Globular Proteins

Biochemistry Team 431

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Globular Proteins

- **Amino acid chains fold into shapes that resemble spheres are called globular proteins**
- **This type of folding increases solubility of proteins in water**
- **Polar groups on the protein's surface**
- **Hydrophobic groups in the interior**
- **Fibrous proteins are mainly insoluble structural proteins**

Hydrophilic groups in outside (Solubility of water)

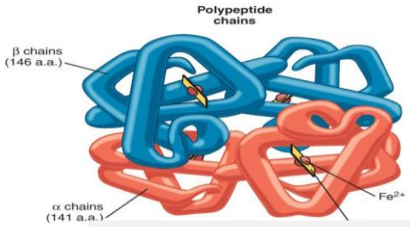
Fibrous proteins are long in shape , so the **Hydrophobic** groups in the outside (example : Collagen

Types of Globular proteins

- **Hemoglobin: oxygen transport function**
- **Myoglobin: oxygen storage/supply function in heart and muscle only.**
- **a1, a2, b-globulins: various functions**
- **g-globulins (immunoglobulins): immune function**
- **Enzymes: catalysis of biochemical reactions**

Hb = 2 a polypeptide chains with heme in each chain + 2 b polypeptide chains with heme in each chain + 2 dimers of ab subunit + 4 O_2 (each heme carry O_2)

Hemoglobin



- **A major globular protein in humans**
- **Composed of four polypeptide chains:**
  - **Two a and two b chains**
- **Contains two dimers of ab subunits**
- **Held together by non-covalent interactions**
- **Each chain is a subunit with a heme group in the center that carries oxygen**
- **A Hb molecule contains 4 heme groups and carries 4 molecules of O2**

The heme is planar structure containing iron.

Each heme carries one molecule of oxygen.

Types of Hemoglobin	
Normal	HbA (97%) , HbA_2 (2%), HbF (1%), HbA_{1c}
Abnormal:	Carboxy Hb ,Sulf Hb, Met Hb

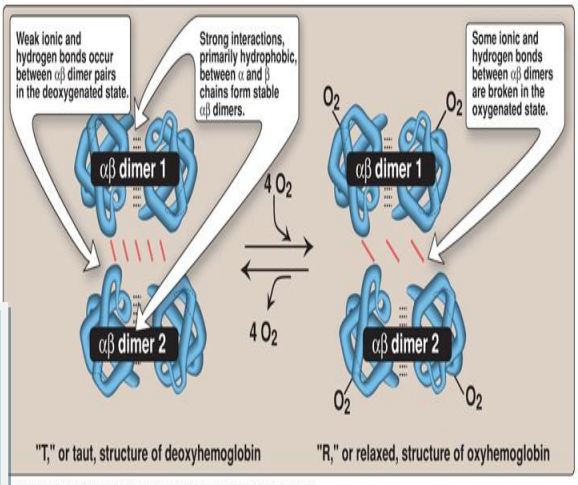
HbA Structure

Hemoglobin function

- **Carries oxygen from the lungs to tissues**
- **Carries carbon dioxide from tissues back to the lungs**
- **Normal level (g/dL):**
  - **Males: 14-16**
  - **Females: 13-15**

HB+O_2=oxyhemogloben and bond is broken (relax).

HB-O_2= deoxyhemogloben and bond is tightened and the number of hydrogen bond (taut)



Oxygen binding to hemoglobin

Fetal hemoglobin (HbF):

- **Major hemoglobin found in the fetus and newborn**
- **Tetramer with two a and two g chains**
- **Higher affinity for O2 than HbA**
- **Transfers O2 from maternal to fetal circulation across placenta**

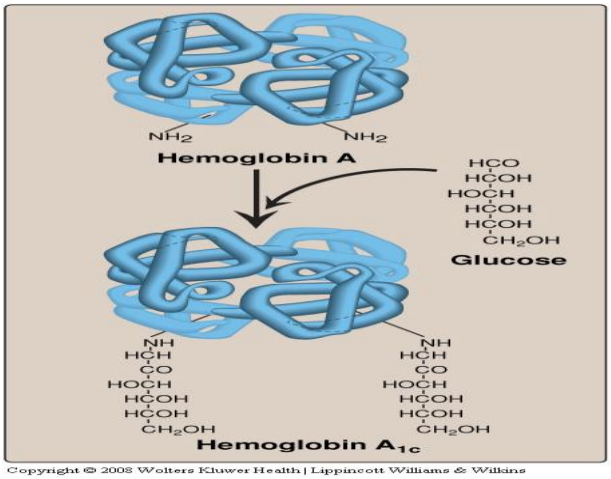
That why HBF is more in fetus so it can get the o_2 from the mother through the placenta.

HbA_2:

- **Appears ~12 weeks after birth**
- **Constitutes ~2% of total Hb**
- **Composed of two a and two d globin chains**

HbA_{1c}:

- **HbA undergoes non-enzymatic glycosylation**
- **Glycosylation depends on plasma glucose levels**
- **HbA1c levels are high in patients with diabetes mellitus**



Abnormal Hbs

- Unable to transport O_2 due to abnormal structure

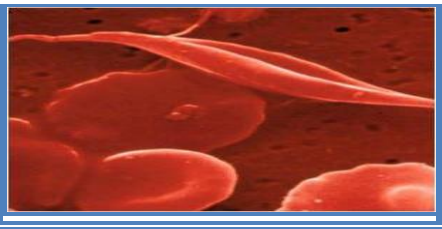
Abnormal Hbs	Characteristic
Carboxy-Hb	CO replaces O_2 and binds 200X tighter than O_2 (in smokers)
Met-Hb	Contains oxidized Fe^{3+} (~2%) that cannot carry O_2"
Sulf-HB	Forms due to high sulfur levels in blood

The normal is **Fe^{2+}**

Sometime if sulfate is too high it might be irreversible. But there is a very low values of it in the blood normally.

It is caused by (Point Mutation)

Hemoglobinopathies

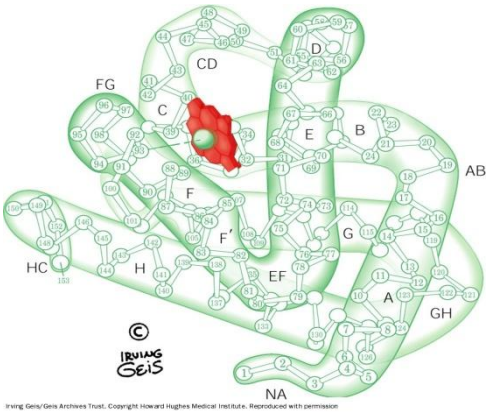
disease	Characteristic
Sickle cell (HbS) disease 	**-Caused by a single mutation in b-globin gene -Glutamic acid at position 6 in HbA is replaced by valine -The mutant HbS contains bs chain -The shape of RBCs become sickled Causes sickle cell anemia**
Hemoglobin C disease:	**-Caused by a single mutation in b-globin gene -Glutamic acid at position 6 in HbA is replaced by lysine -Causes a mild form of hemolytic anemia**
Methemoglobinemia	**- Caused by oxidation of Hb to ferric (Fe3+) state -Methemoglobin cannot bind oxygen -Caused by certain drugs, reactive oxygen species and NADH-cytochrome b5 reductase deficiency -Chocolate cyanosis: brownish-blue color of the skin and blood**
Thalassemia: **-Defective synthesis of either a or b-globin chain due to gene mutation**	**a-thalassemia:** **-Synthesis of a-globin chain is decreased or absent -Causes mild to moderate hemolytic anemia b-thalassemia: -Synthesis of b-globin chain is decreased or absent , -Causes severe anemia -Patients need regular blood transfusions**

Myoglobin

- A globular hemeprotein in heart and muscle
- Stores and supplies oxygen to the heart and muscle only
- Contains a single polypeptide chain forming a single subunit with eight a-helix structures
- The interior of the subunit is composed of nonpolar amino acids

Structure of myoglobin

- The charged amino acids are located on the surface
- The heme group is present at the center of the molecule
- Myoglobin gives red color to skeletal muscles
- Supplies oxygen during aerobic exercise

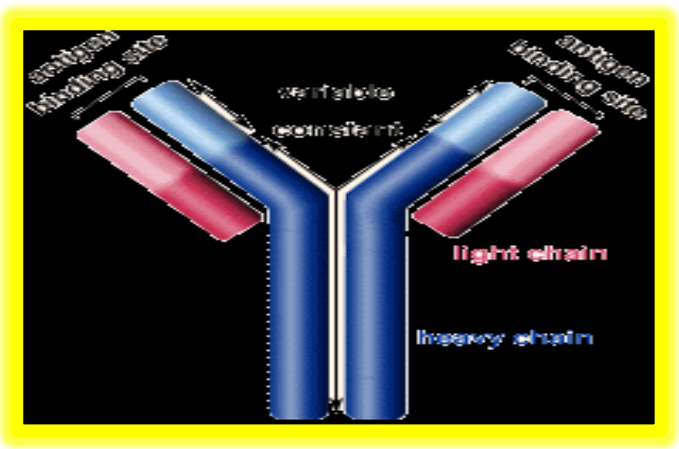


Myoglobin in disease

- Myoglobinuria: Myoglobin is excreted in urine due to muscle damage (rhabdomyolysis)
- May cause acute renal failure
- Specific marker for muscle injury
- Less specific marker for heart attack

Immunoglobulins

- Defensive proteins produced by the B-cells of the immune system
- Y-shaped structure with 2 heavy and 2 light polypeptide chains
- Neutralize bacteria and viruses
- Types: IgA, IgD, IgE, IgG, IgM



Review Question

1- <u>The Normal level of Hemoglobin in the male is :</u>

A- 14-16 (g/dL)

B-12-14 (g/dL)

C- 13-15(g/dL)

D-16-20(g/dL)

<u>2-which of the following statement is correct about Fetal hemoglobin (HbF)</u>

A-specific marker for muscle injury

B-Contains two dimers of ab subunits

C-Contains Tetramer with two a and two g chains

D- Contains a single polypeptide chain forming a single subunit with eight a-helix structures

<u>3-which of the following is correct regarding Sickle cell disease ?</u>

A-Glutamic acid at position 5 in HbA is replaced by valine

B-Glutamic acid at position 6 in HbA is replaced by lysine

C-Caused by oxidation of Hb to ferric (Fe^{3+}) state

D-non above

<u>4- which of the following is correct regarding b-thalassemia</u>

A-Causes mild to moderate hemolytic anemia

B-Causes severe anemia

C- the patient suffers from Chocolate cyanosis

D-Caused by a single mutation in b-globin gene

- **Answers**

1-A

2-C

3-D

4-B