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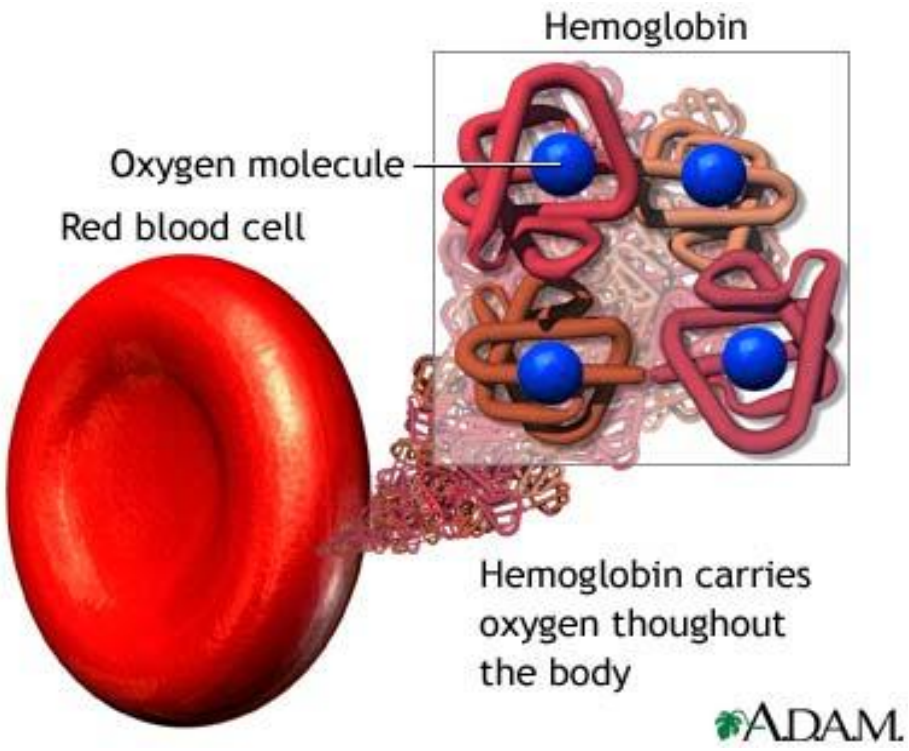


What is the hemoglobin (HB)?

hemeprotein found only in red blood cells

what is it function?

It binds reversibly to O2 , so it is O2 transporter from lung to tissues

It is formed of 2 components :

heme as prosthetic group * and **globine** that is protein

***prosthetic group** → non-protein molecule attached to the protein to make it functioning.

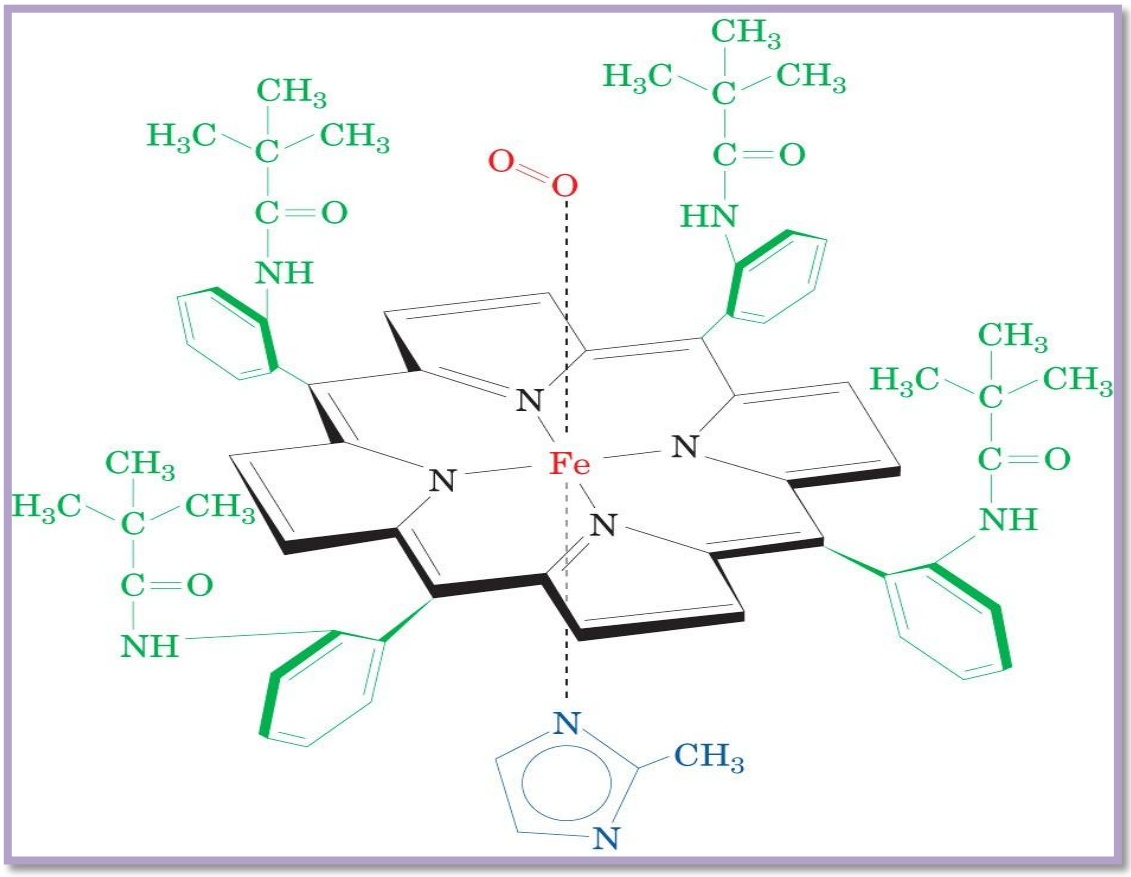
The heme group is formed of :

1-protoporphyrine IX (9) that form a ring

2-ferreus iron Fe^{++} that is located at the center of the heme

Ferreus iron has 6 bonds , **they are :**

4 bonds with 4 nitrogens (N) of the protophyrine ring , 1 with histidine residue of globin chain and the last to the O2



HB type	Formed of	Normal level	Found in	Relation with O2	function
HB A	α 2 β 2	97% Male 14-16g/dl Female 13-15 g/dl	Adult	Affected by Three allosteric effectors	-Carries O_2 from the lungs to tissues -Carries CO_2 from tissues back to the lungs
HB F	α 2 γ 2	1 %	Fetus and newborn	Higher O2 affenety than HB A	Transfers O_2 from maternal to fetal circulation across placenta
HB A_2	α 2 δ 2	2 %	Appears 12 weeks after birth		
HBA_{1c}	Hb A undergoes non-enzymatic glycosylation (depending on plasma glucose)				HbA1c levels are high in patients with diabetes mellitus
Carboxy-Hb	CO carried by HB instead of O_2				CO replaces O_2 and binds 200X tighter than O_2 (in smokers)
Met-Hb	Contains oxidized Fe^{3+}	~2%		cannot carry O_2	
Sulf-HB	due to high sulfur levels in blood				irreversible reaction

Normal HB

Abnormal HB

Hbs : Unable to transport O_2 due to abnormal structure

HB A

Composed of four polypetide chains:

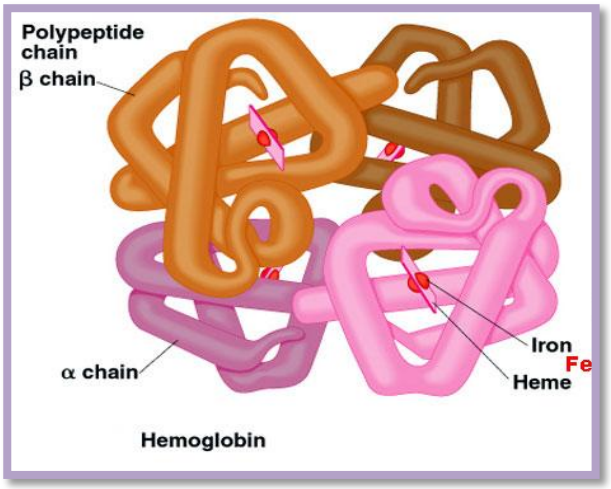
Two α and two β chains

Contains two dimers of αβ subunits

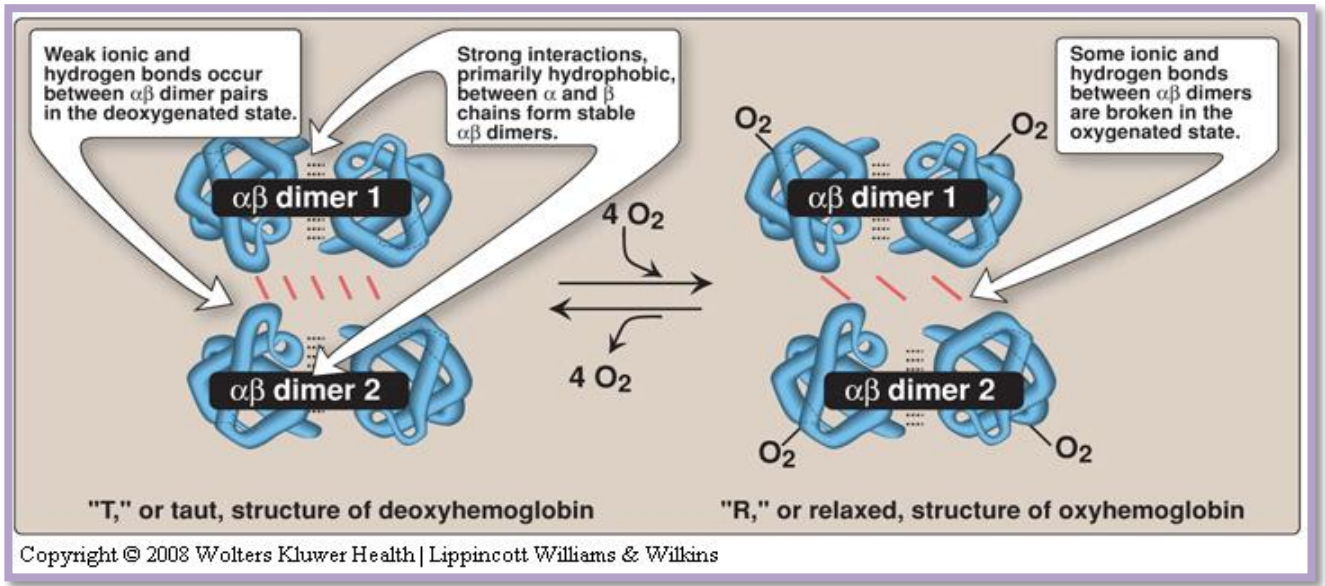
α & β chains Held together by non-covalent hydrophopic interactions

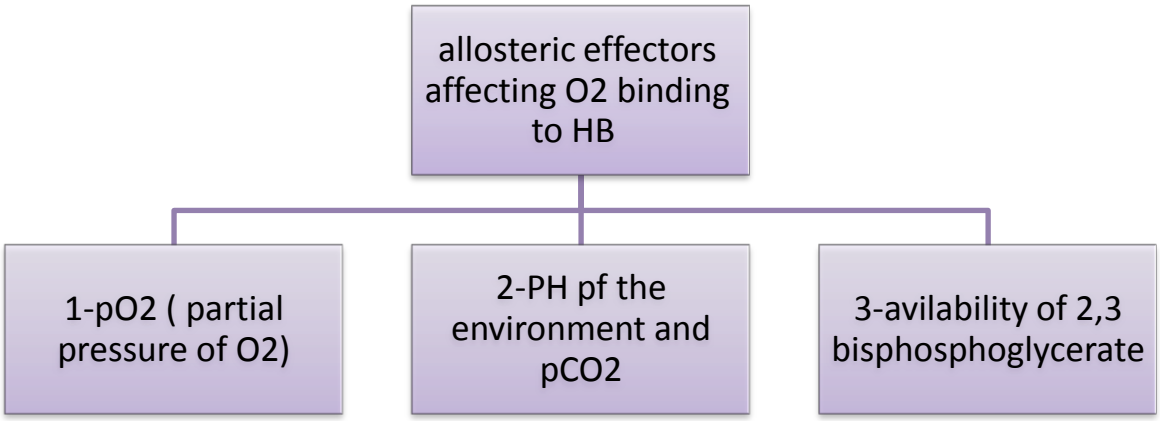
the bonds **between the 2 dimers αβ=αβ** is week ionic and hydrogene

Each chain is a subunit with a heme group in the center that carries oxygen, so the HB is able to carry 4 O2 molecules (because it`s formed of 4 chains



HB structure	Form of HB is	movement	O2 affinity
T (taut) form	Deoxy HB (not attatched with HB	The movement of dimers is constrained	Low affinity
R (relaxed) form	Oxy HB (attatched with HB)	dimers have more freedom of movement	High affinity





O_2Dissociation Curve:

It is sigmoidal shaped curve → indicates the cooperation of subunits in O_2 binding

(so when ↑pO_2 → ↑saturation of HB to O_2→Increasing the HB affinity to O_2)

That means Binding of O2 to one heme group increases O2 affinity of others and that`s called (heme-heme interaction) that the affinity of hemoglobin for the last oxygen bound is approximately 300 times greater than its affinity for the first oxygen bound.

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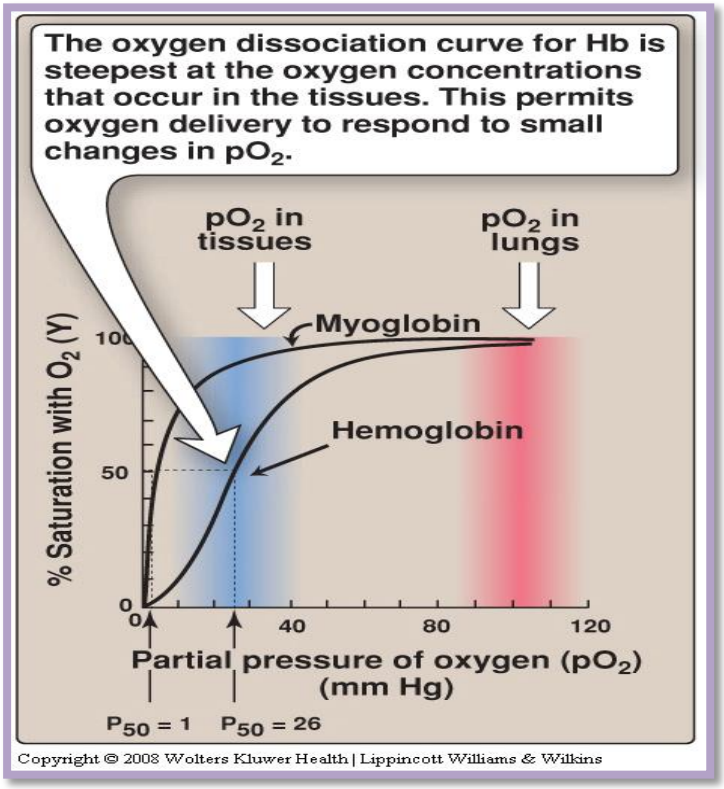
So oxygenation favors → R form

Deoxygenation favors → T form



The ellosteric factor	What is it	When / where increase	When / where decrease
1- pO2 indecates affinity of HB to O2	the pressure at which Hb is 50% saturated with O2 that means the pressure needs to make the haltf of HB saturated with O2.	In lungs will cause: High affinity → slow unloading of O2. Saturation in lung 100% because the PO2 is 100mm. So O2 will be taken from the lungs.	In tissues Will cause Low affinity → fast unloading of O2so saturation reduced because the Po2 in tissues is 40mm So O2 will be delivered to tissues.
2- PH+CO2 = Bohr Effect	Bohr effect : - removes insoluble CO2 from blood stream - Produces soluble bicarbonate	In the lungs : The free Hb (after releasing of O2 into the tissues) binds to two protons Protons are released and react with HCO3 – to form CO2 gas The proton-poor Hb now has greater affinity for O2 .	In tissues : They have ↓ PH (acidic) than the lungs Due to proton generation: CO2 + H20 → HCO3- + H+ Proton ↓O2 affinity of HB→ easier O2 release into the tissues.
3- 2,3bisphosphoglycerate (BPG)	-Binds to deoxy-Hb and stabilizes the T-form -When oxygen binds to Hb, BPG is released	In high altitude as a compensatory mechanism to decrease O2 affinity of HB and deliver it faster to tissues -High altitude→ ↓O2 concentration →hypoxia→↑2,3BPG→ ↓O2 affinity→↑O2 delivery to tissues	

So as a conclusion: