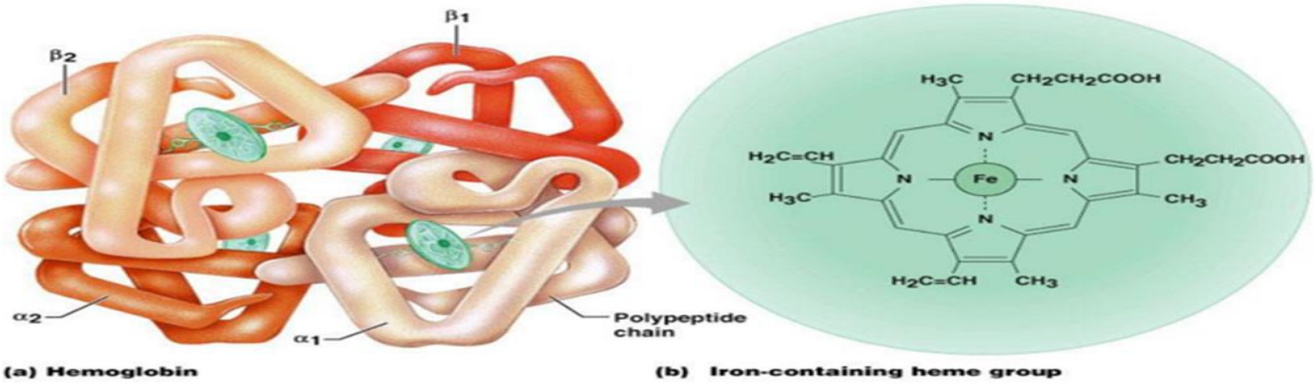
Lecture Three : Hemoglobin structure, types, synthesis, levels in blood

- Hemoglobin (also spelled haemoglobin and abbreviated Hb or Hgb) is the ironcontaining oxygen-transport metalloprotei n in the red blood cells .
- Each molecule of haemoglobin contains four polypeptide (globin) chains and four molecules of haem.
- Globin in adult consist of two alpha (α) chain containing 141 amino acid and two beta (β (chains containing 146 amino acids
- A healthy individual human has 12 to 20 grams of hemoglobin in every 100 mL of blood

Hemoglobin (Hb) structure:

- Each human red blood cell contains approximately 270 million hemoglobin molecules,
- it is a large tetrameric molecule, composed of four globular protein subunits
- Each of four subunits contains; heme group and a globin chain (4 heme and 4 globin subunits
- The four subunits of hemoglobin, each consisting of a heme group surrounded by a globin chain, are held together by salt bonds,



Heme:

- Is the prosthetic group of hemoglobin, is a complex of protoporphyrin IX ring and iron.
- Iron has to be in the ferrous state (Fe2+), otherwise it will not bind to Hb, ferrous iron located in the center of the protoporphyrin ring,
- each heme subunit can carry one molecule of oxygen bound to the central ferrous iron; thus,
- each hemoglobin molecule can carry four molecules of oxygen.

Globin:

- The composition of the globin polypeptide chain is responsible for the different functional and physical properties of hemoglobin.
- Important amino acids that formed circular polypeptide chain of globin include Lysine, Leucine, Aspartate, Glutamate acid and Arginine.
- Four types of globin chains alpha: α, beta β, gama γ and delta δ
- Adult hemoglobin HbA composed from 2 α chains and 2 β chains
- Alpha globin chain composed from 141 amino acids but other chains of globin contains 146 amino acids

Types of Hemoglobin in humans

- Hemoglobin is a heterotetramer composed of 2 α and 2 β polypeptide globin subunits،
- Hemoglobin was one of the first proteins to be sequenced and the globin genes were among the earliest to be cloned, more than 1000 naturally occurring human hemoglobin variants with
- single amino acid substitutions throughout the molecule have been discovered, mainly through their clinical and/or laboratory manifestations.

A-normal types:

1. In adults, these are normal percentages of different hemoglobin molecules

- **HbA: 95% to 98%**
- **HbA2: 2% to 3%**
- **HbF: 0.8% to 2%**

2.In infants and children, these are normal percentage of HbF molecules:

HbF (newborn): 50% to 80% (0.5 to 0.8), decrease after 6 months: 8%, and more than 6 months become 1 - 2%.

1. In the embryo:

- **Gower 1 (δ2ε2)**
- **Gower 2 (α2ε2)**
- **Hemoglobin Portland (δ2γ2)**

2. In the fetus:

- **Hemoglobin F (α2γ2)**

3. In adults:

- **Hemoglobin A (α2β2) - a normal amount 96-98%**

B-abnormal types:

After electrophoresis of hemoglobin, inherited blood disorder in which the body makes an abnormal form of hemoglobin

- **HbH (thalassemia),**
- **HbSS (Sickle cell anemia)**
- **Hb SC, Hb C**
- **Methemoglobin**
- The level of Hb F can be elevated in persons with sickle-cell disease and thalassemia

Hb derivatives: When hemoglobin bind with substances other oxygen produces: All these compound are toxic because incapable to transport O2

- Oxyhemoglobin
- Deoxyhemoglobin
- Methaemoglobin: that formed when Hb bind with KCN (potassium cyanid), Fe+2 converted to Fe+3 and heme converted to hemin
- Carboxyhaemoglobin: formed after CO bind with Hb
- Sulf haemoglobin: come from bind of H2S with Hb

Hemoglobin synthesis:

- About 65% of hemoglobin synthesis occurs in the nucleated stages of RBC maturation and 35% during the reticulocyte stage (nunucleatd).
- **Important factors in hemoglobin synthesis:** Vitamin C, B6, B12, folic acid copper, iron amino acids and residual of hemoglobin results from destroyed old RBC.
- hydrophobic contacts, and hydrogen bonds in a tetrahedral formation giving the hemoglobin molecule a nearly spherical shape

Hemoglobin functions:

1. Hemoglobin is an oxygen carrier.
2. It is a carbon dioxide carrier.
3. Maintains the shape of the red blood cells.
4. Acts as a buffer saver.
5. That interacts with other ligands.
6. Hemoglobin degradation accumulates physiologically active catabolites.

Factors effect on affinity between hemoglobin and O2:

1- PH: the affinity of hemoglobin to oxygen is positively correlated with blood acidity (H+)، the degree of hemoglobin affinity is related to the degree of acidity of the blood, a low pH of the blood means a decrease in the degree of affinity of hemoglobin to combine with oxygen. low PH = low affinity.

2- PCO2 partial pressure of carbon dioxide that have inversely effect on affinity.

3- Temperature have inversely effect on affinity.These three factors, PCO2, PH and temperature called Bohr effect

4- 2,3BPG concentration, also have inversely effect

5- Carbon monoxide CO: it is known as the silent killer since it has no colour or smell, has10 times greater affinity for haemoglobin than oxygen, this means that less oxygen will actually be delivered to our tissues. (make as acompetition for O2 because that it has positive correlation

6- The presence of unusual hemoglobin species, Methaemoglobin, carboxyhaemoglobin and fetal haemoglobin that have positive effect and Sulfhaemoglobin have inversely effect.

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