the polypeptide portion.

The different types of chains are designated alpha chains, beta chains, gamma chains, and delta chains. The most common form of hemoglobin in the adult human being, hemoglobin A, is a combination of two alpha chains and two beta chains. Hemoglobin A has a molecular weight of 64,458. Because each hemoglobin chain has a heme prosthetic group containing an atom of iron, and because there are four hemoglobin chains in each hemoglobin molecule, one finds four iron atoms in each hemoglobin molecule; each of these can bind loosely with one molecule of oxygen, making a total of four molecules of oxygen (or eight oxygen atoms) that can be transported by each hemoglobin molecule. The types of hemoglobin chains in the hemoglobin molecule determine the binding affinity of the hemoglobin for oxygen. Abnormalities of the chains can alter the physical characteristics of the hemoglobin molecule as well. For instance, in sickle cell anemia, the amino acid valine is substituted for glutamic acid at one point in each of the two beta chains. When this type of hemoglobin is exposed to low oxygen, it forms elongated crystals inside the red blood cells that are sometimes 15 micrometers in length. These make it almost impossible for the cells to pass through many small capillaries, and the spiked ends of the crystals are likely to rupture the cell membranes, leading to sickle cell anemia.



Iron transport and metabolism

Iron Metabolism

Because iron is important for the formation not only of hemoglobin but also of other essential elements in the body (e.g., myoglobin, cytochromes,

cytochrome oxidase, peroxidase, catalase), it is important to understand the means by which iron is utilized in the body. The total quantity of iron in the body averages 4 to 5 grams, about 65 per cent of which is in the form of hemoglobin. About 4 per cent is in the form of myoglobin, 1 per cent is in the form of the various heme compounds that promote intracellular oxidation, 0.1 per cent is combined with the protein transferrin in the blood plasma, and 15 to 30 per cent is stored for later use, mainly in the reticuloendothelial system and liver parenchymal cells, principally in the form of ferritin.

Destruction of Hemoglobin.

When red blood cells burst and release their hemoglobin, the hemoglobin is phagocytized almost immediately by macrophages in many parts of the body, but especially by the Kupffer cells of the liver and macrophages of the spleen and bone marrow. During the next few hours to days, the macrophages release iron from the hemoglobin and pass it back into the blood, to be carried by transferrin either to the bone marrow for the production of new red blood cells or to the liver and other tissues for storage in the form of ferritin. The porphyrin portion of the hemoglobin molecule is converted by the macrophages, through a series of stages, into the bile pigment bilirubin, which is released into the blood and later removed from the body by secretion through the liver into the bile.

The common cause of Jaundice are:

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.