

Hemoglobin & Myoglobin

By Tess Warchalowski



Clinical

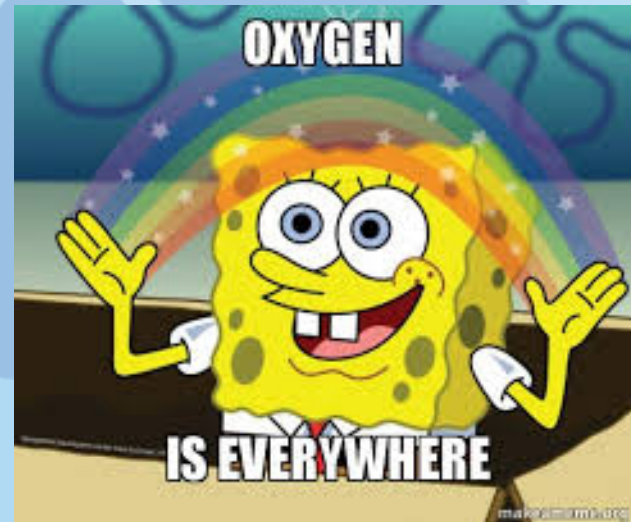
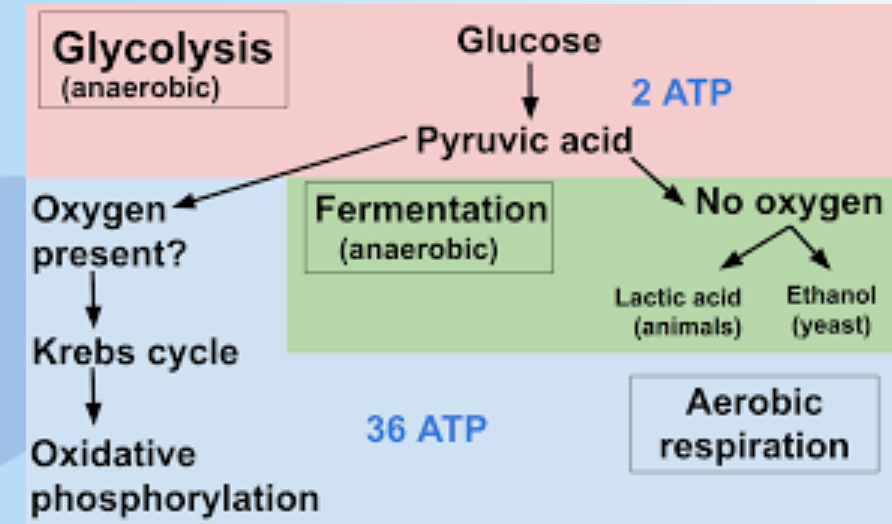
Your professor asks you why his skin is blue- what do you answer?



- A) He had a wild night out
- B) He's been hypoxemic for a while
- C) He recently had an infection and is taking the antibiotic dapsons
- D) He is a Smurf

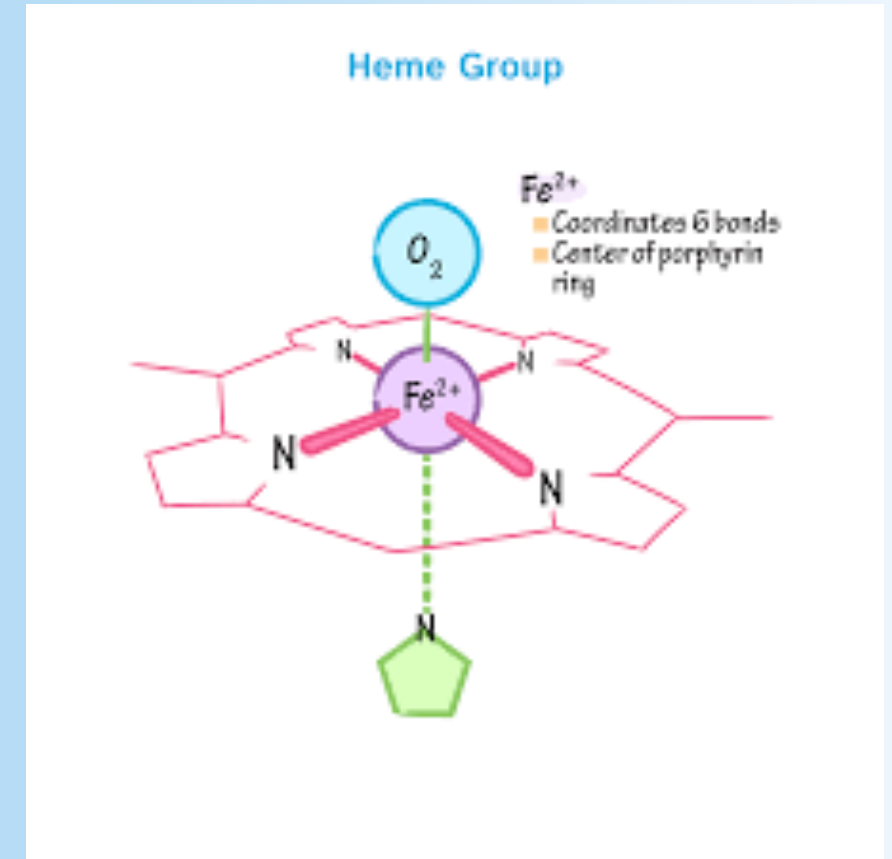
Basics

- We need oxygen for life! = **Produces More ATP**
- Problem= O₂ has low solubility In blood
- **Free oxygen is harmful to tissues !**
- Need something to transport it



Heme Structure

- Normal adult hemoglobin has 4 hemes
- Protoporphyrin IV + Fe^{2+}
- 1 heme= binds one O_2
- Key for most living cells!

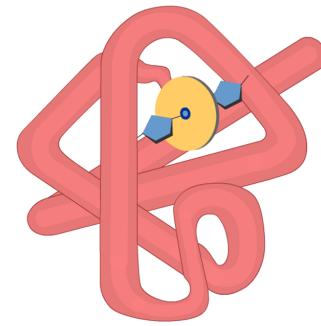


Myoglobin

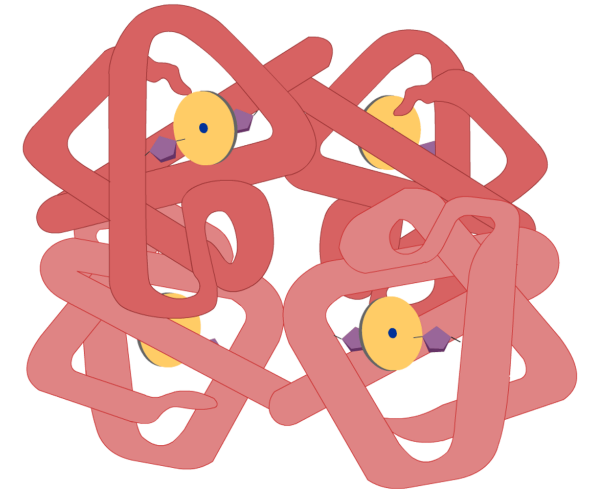
- Stores O₂ in heart and Skeletal muscle
- Binds 1 O₂ molecule!!
- High O₂ affinity (too strong!)

Clinical

- High myoglobin levels indicate muscle breakdown!
 - Myocardial infarction
 - Rhabdomyolysis



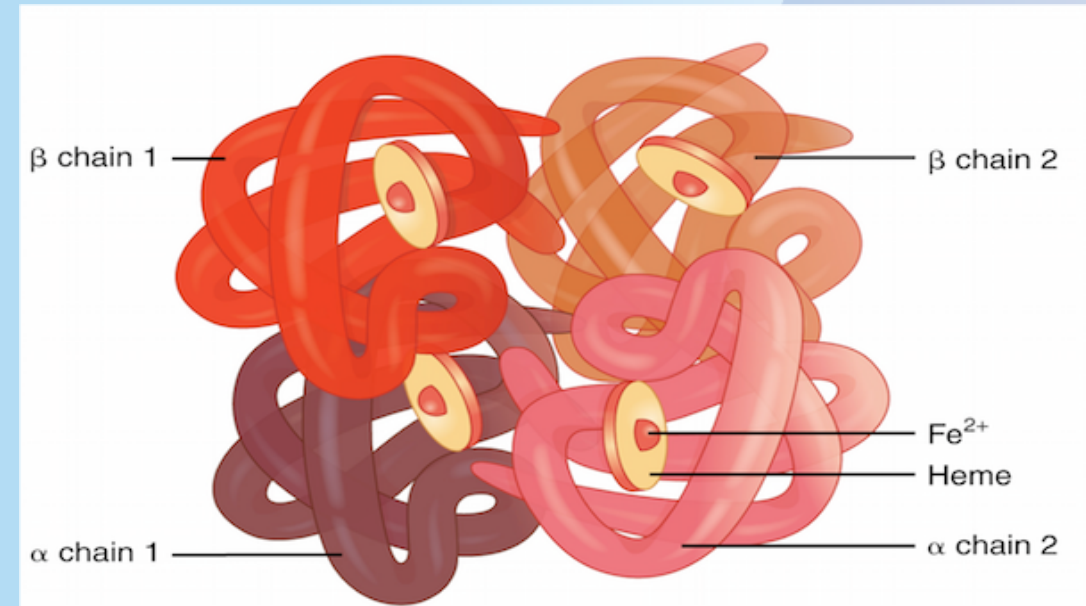
Myoglobin



Hemoglobin

Hemoglobin

- Found in RBC- O₂ transport!
- Binds 4 O₂ molecules
- Composed of 2 dimers (4 units in total)
 - Alpha
 - Beta
 - Gamma
 - Delta
- Sub types
 - **HbA: 2 alpha, 2 Beta**
 - HbF: 2 alpha, 2 Gamma
 - HbS: many types, 2 alpha, beta chains= mutated

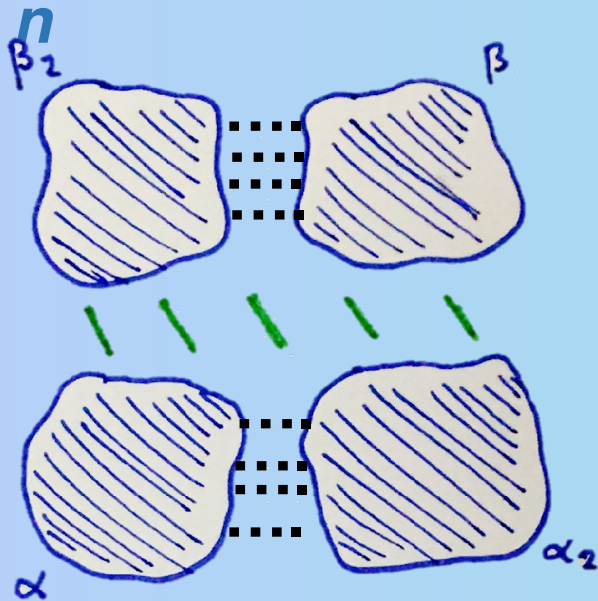


Hb + Oxygen
= Relaxed

T vs R form

T form

Deoxyhemoglobin

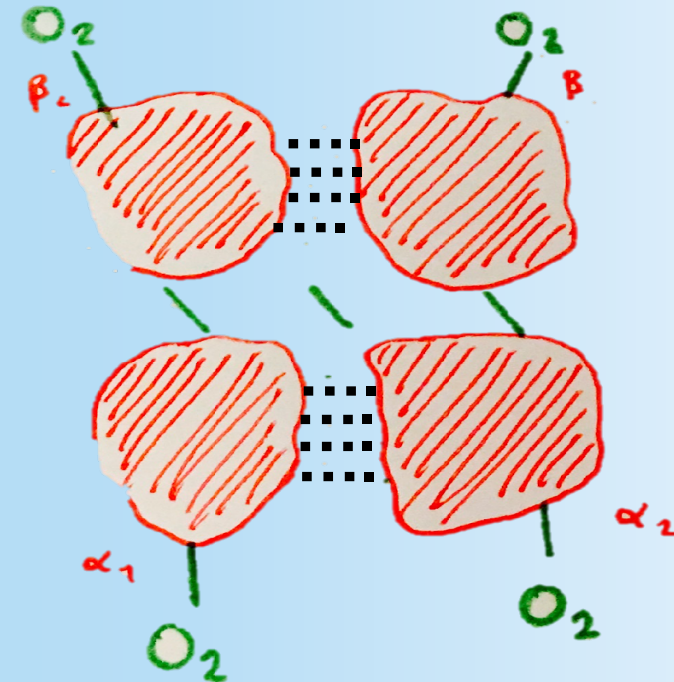


O_2



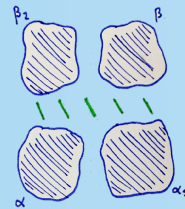
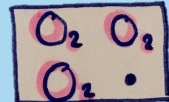
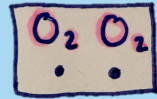
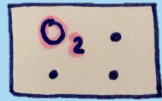
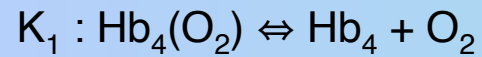
R form

Oxyhemoglobin

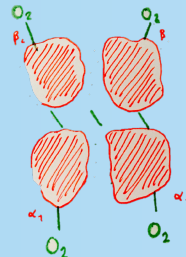


Hemoglobin Cooperativity

- Hb affinity for O₂ depends on ppO₂
- Affinity for O₂ increases with more O₂ binding



T form



R form

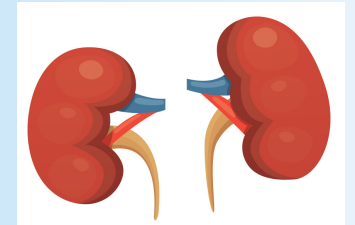
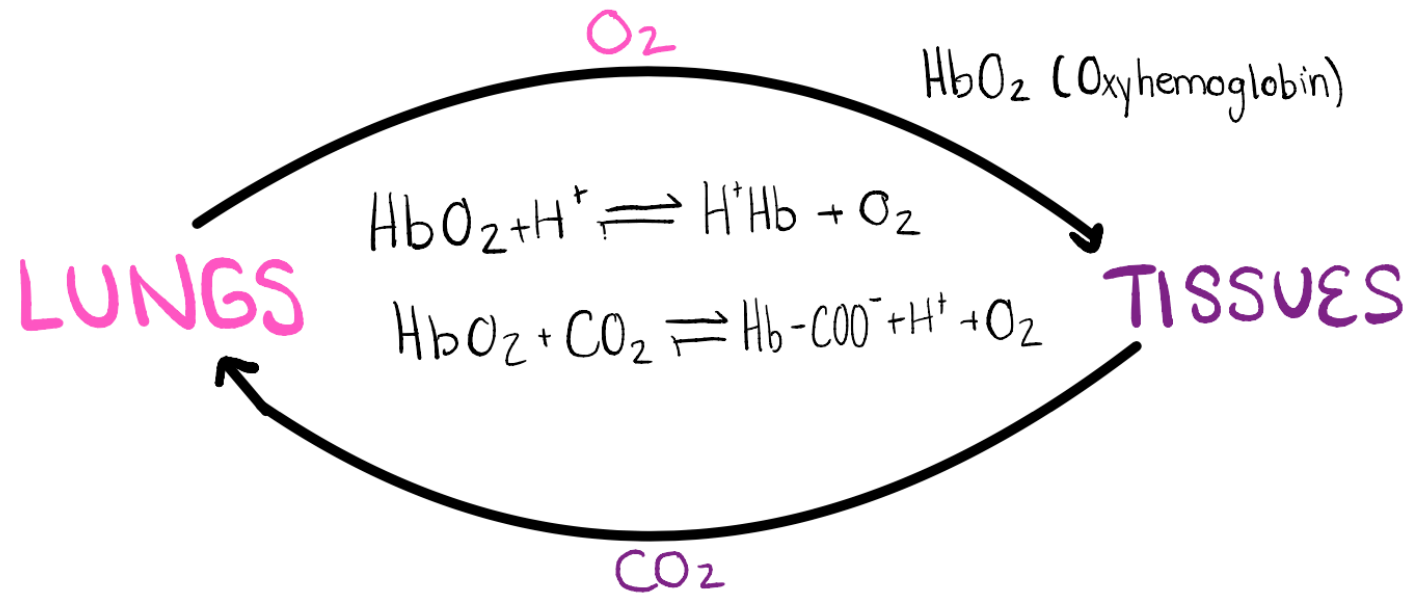
TISSUES



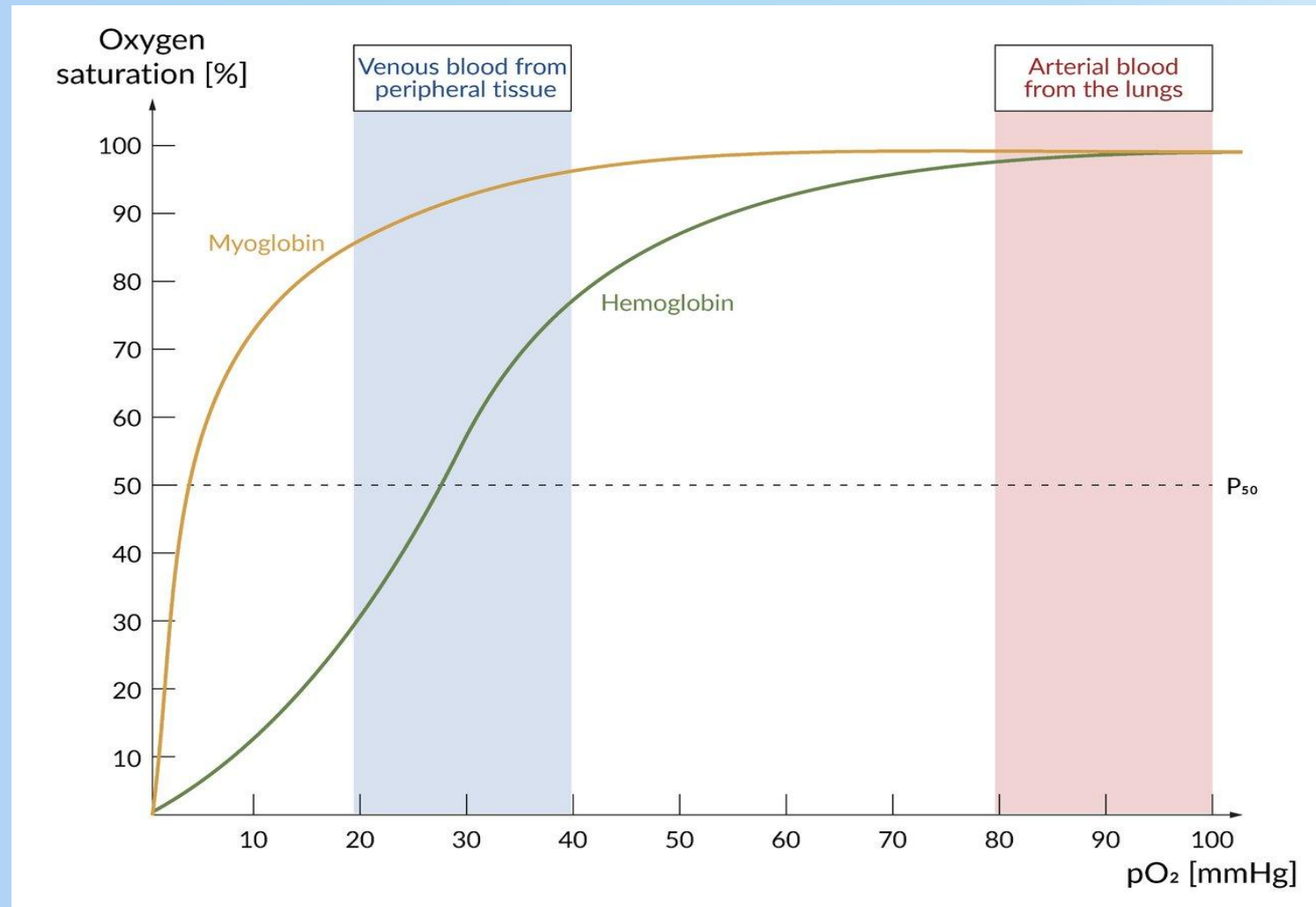
LUNGS

Bohr Effect

- We now know how Hb gets O₂- but how do we get O₂ from our blood to our tissues?
- O₂ binding affinity is inversely proportional to pH (H⁺) and CO₂ concentration



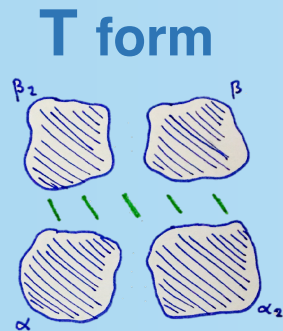
O2- Hemoglobin Dissociation curve



Cadet face RIGHT



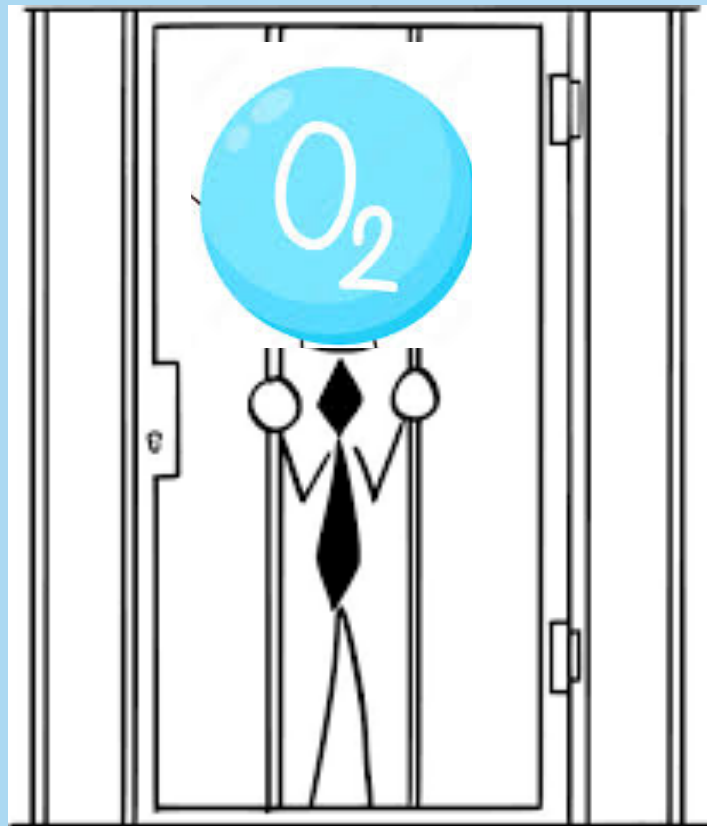
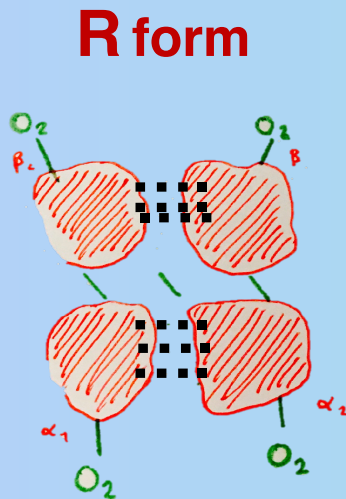
- Dec Hb affinity for O₂- inc tissue oxygenation
- C= CO₂
- A= Acid
- D= 2,3 BPG
- E= Exercise
- T= Temp inc



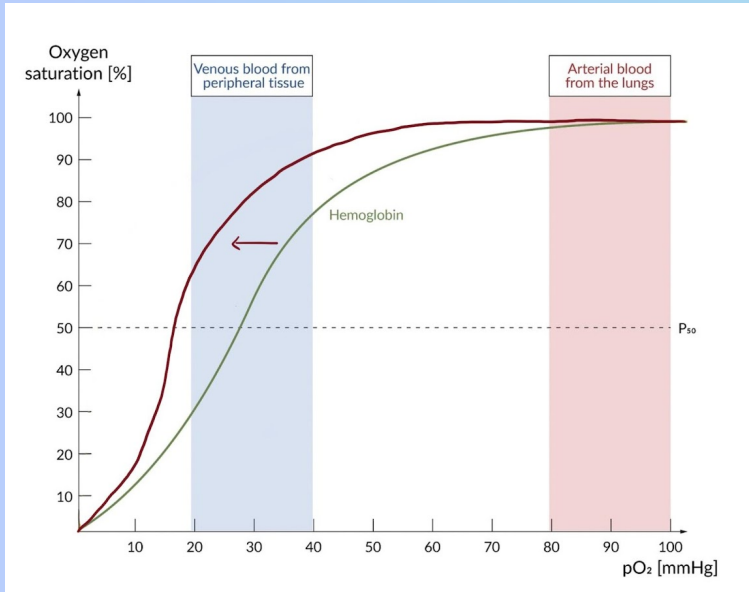
Left shift= Oxygen is locked up



- Inc Hb affinity for O_2 - dec tissue oxygenation (inc Erythrocytosis)



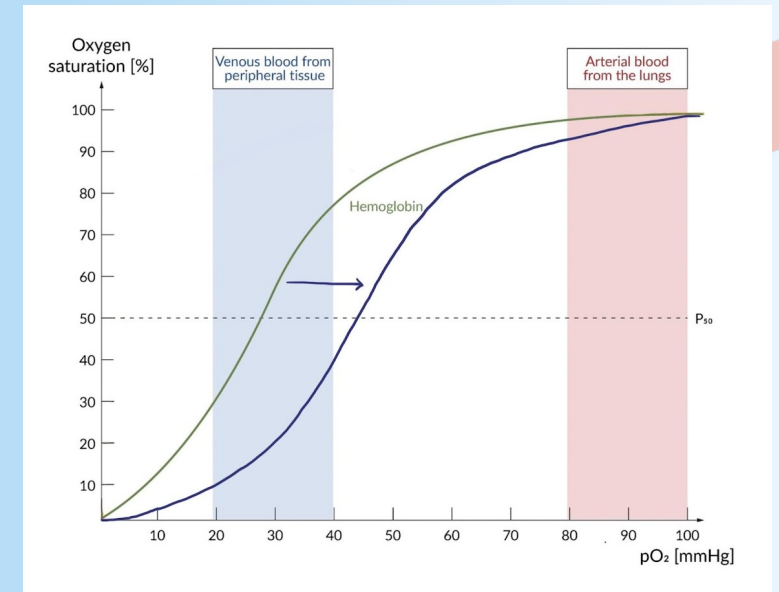
Shift overview



↑ pH (or H⁺), ↑ pCO₂, ↑ 2,3-BPG

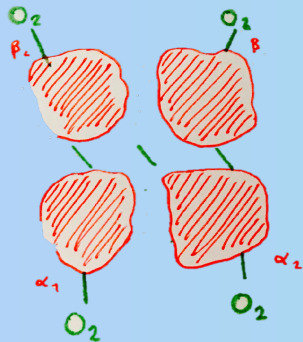


↓ pH (or H⁺), ↓ pCO₂, ↓ 2,3-BPG



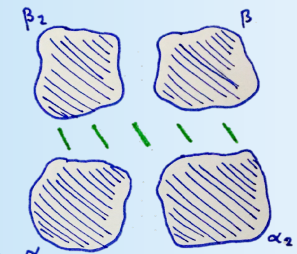
R form

↑ affinity to O₂
(Harder to unload O₂)

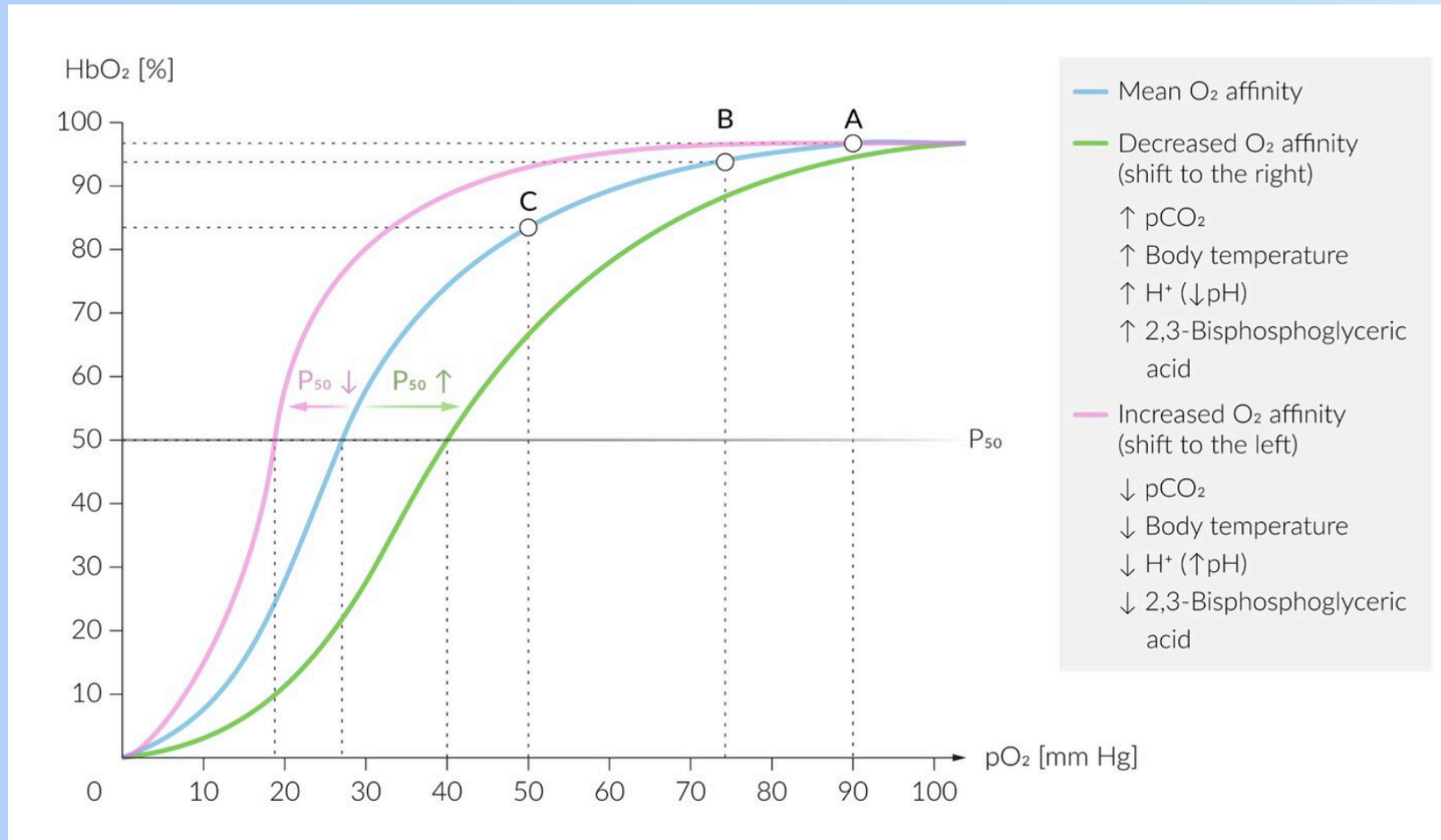


T form

↓ affinity to O₂
(Easier to unload O₂)

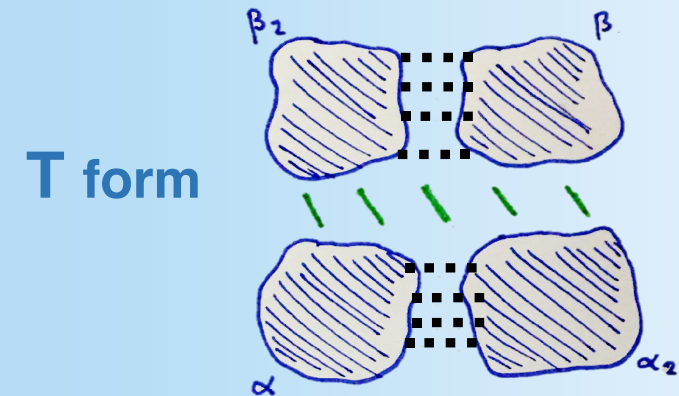


Shifts



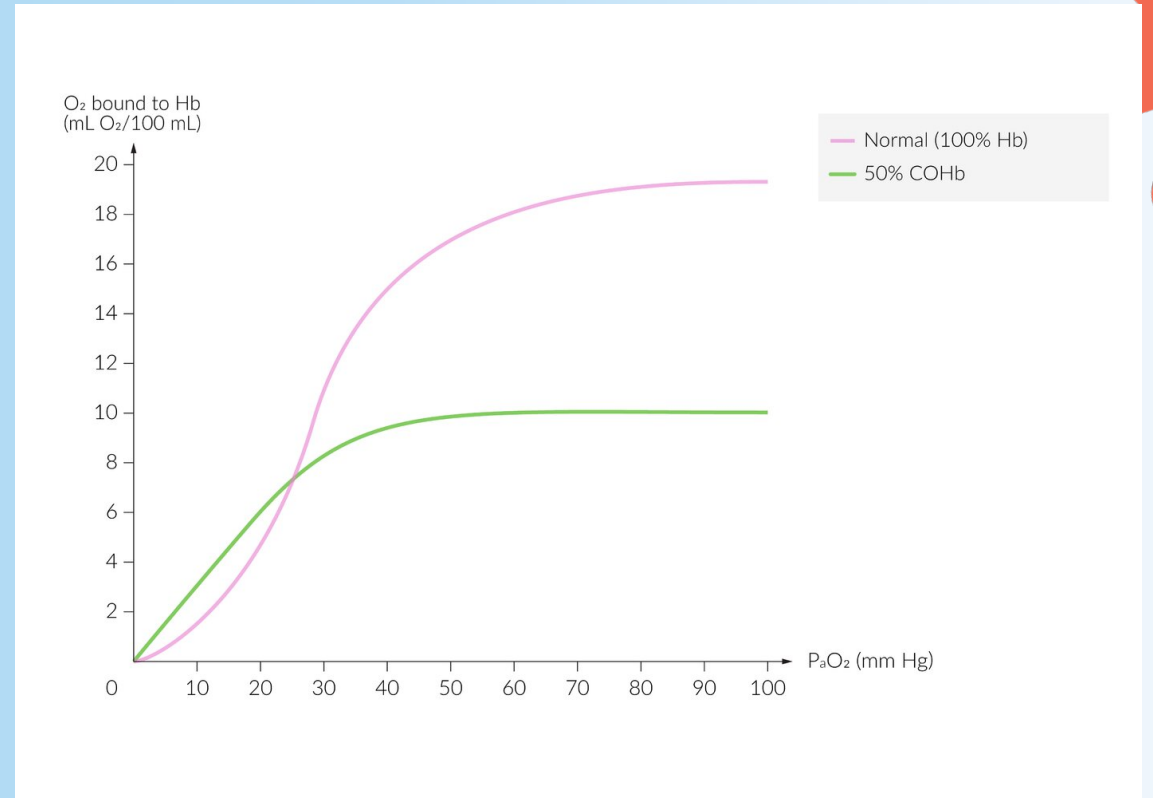
2,3-Bisphosphoglycerate

- Regulates O₂ binding to Hb
- **Stabilizes the T form**
- More T form= decreased Hb O₂ affinity
- increased production in states of low O₂
- Binds B chains



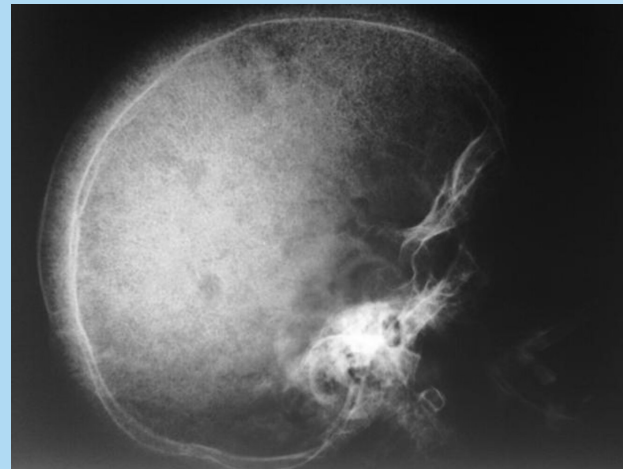
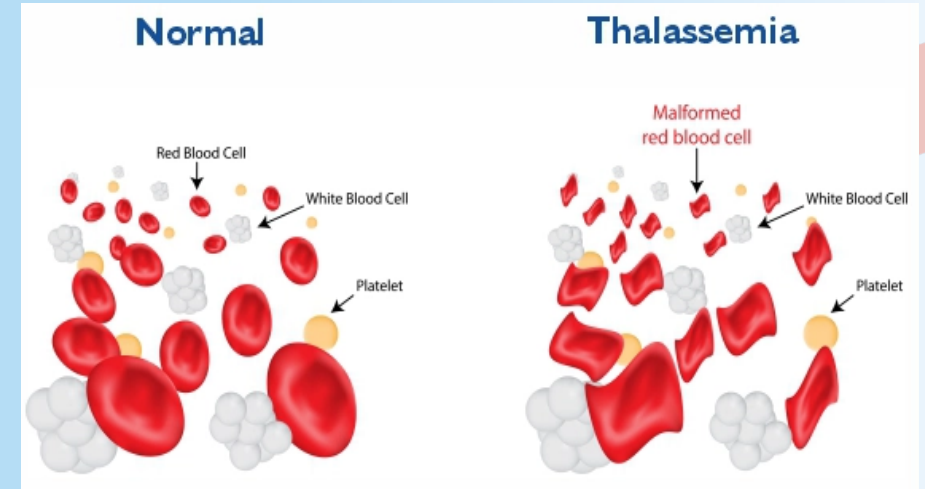
Carbon Monoxide

- PATHOLOGICAL- if $>1\%$
- **Binds the R form-** stabilizes oxygen form/ binding
- Hb CANNOT release O₂
- Symptoms depend on amount of CO in blood
 - 15%= headache
 - 50% = loss of consciousness
 - $> 60\%$ = death



Thalassemia

- Mutations in alpha or beta globin chains
- Alpha chain has **4 alleles**
 - 1= silent
 - 2= trait
 - 3= disease
 - 4= Hydrops fetalis
- Beta chains has **2 alleles**
 - 1= minor
 - 2= major



Clinical

- You're doing your 6th year emergency medicine rotation at the University Hospital in Prokocim . It's 8 am on a Monday morning and the man in the photo below walks in. Your professor asks you why his skin is blue- what do you answer?



- A) He had a wild night out
- B) He's been hypoxemic for a while
- C) He recently had an infection and is taking the antibiotic dapsons
- D) He is a Smurf

Methemoglobinemia

- **Normally iron is in its Fe^{2+} (ferrous) form**
 - Here the iron attached to Hb is in its oxidized- Fe^{3+} (ferric) form
- $> 1\%$ of iron is in Fe^{3+} form- cannot participate in O_2 delivery
- Symptoms appear when methemoglobin (Fe^{3+}) is $> 10\%$ of total Hb
- Inherited or acquired
 - Acquired via anesthetics, dapsone, etc



Clinical

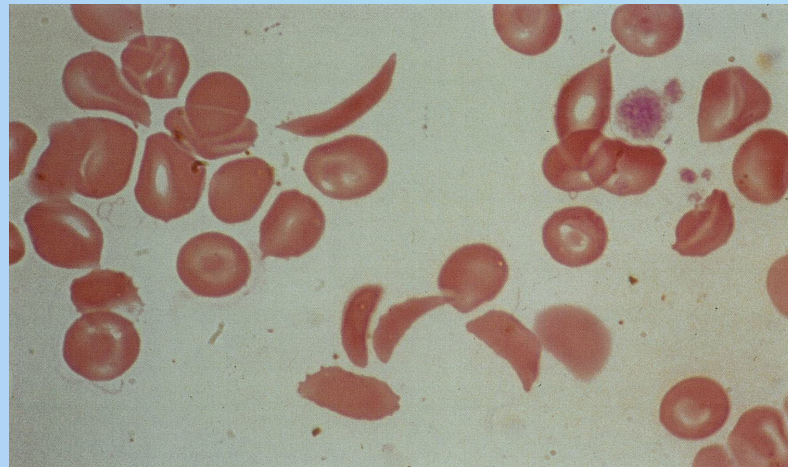
- You are doing your 6th year away clinical rotations in Nigeria and a mother brings her 4 year old child to clinic. The child presents with breathlessness and symptoms as shown in the pictures, what is your diagnosis ?



- A) Child is normal
- B) Thalassemia (subtype)
- C) Sickle Cell Anemia
- D) Methemoglobinemia

Sickle Cell Anemia

- Point mutation in B globin chain causes **valine** → **glutamate**
- Causes formation of HbS, polymerizes when deoxygenated
- Homozygous mutations= **HbSS= sickle cell disease**
- Symptoms occur in conditions when the curve is shifted **RIGHT**
- Heterozygous= **HbSA= sickle cell trait**
 - Symptoms like disease under certain conditions



Quiz time 😊



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