Hematology

HEMOGLOBIN

LEC 5

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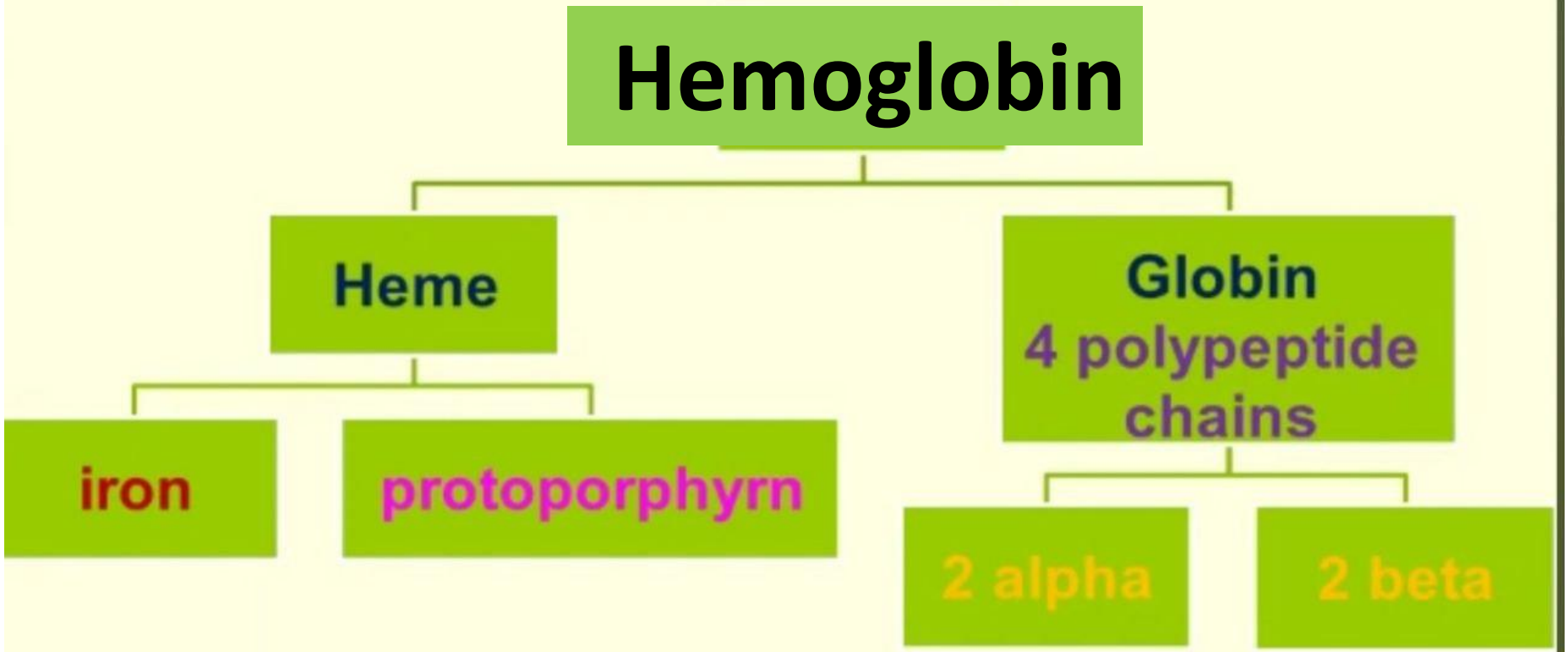
- **HEMOGLOBIN (Hb)**

- **Hb** 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.
- The major organ in the human body depends on oxygenation for **growth** and **function**, and this process is ultimately under the control of hemoglobin.

Function of Hemoglobin

1. Hemoglobin is an oxygen carrier.
2. Hemoglobin is a carbon dioxide carrier.
3. Hemoglobin gives the red color to blood.
4. Hemoglobin maintains the shape of RBCs
5. Hemoglobin acts as a buffer.
6. Hemoglobin interacts with other ligands.

Structure of haemoglobin



Hemoglobin Structure

The hemoglobin molecule consists of two primary structures:

1. **Globin portion:** Hemoglobin is made up of **four protein molecules** (globulin chains) that are connected together. These consist of amino acids linked together to form a polypeptide chain.

The most significant chains for adult hemoglobins are the alpha and beta chains.

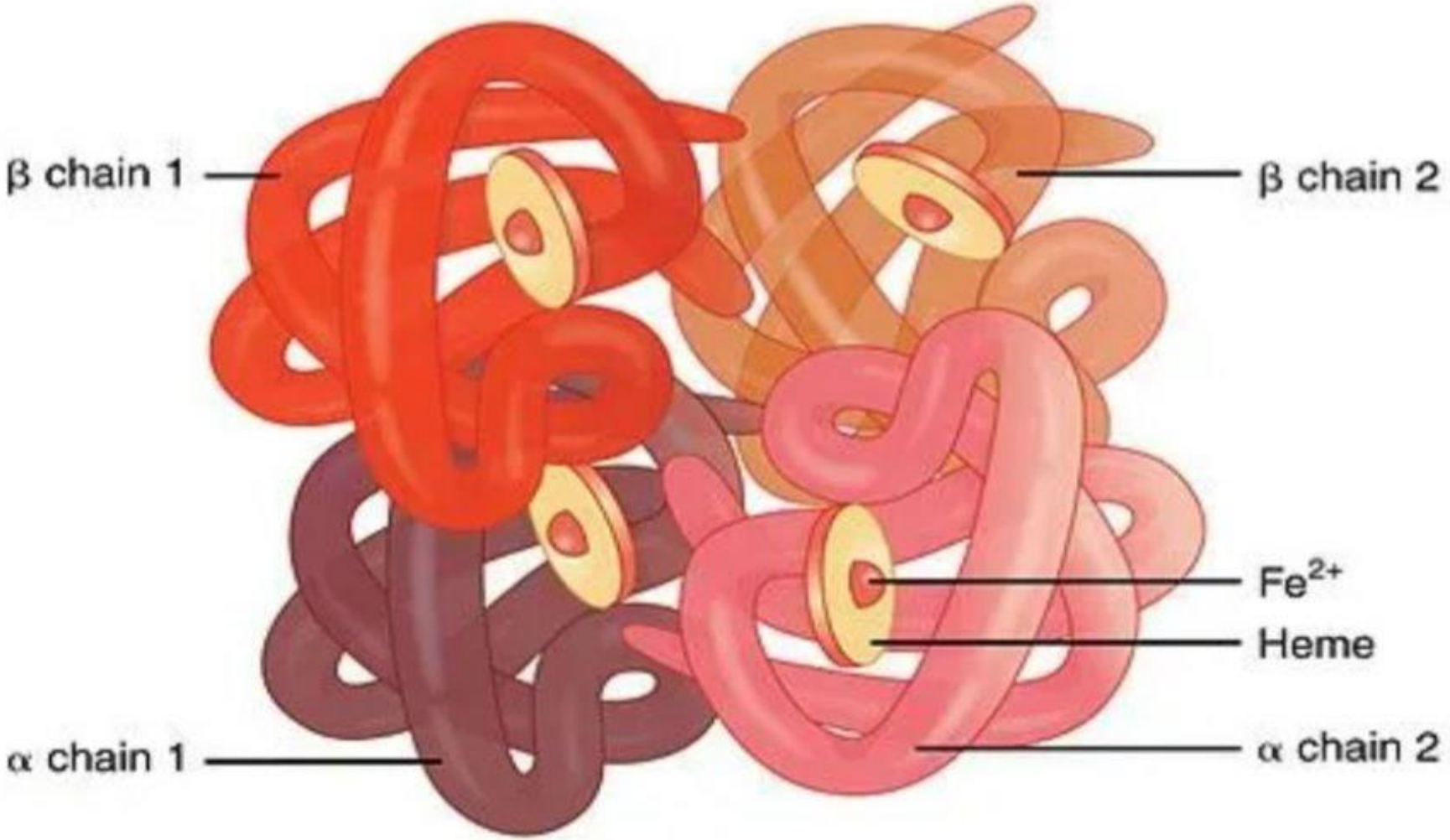
1- Alpha chains have **141** amino acids,

2- Beta chains have **146** amino acids in a unique arrangement.

2. Heme portion: Each globulin chain contains an important central structure called the **heme molecule**. This structure involves four iron atoms in the ferrous state (Fe^{+2}) (because iron in the ferric state (Fe^{+3}) cannot bind oxygen) surrounded by porphyrin ring, a structure formed in the nucleated red cells.

* Porphyrin is the final product in the synthesis of the heme molecule. Once **iron** combines with **porphyrin** to form the **complete heme molecule**. The heme and globin portions of the hemoglobin molecule are linked together by chemical bonds.

Structure of hemoglobin



(a)

- **Synthesis of Hemoglobin**

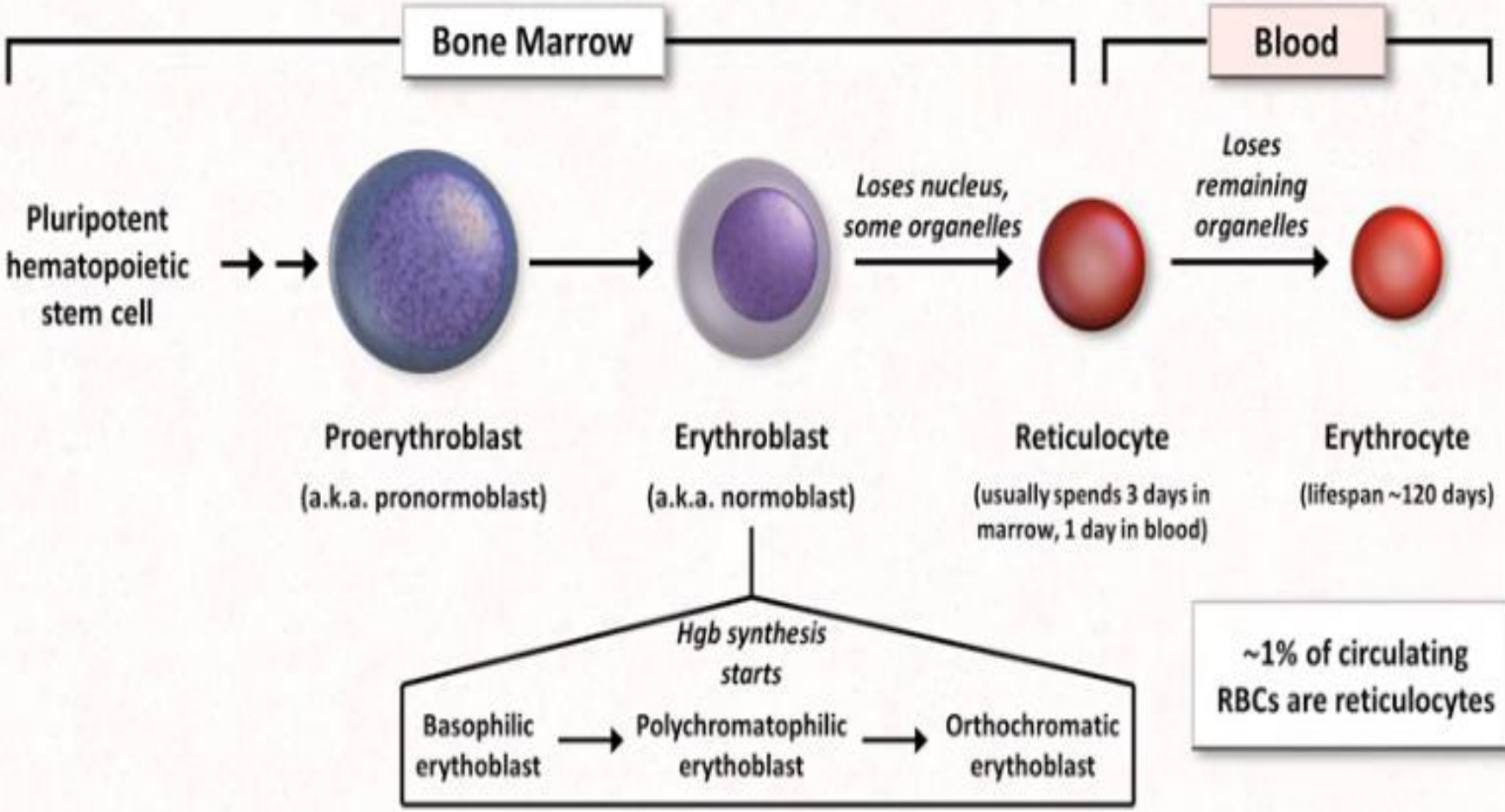
- Hemoglobin is synthesized in a complex series of steps. The heme part is synthesized in the mitochondria and immature red blood cells, while the globin protein parts are synthesized by ribosomes.
- Production of Hb continues in the cell throughout its early development from the proerythroblast (65%) to the reticulocyte (35%) in the bone marrow.

- Even after the loss of the nucleus in mammals, residual ribosomal RNA allows further synthesis of Hb until the reticulocyte loses its RNA after entering the vascular.

- Normal mature red cells have a full complement of hemoglobin, which occupies a more than one half of the surface area of the red cell and each red cell contains approximately 270 million hemoglobin molecules.

Erythropoiesis

(RBC Production and Maturation)



- **Normal Hemoglobin Types:**

- **1. Embryonic hemoglobins** Hb **Gower-1** (2ζ2ε), Hb **Portland** (2ζ2γ), and Hb **Gower-2** (2α2ε), are synthesized and remain in the embryo for the 3 months.

- **2. Fetal hemoglobin (Hb. F)** (2α2γ), begins to be synthesized at approximately 3 months in fetal development and remains as the majority hemoglobin at birth.

- **3. Adult hemoglobins (Hb. A)**, Between 3 and 6 months post-delivery, the amount of gamma chains declines and the amount of beta chains increases

❖ **Hb. A**: composes about 95% – 98 % of Hb. found in your body and contains $2\alpha 2\beta$ chains.

❖ **Hb. A2**: makes up 1.5% – 3.2 % of the Hb. It has $2\alpha 2\delta$ chains.

❖ **Hb. F**: makes up 0.5% – 0.8 % of the Hb. It has $2\alpha 2\gamma$ chains.

- **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 (βS) chains and two normal alpha (α) chains.
- The presence of hemoglobin S causes the red blood cell to deform and convert to sickle shape when exposed to decreased amounts of oxygen (such as might happen when someone exercises).

- **Sickled red blood cells can caused:**

- block small blood vessels,
- causing pain
- impaired circulation,
- decrease the oxygen-carrying capacity of the red blood cell,
- decrease the cell's lifespan.

A single beta (βS) copy does not cause symptoms unless it is combined with another hemoglobin mutation, such as that causing Hb C (βC).

- **2. Hemoglobin C (HbC)** is an abnormal hemoglobin in which glutamic acid replaced with a lysine amino acid due to a point mutation in beta-globin chain. The patients with **hemoglobin C trait** (HbAC) (heterozygotes) are phenotypically normal, while patients with **hemoglobin C disease** (HbCC) (homozygotes) may have chronic hemolytic anemia (mild anemia).

- **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. patients who are homozygous for Hb E (have two copies of βE) 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 no causing 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 M, Hemoglobin J, 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 years of age. Hb F may be elevated in several congenital disorders. Levels can be normal to increase 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 disease (HbH)** is a form of **alpha thalassemia** in which moderately severe anemia develops due to reduced formation of alpha globin chains. Normally, there are four genes to produce alpha globin chains. When three out of **four** of these genes become **inactive**, called of hemoglobin H. 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.

- 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 **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.

- 3. **Hemoglobin E – beta thalassemia:** Individuals who are doubly heterozygous for hemoglobin E and beta thalassemia have an anemia that can differ 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.

- **The normal ranges:**
- The normal range of hemoglobin varies depending upon on **age** and **sex.**

- 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.
- 9. Pregnant women: 11 - 14 g/dL

- **Oxygen saturation**
- In general, hemoglobin can be saturated with oxygen molecules (oxyhemoglobin), or desaturated with oxygen molecules (deoxyhemoglobin).