LEC/4

Hemoglobin

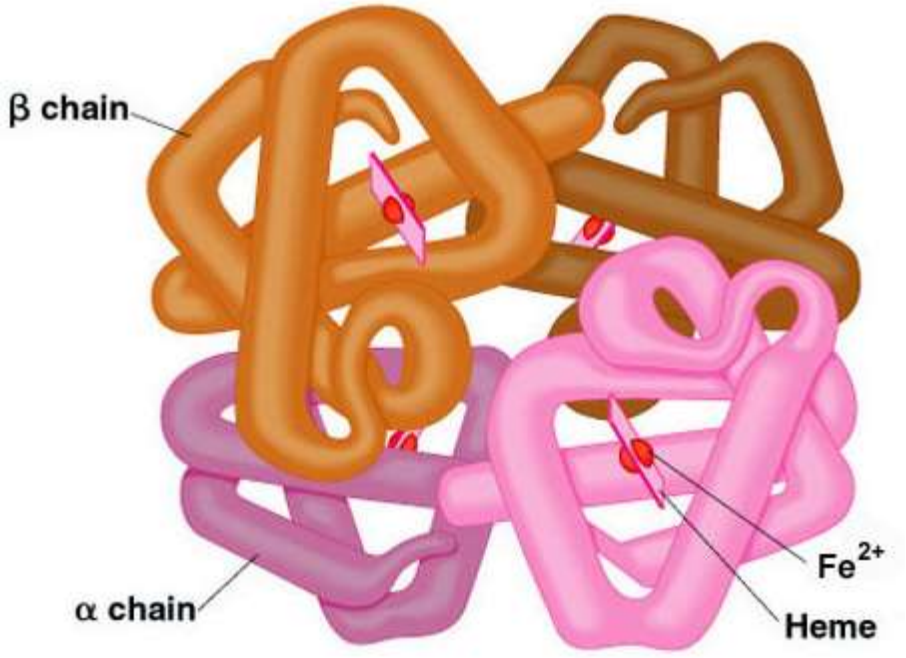
What is hemoglobin?

Hemoglobin is the specialized protein molecule in red blood cells that carries oxygen from the lungs to the body's tissues and returns carbon dioxide from the tissues back to the lungs.

Hemoglobin is made up of four protein molecules (globulin chains) that are connected together. The normal adult hemoglobin (Hb.) molecule contains two alpha-globulin chains and two beta-globulin chains. In fetus and infants, beta chains are not common and the hemoglobin molecule is made up of two alpha chains and two gamma chains. As the infant grows, the gamma chains are gradually replaced by beta chains, forming the adult hemoglobin structure.

Each globulin chain contains an important central structure called the heme molecule. Embedded within the heme molecule is iron that is vital in transporting oxygen and carbon dioxide in our blood. The iron contained in hemoglobin is also responsible for the red color of blood.

Hemoglobin also plays an important role in maintaining the shape of the red blood cells. In their natural shape, red blood cells are round with narrow centers similar to a donut without a hole in the middle. Abnormal hemoglobin structure can, for that reason, disorder the shape of red blood cells and hold back their function and flow through blood vessels.



Normal Hemoglobin Values :

The hemoglobin level is expressed as the amount of hemoglobin in grams (gm) per deciliter (dL) of whole blood, a deciliter being 100 milliliters.

The normal ranges for hemoglobin depend on the age and, beginning in adolescence, the gender of the person. **The normal ranges are:**

1. Newborns: 17 - 22 gm/dL.
2. One (1) week of age: 15 - 20 gm/dL.
3. One (1) month of age: 11 - 15gm/dL.
4. Children: 11 - 13 gm/dL.
5. Adult males: 14 - 18 gm/dL.
6. Adult women: 12 - 16 gm/dL.
7. Men after middle age: 12.4 - 14.9 gm/dL.
8. Women after middle age: 11.7 - 13.8 gm/dL.

All of these values may vary slightly between laboratories. Some laboratories do not differentiate between adult and "after middle age" hemoglobin values.

Normal Hemoglobin Types:

Normal hemoglobin types found in our body include Hb. A, Hb. A2 ,and Hb. F.

Hb. A : composes about (95 – 98) % of Hb. found in your body and contains two alpha protein chains and two beta protein chains.

Hb. A2 : makes up a smaller portion (1.5 – 3.2) % of the Hb. in your body. It has two alpha and two delta protein chains.

Hb. F : makes up (0.5 – 0.8)% of the Hb. found in your body. It has two alpha and two gamma protein chains.

- 65 % of haemoglobin is synthesized in the erythroblasts .
- 35 % of haemoglobin is synthesized at reticulocyte stage .
- – Haem synthesis occurs largely in the mitochondria by series of biochemical reactions .

Common Hemoglobin Variants:

1. **Hemoglobin S :-** This is the primary hemoglobin in people with sickle cell disease. Descent carry the sickle Hb mutation in one of their two beta genes. Persons with Hb S disease have two abnormal beta (β^S) chains and two normal alpha (α) chains. The presence of hemoglobin S causes the red blood cell to deform and think a sickle shape when exposed to decreased amounts of oxygen (such as might happen when someone exercises). Sickled red blood cells can block small blood vessels, causing pain and impaired circulation, decrease the oxygen-carrying capacity of the red blood

cell, and decrease the cell's lifespan. A single beta (β^S) copy does not cause symptoms unless it is combined with another hemoglobin mutation, such as that causing Hb C (β^C).

2. **Hemoglobin C :-** About 2-3% of people of West African descent are heterozygotes for hemoglobin C (have one copy of β^C). Hemoglobin C disease (seen in homozygotes – those with two copies of β^C) is rare and relatively mild. It usually causes a minor amount of hemolytic anemia and a mild to moderate enlargement of the spleen.
3. **Hemoglobin E :-** Hemoglobin E is one of the most common beta chain hemoglobin variants in the world. It is very common in Southeast Asia, especially in Cambodia, Laos, and Thailand and in individuals of Southeast Asian descent. People who are homozygous for Hb E (have two copies of β^E) generally have a mild hemolytic anemia, microcytic red blood cells, and a mild enlargement of the spleen. A single copy of the hemoglobin E gene does not cause symptoms unless it is combined with another mutation, such as the one for beta thalassemia trait.

Less Common Hemoglobin Variants:

There are many other variants. Some are silent – causing no signs or symptoms – while others affect the functionality **and/or** stability of the hemoglobin molecule. Examples of other variants include: **Hemoglobin D, Hemoglobin G, Hemoglobin J, Hemoglobin M, and Hemoglobin Constant Spring**, a mutation in the alpha globin gene that results in an abnormally long alpha (α) chain and an unstable hemoglobin molecule. Additional beta chain variant examples are:

1. **Hemoglobin F : -** Hb F is the primary hemoglobin produced by the fetus, and its role is to transport oxygen efficiently in a low oxygen environment. Production of Hb F stops at birth and decreases to adult levels by 1-2 years of age. Hb F may be elevated in several congenital disorders. Levels can be normal to increased in beta thalassemia and are frequently increased in individuals with sickle cell anemia and in sickle cell-beta thalassemia.

   Hb F levels are also increased in a rare condition called Hereditary Persistence of Fetal Hemoglobin (HPFH). This is a group of inherited disorders in which Hb F levels are increased without the signs or clinical features of thalassemia.
2. **Hemoglobin H :-** Hb. H is an abnormal hemoglobin that occurs in some cases of alpha thalassemia. It is composed of four beta (β) globin chains and is produced in response to a severe shortage of alpha (α) chains. Although each of the beta (β) globin chains is normal, the tetramer of 4 beta chains does not function normally.

It has an increased affinity for oxygen, holding onto it instead of releasing it to the tissues and cells.

3. **Hemoglobin Barts :-** Hb Barts develops in fetuses with alpha thalassemia. It is formed of four gamma (γ) protein chains when there is a shortage of alpha chains, in a method similar to the formation of Hemoglobin H. Hb Bart's disappears shortly after birth due to decreasing gamma chain production.

- A person can also inherit two different abnormal genes, one from each parent. This is known as being compound heterozygous or doubly heterozygous. Several different clinically significant combinations are listed below.

1. **Hemoglobin SC Disease.** Inheritance of one beta S gene and one beta C gene results in Hemoglobin SC Disease. These individuals have a mild hemolytic anemia and moderate enlargement of the spleen. Persons with Hb SC disease may develop the same vaso-occulsive (blood vessel blocking) complications as seen in sickle cell anemia.
2. **Sickle Cell – Hemoglobin D Disease :** Individuals with sickle cell – Hb D disease have inherited one copy of hemoglobin S and one of hemoglobin D-Los Angeles (or D-Punjab).
3. **Hemoglobin E – beta thalassemia :** Individuals who are doubly heterozygous for hemoglobin E and beta thalassemia have an anemia that can vary in severity, from mild (or asymptomatic) to severe.
4. **Hemoglobin S – beta thalassemia :** Sickle cell – beta thalassemia varies in severity, depending on the beta thalassemia mutation inherited. Some mutations result in decreased beta globin production ($beta^+$) while others completely reduce it ($beta^0$). Sickle cell – $beta^+$ thalassemia tends to be less severe than sickle cell – $beta^0$ thalassemia. Patients with sickle cell – $beta^0$ thalassemia tend to have more irreversibly sickled cells, more common vaso-occlusive problems, and more severe anemia than those with sickle cell – $beta^+$ thalassemia.