

# Biochemistry Team

## Globular Proteins 2<sup>nd</sup> Lecture

Done by:

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## Globular Protein

Amino acid chains fold into shapes that resemble **spheres** called **globular proteins**

This type of folding increases solubility of proteins in water

Polar groups on the protein's surface

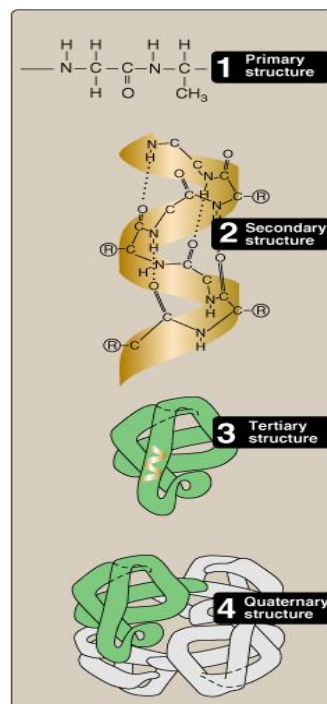
Hydrophobic groups in the interior

Fibrous proteins are mainly insoluble structural proteins.

باختصار الـ **Globular proteins** كروي بحيث أن محيطه يذوب في الماء أما الجزء الداخلي لا يذوب في الماء

### Protein Structures (phases)

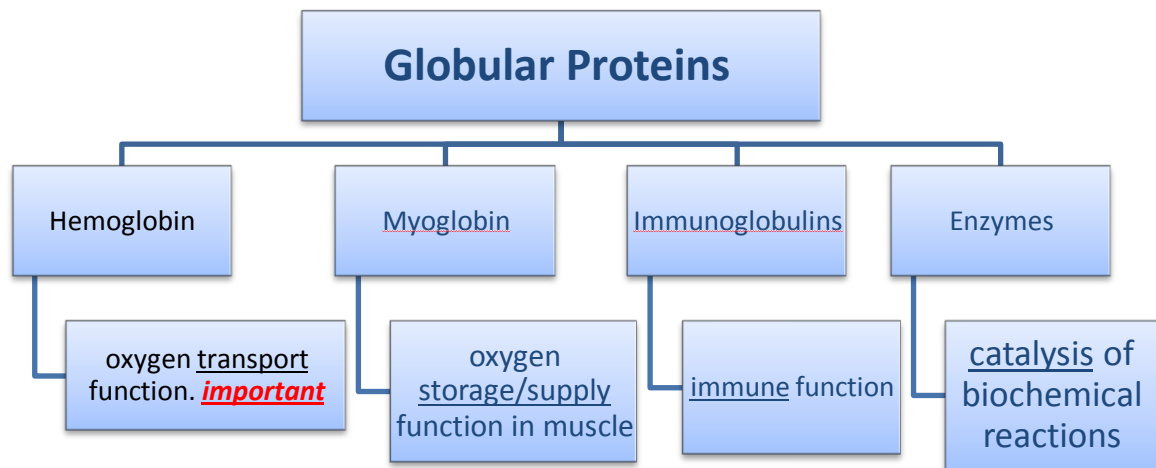
just to understand !



**Figure 2.1**

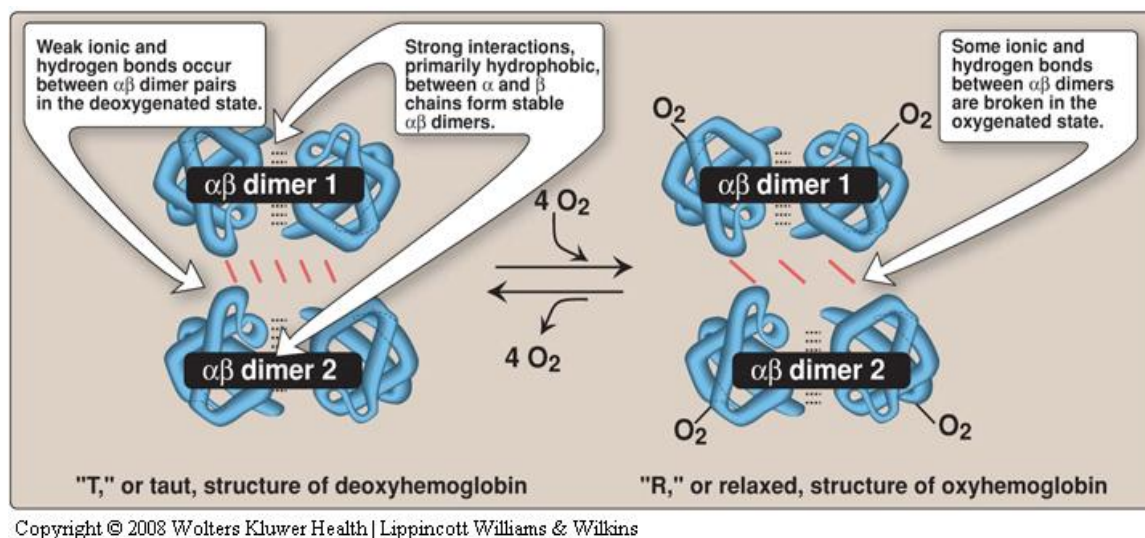
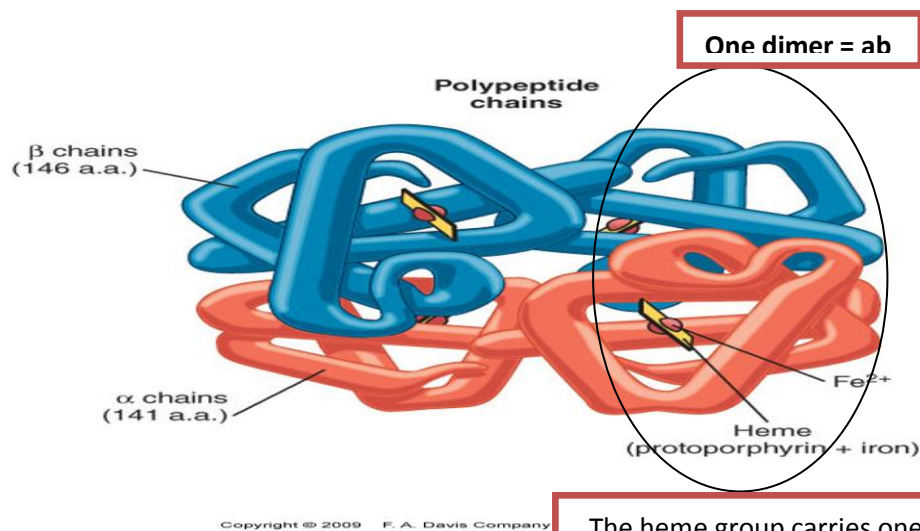
Four hierarchies of protein structure.

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### 1st type: Hemoglobin

- Major globular protein in humans
- Composed of **four** polypeptide chains:
  - Two  $\alpha$  and two  $\beta$  chains ( subunits)  
( Beta more important than alfa)
- Contains two dimers of  $\alpha\beta$  subunits
- Held together by non-covalent bonds  
(ionic or hydrogenic bond) interactions
- Each chain is a subunit with a heme group in the center that carries oxygen.
- 1 Hb molecule contains 4 heme groups and carries 4 molecules of  $O_2$ .



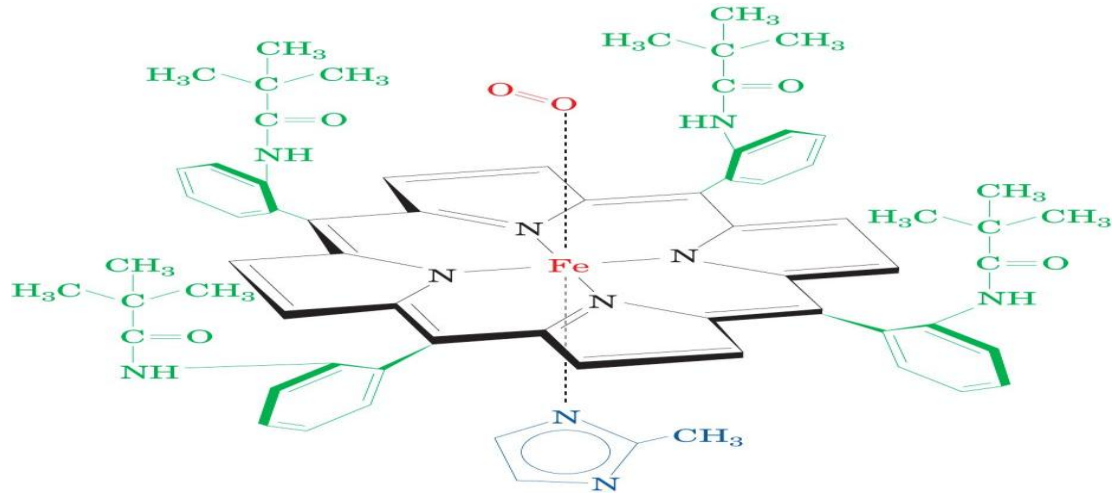
Non covalent bond will be weak bond in present of O<sub>2</sub>

## ■ - The heme group:

A complex of protoporphyrin IX and ferrous iron (Fe<sup>2+</sup>)

- Fe<sup>2+</sup> is present in the center of the heme
- Binds to four nitrogen atoms of the porphyrin ring
- Forms two additional bonds with:
  - Histidine residue of globin chain
  - Oxygen

في مركب الهيم:  
الحديد يرتبط بأربع روابط مع النيتروجين ،  
و الرابطة الخامسة مع الـ Histidine (أسفل)  
و السادسة مع جزئ أوكسجين.



### - Forms of Hemoglobin

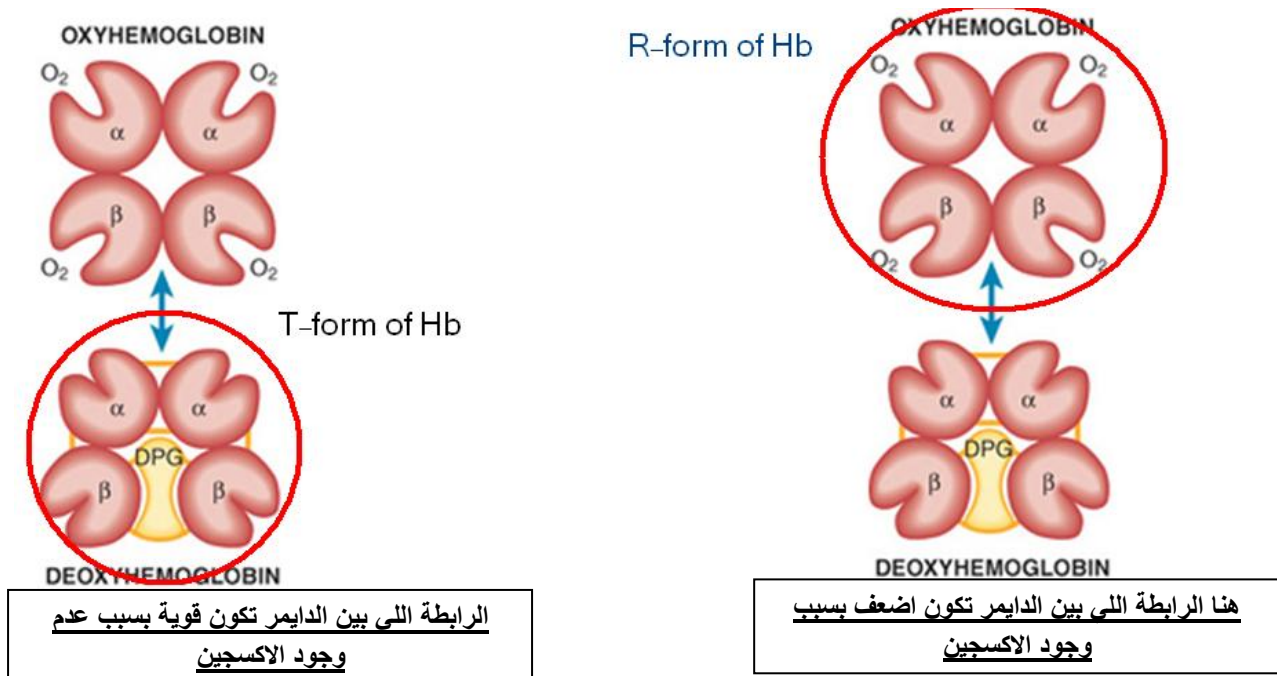
T-form of Hb

R-form of Hb

- The deoxy form of Hb
- **Taut form**
- The movement of dimers is constrained
- **Low-oxygen-affinity form**

- The oxygenated form of Hb
- **Relaxed form**
- The dimers have more freedom of movement
- **High-oxygen-affinity form**

## Comparing of Hb's Forms



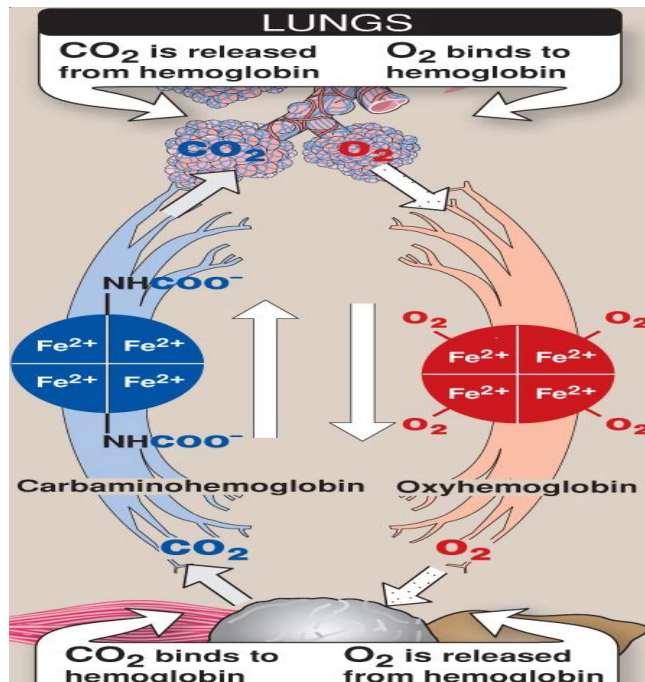
### - Hemoglobin function:

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

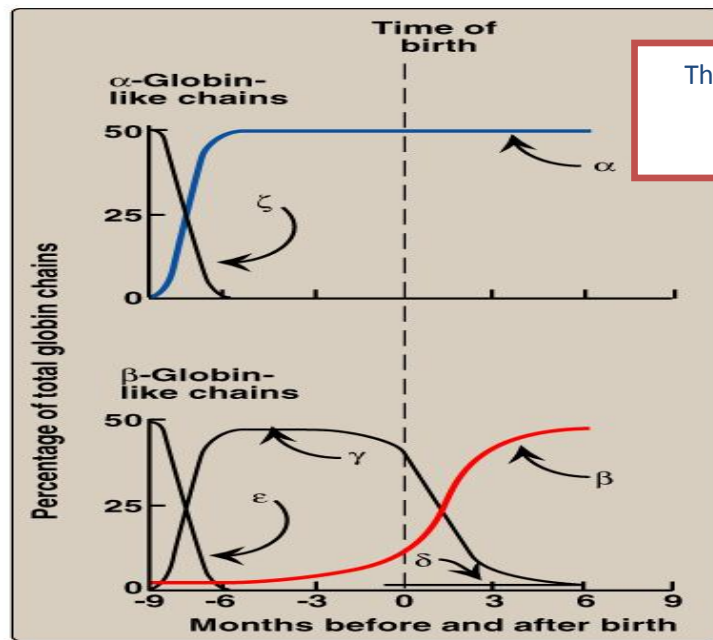


## - Types Of Hb

### 1-Fetal hemoglobin (HbF): (actually, fetal has NO HbA)

- Major hemoglobin found in the fetus and newborn (until 28 days)
- Tetramer with two  $\alpha$  and two  $\gamma$  chains
- Higher affinity for O<sub>2</sub> than HbA
- Transfers O<sub>2</sub> from maternal to fetal circulation across placenta.

هذا النوع ينقل الأكسجين من البلاسنتا للجنين  
ويختفى بعد الولادة (يوجد بنسبة ضئيلة جدا)



This pic just to show how Hb changes during & after birth

**Figure 3.14**  
Developmental changes in hemoglobin.  
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Appears ~12 weeks after birth

Constitutes ~2% of total Hb ■

Composed of two α and two δ globin chains.

γ	→	HbF
α	→	HbA
δ	→	HbA <sub>2</sub>



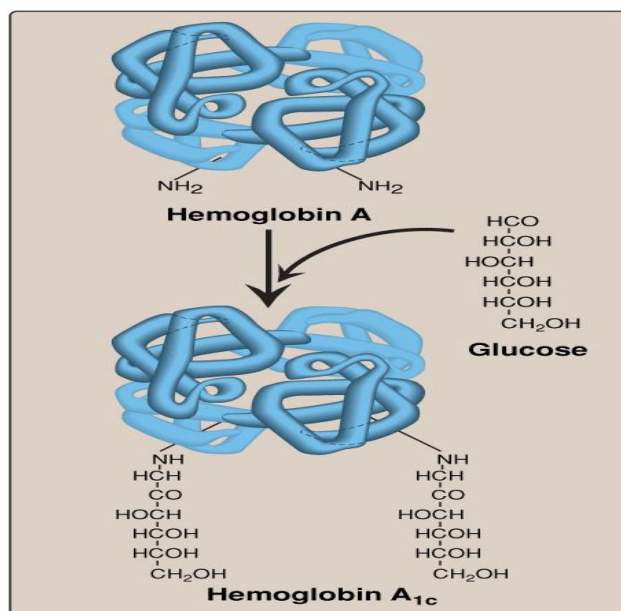


### 3-HbA<sub>1c</sub>

HbA undergoes non-enzymatic glycosylation

Glycosylation depends on plasma glucose levels

HbA<sub>1c</sub> levels are high in patients with diabetes mellitus



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**Glycosylation: add sugar to protein**

A table with Hb Types

Normal:	
له الأغلبية في الهيموقلوبين الطبيعي	HbA (97%)
تجده في الرضيع حتى ٣ أشهر	HbA <sub>2</sub> (2%)
في الجنين	HbF (1%)
في مرضى السكر	HbA <sub>1c</sub>
Abnormal:	
	Carboxy Hb
	Met Hb
	Sulf Hb

## - Hemoglobinopathies

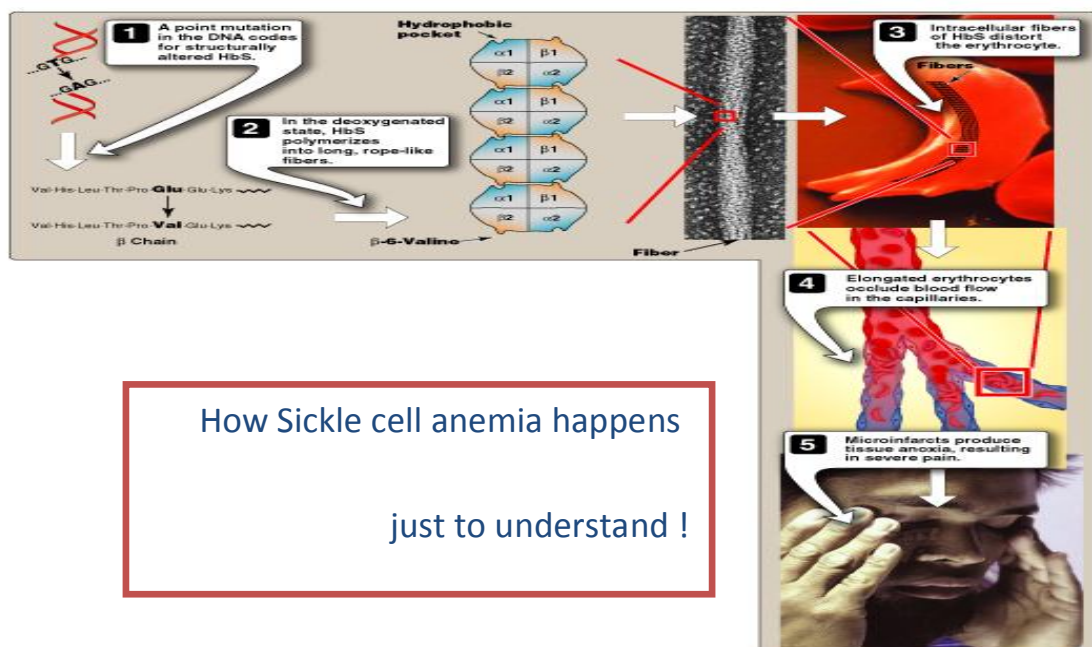
**\*Disorders of hemoglobin caused by:**  
 Synthesis of **structurally** abnormal Hb  
 Synthesis of insufficient **quantities** of normal Hb  
 Combination of **both**

### 1-Sickle cell (HbS) disease

Caused by a single mutation in  $\beta$ -globin gene  
 Glutamic acid in HbA is replaced by valine

The mutant HbS contains  $\beta$  chain  
 The shape of RBCs become sickled  
 Causes sickle cell anemia

المرض هذا يكون فيه تغير بسلسلة الببتا حيث يأتي الفالين بدلا عن القلوتاميك اسيد



How Sickle cell anemia happens

just to understand !

**Figure 3.21**  
 Molecular and cellular events leading to sickle cell crisis.

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**2-Hemoglobin C disease:**

Caused by a single mutation in  $\beta$ -globin gene

Glutamic acid in HbA is replaced by **lysine**

Causes a mild form of hemolytic anemia

**3-Thalassemia:**

Defective synthesis of either  $\alpha$  or  $\beta$ -globin chain due to gene mutation

 **$\alpha$ -thalassemia:**

Synthesis of  $\alpha$ -globin chain is decreased or absent

Causes mild to moderate hemolytic anemia

 **$\beta$ -thalassemia:**

Synthesis of  $\beta$ -globin chain is decreased or absent

Causes severe anemia

Patients need regular blood transfusions

**4-Methemoglobinemia:**

Caused by oxidation of Hb to ferric ( $\text{Fe}^{3+}$ ) 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

**5-Abnormal Hbs:**

Unable to transport  $\text{O}_2$  due to abnormal structure

**Carboxy-Hb: CO replaces  $\text{O}_2$  and binds 200X tighter than  $\text{O}_2$  (in smokers)**

**Met-Hb: Contains oxidized  $\text{Fe}^{3+}$  (~2%) that cannot carry  $\text{O}_2$**

**Sulf-HB: Forms due to high sulfur levels in blood (irreversible reaction)**

يعني اذا ارتبط الهيموقلوبين مع السولفات يستحيل فصلهم

	Set of changes	Changes	Disease
HbS	Beta chain	Glutamic acid TO valine	Sickle cell anemia
HbC	Beta chain	Glutamic acid TO lysin	Mild hemolytic anemia
Meth-Hb	ferrus	Fe++ TO Fe+++	Methemoglobinemia
Thalassemia	Beta chain	يقل انتاج الهيموقلوبين	Severe anemia
	Alfa chain		Mild anemia

- 2<sup>nd</sup> Type of Globular Protein :

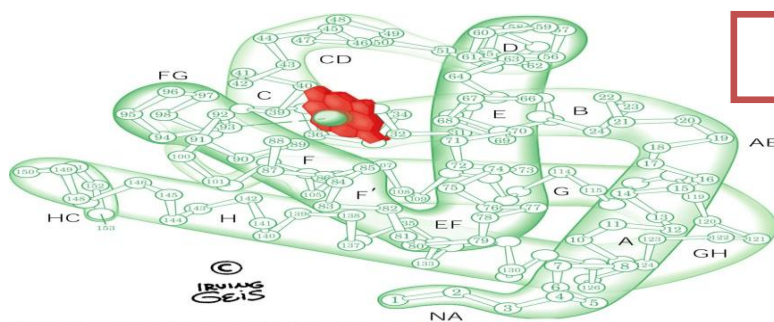
### Myoglobin

A globular hemeprotein in heart and muscle

Stores and supplies oxygen to heart and muscle

Contains a single polypeptide chain forming a single subunit with eight  $\alpha$ -helix structures

The interior of the subunit is composed of nonpolar amino acids



Structure of Myoglobin

## Cont. Myoglobin

The charged ( **polar** ) 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

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.

أهم نقطة في بروتين الميوغلوبين ، أنه يحمل جزئ  
أوكسجين واحد فقط !

أما الهيموغلوبين فيحمل أربع جزيئات أوكسجين.