وَقُل رَّبِّ زِدْنِي عِلْمًا

النادي الطبي

RESPIRATORY SYSTEM

HAYAT BATCH

SUBJECT : Biochemistry

LEC NO. : 4

DONE BY : Esra'a Khaled

Respiratory System

Role of hemoglobin in acid base balance

* بداية المحاضرة في مراجعة سريعة للهيموغلوبين

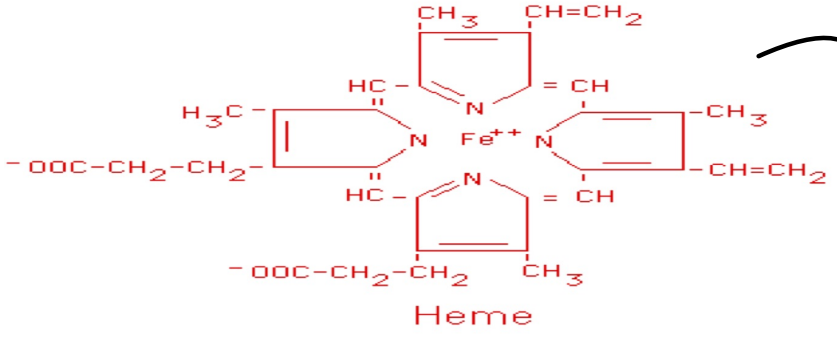
Hemoglobin : Heme + globin

Formed of 4 polypeptide chains , Each polypeptide chain is formed of 7 or 8 helices which are termed A-B-C-D...

* α-chain → 141 A.A / on chromosome 16

* β-γ-& chains → 146 A.A / on chromosome 11

* Hb A is composed of two identical dimers (αβ)1 and (αβ)2



- Porhyrin ring , 4 pyrrole ring
- ferrous iron
- has 6 valencies
- carries O2

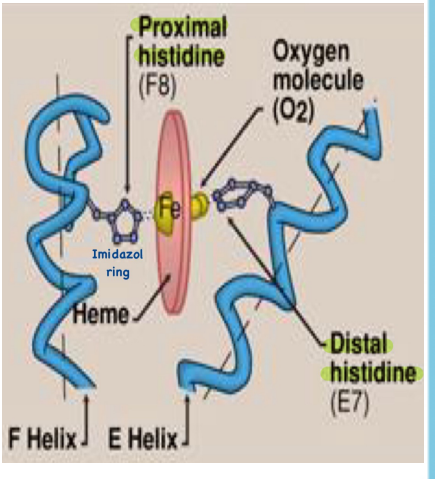
*Each polypeptide binds a heme molecule at its center (4 heme residues per Hb molecule) and lies in a pocket (hdrophobic cleft) between E and F helices

*The iron of heme is coordinated with the nitrogen of the imidazole ring of one histidine .

In F helix → proximal histidine

In E helix → distal histidine

lies near the heme but is not bonded to it and it stabilizes binding of oxygen to heme and destabilizes binding of carbon monoxide



* The 2 polypeptide chains of each dimer are tightly held together by hydrophobic bonds بين α و β

*Each dimer is held relatively loosely to the other dimer by ionic and hydrogen bonds بين αβ و αβ

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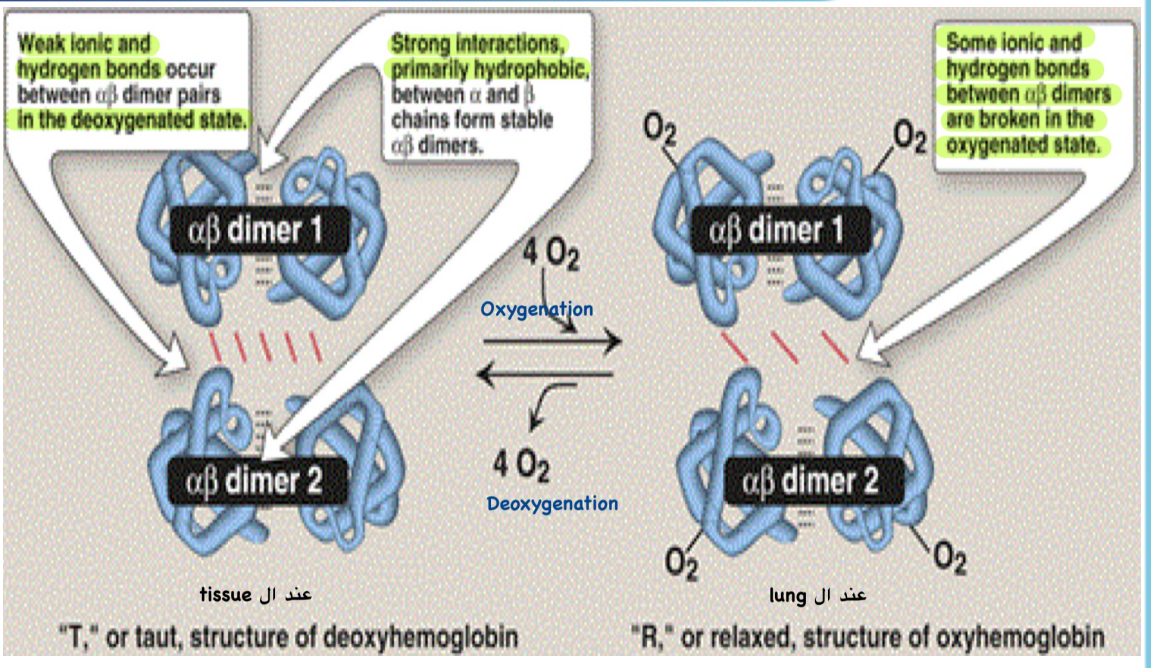
Respiratory System

There are 2 forms of Hb : Tense and relax



* Binding of oxygen to Hb is facilitated by previous binding of other oxygen molecules (cooperative binding kinetics)

* The affinity of Hb for the last oxygen molecule is about 300 times greater than for the first oxygen molecule

* This pulls the proximal histidine towards the porphyrin ring and is accompanied by deprotonation of the imidazole ring of histidine and of N-terminal amino groups in the peptide chain

* This leads to rupture of salt bonds between globin chains, and Hb changes from the T to R state , increasing its affinity for oxygen

* This is sometimes called heme-heme interaction

T form (Hb)	R form (Hb)
1. Tense form 2. more ionic bonds 3. Stabilized by protonation 4. Stabilized by deoxygenation 5. Lower affinity for O2	1. Relaxed form 2. Less ionic bonds 3. stabilized by deprotonation 4. Stabilized by oxygenation 5. Higher affinity for O2

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Respiratory System

Allosteric properties of Hb

Other Site

* The ability of Hb to reversibly bind oxygen is affected by :
  1. PO2
  2. PH of the environment
  3. PCO2
  4. Availability of 2,3-bisphosphoglycerate

* called allosteric effectors because their interaction at one site on the Hb molecule affects the binding of oxygen to heme groups at other locations on the molecule

1. CO2 : $Hb-NH_2 + CO_2 \rightarrow Hb-NH-COO^- + H^+$

This gives Hb a negative charge , increases the formation of ionic bonds, which stabilizes the T-form
The affinity of Hb for oxygen decreases , helping delivery of oxygen to the tissues

2. PH (The Bohr effect) : $Hb-O_2 + H^+ \rightarrow Hb-H^+ + O_2$

Most of the CO2 delivered by the tissues to the blood is converted to H2CO3 in the red blood cells

H2CO3 liberates hydrogen ions ($H_2CO_3 \rightarrow HCO_3^- + H^+$) which protonate the N-terminal amino groups of the α- subunits and the C-terminal histidine of the β- subunits , stabilizing the T-form

* Bohr effect : The influence of pH and pCO2 to facilitate oxygenation of Hb in the lungs and deoxygenation at the tissues

3. 2,3-Bisphosphoglycerate :

carries 5 negative charges and is derived from oxidation of glucose (glycolysis) in red cells .

* It binds to a positively charged pocket in Hb between the 2 β chains

* Binding favors the T-form of Hb , reducing affinity for oxygen and helping delivery of oxygen to tissues

* BPG increases in RBCs in case of chronic anemia and hypoxia

* Adding inosine to blood keeps the level of BPG normal in RBCs

* Chloride shift (hamburger effect) : Entering a chloride ions from the plasma to the cells

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