Hemoglobin & Myoglobin

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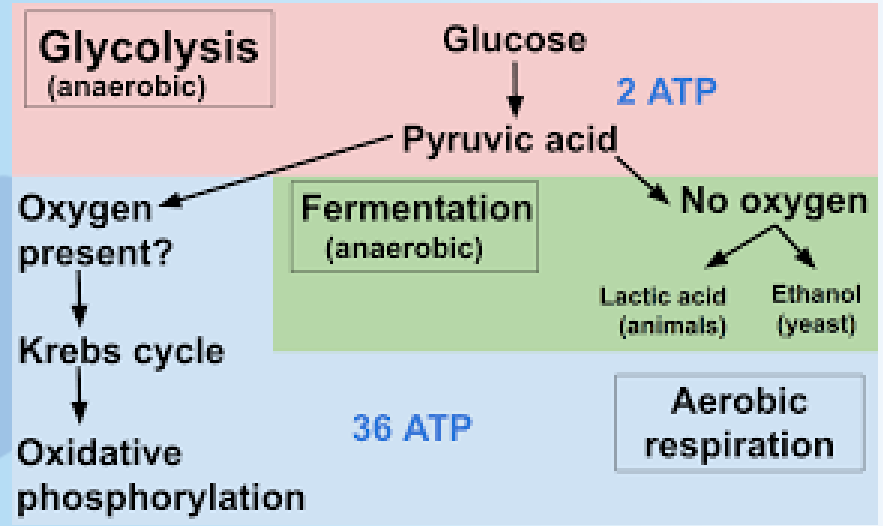
Clinical

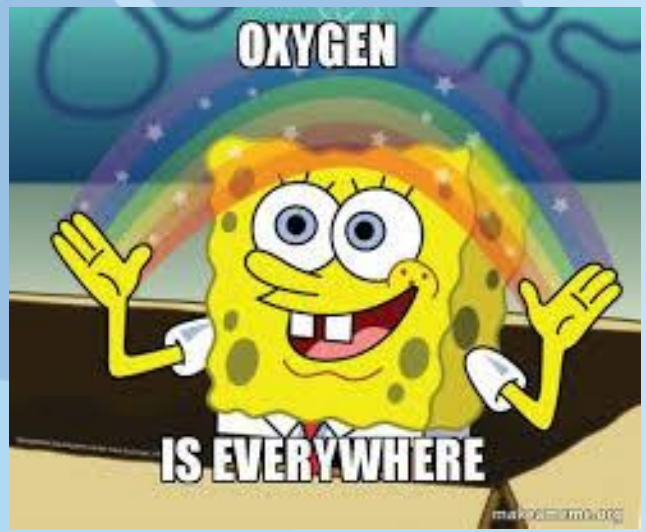
Your professor asks you why his skin is blue- what do you answer?

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 dapsone
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





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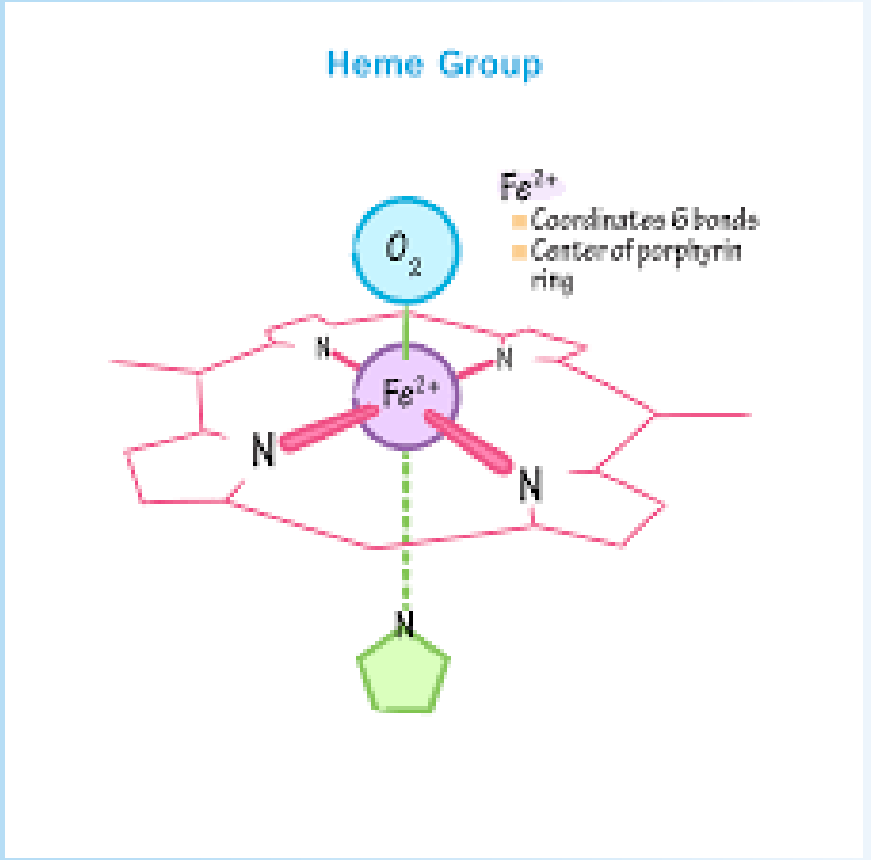
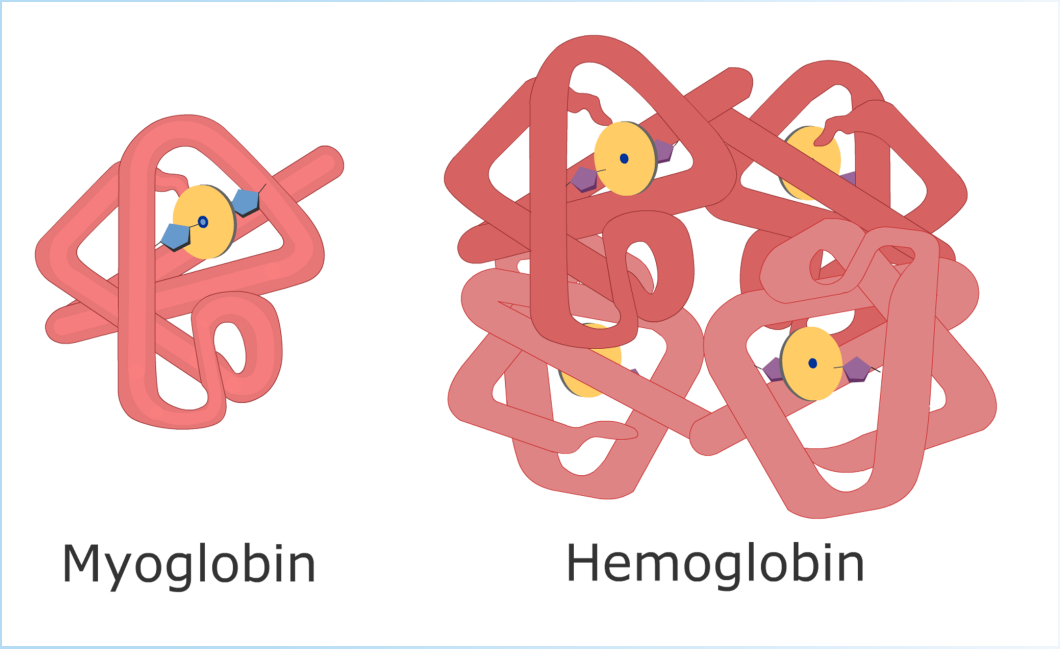
Heme Structure

- Normal adult hemoglobin has 4 hemes
- Protoporphyrin IV + Fe 2+
- 1 heme= binds one O2
- Key for most living cells!



Myoglobin

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

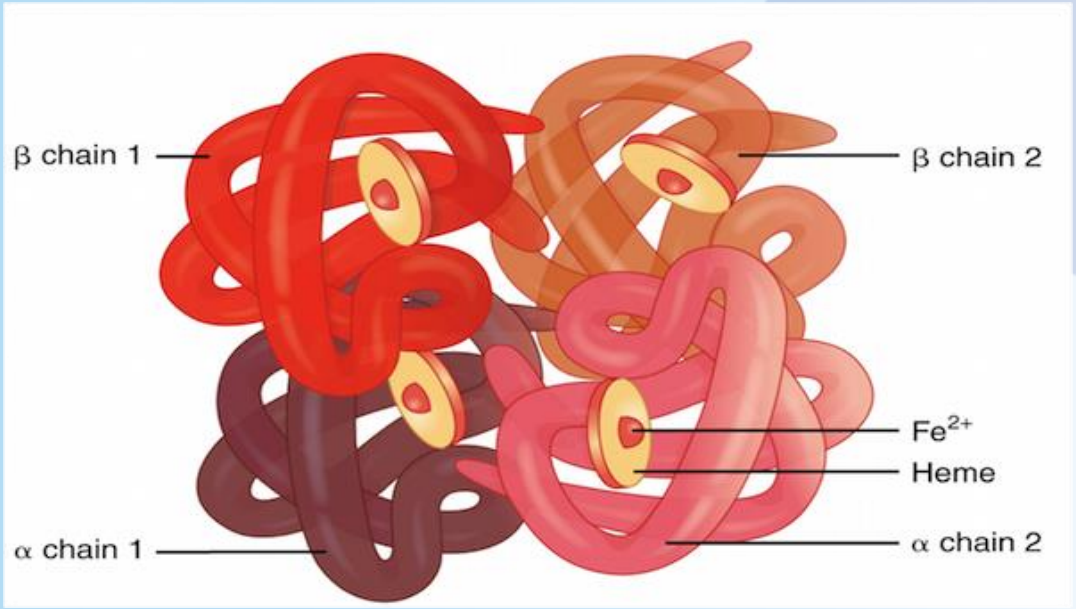


Clinical

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

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

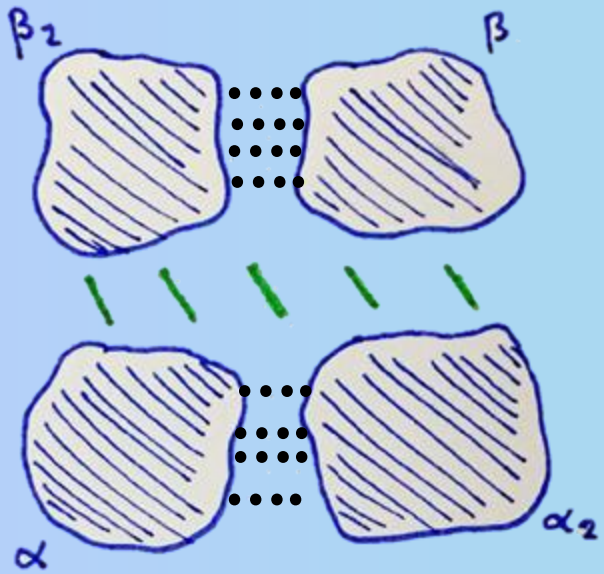


T vs R form

Hb + Oxygen
= Relaxed

T form

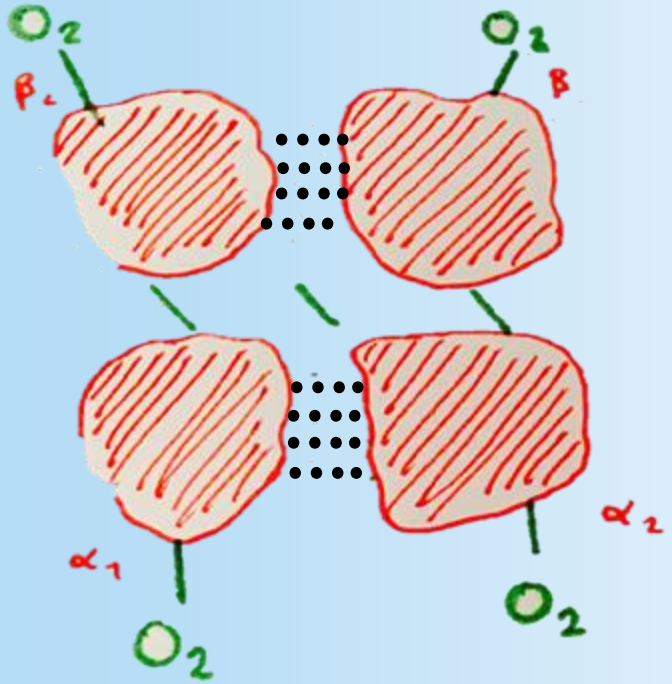
Deoxyhemoglobin



O_2

R form

Oxyhemoglobin



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Hemoglobin Cooperativity

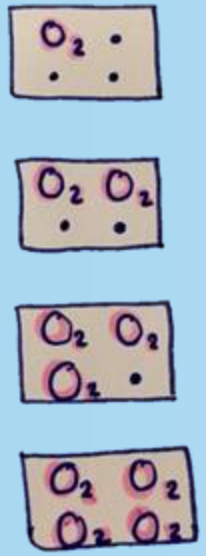
- Hb affinity for O2 depends on ppO2
- Affinity for O2 increases with more O2 binding

$K_1 : Hb_4(O_2) \Leftrightarrow Hb_4 + O_2$

$K_2 : Hb_4(O_2)_2 \Leftrightarrow Hb_4(O_2) + O_2$

$K_3 : Hb_4(O_2)_3 \Leftrightarrow Hb_4(O_2)_2 + O_2$

$K_4 : Hb_4(O_2)_4 \Leftrightarrow Hb_4(O_2)_3 + O_2$



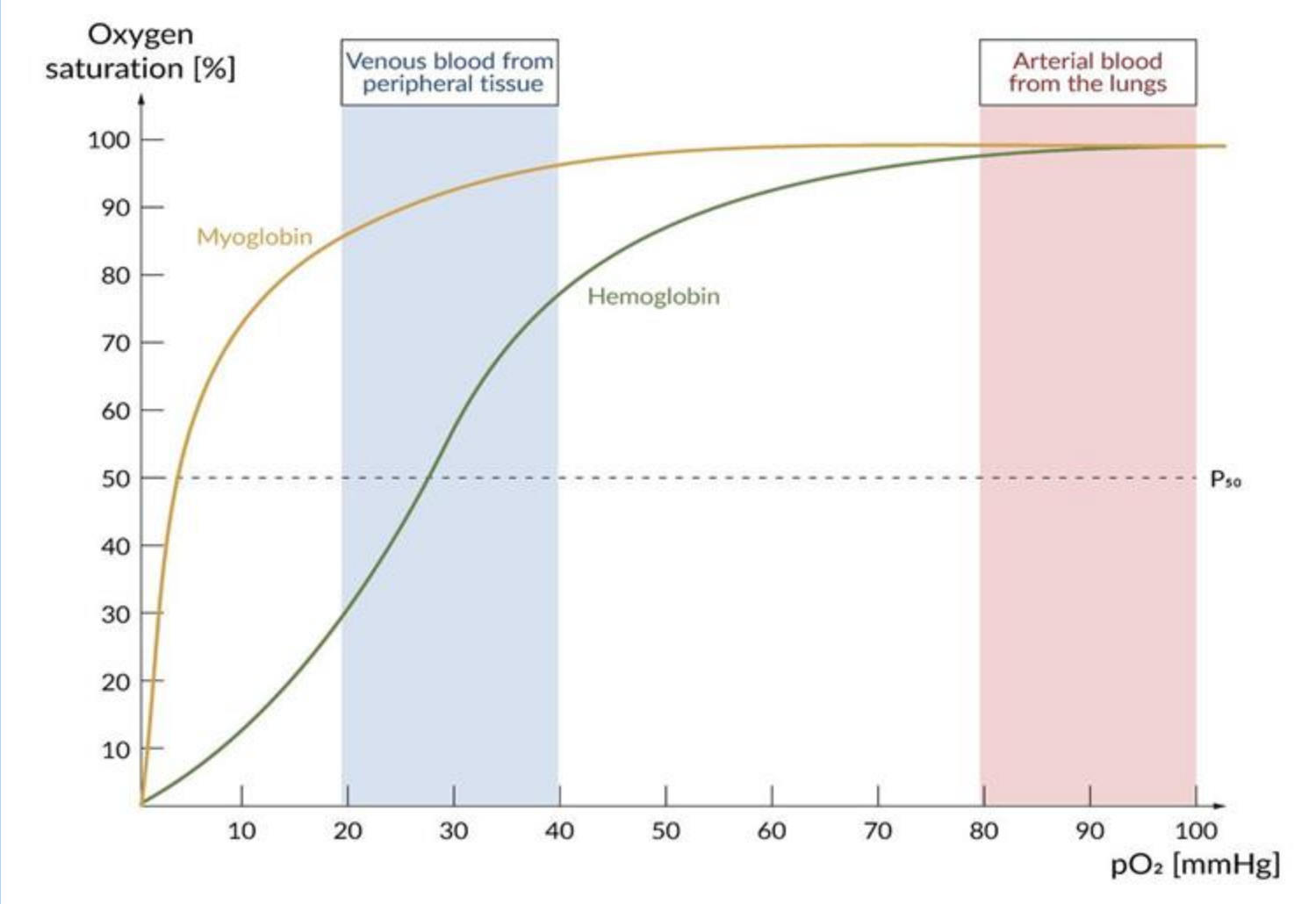
T form

R form

TISSUES

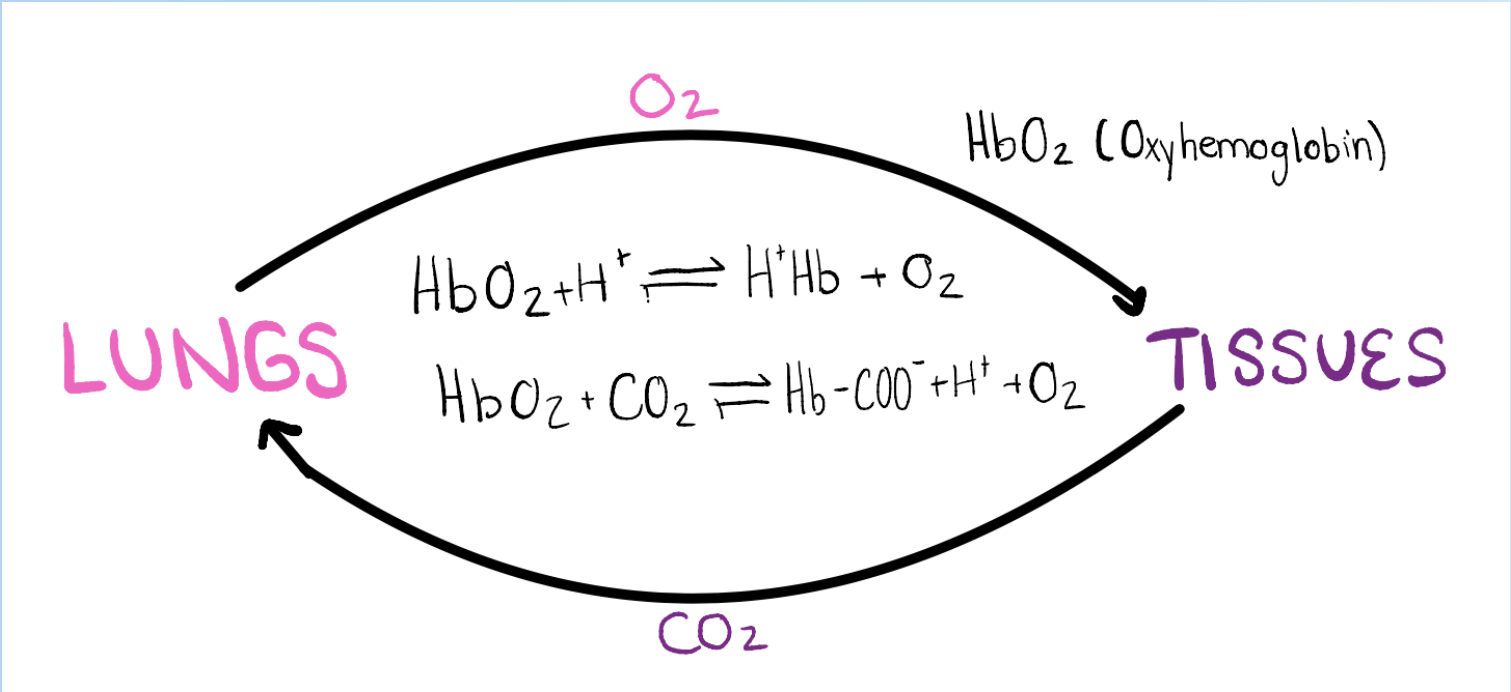
LUNGS

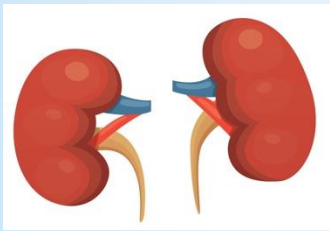
O2- Hemoglobin Dissociation curve



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**





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Cadet face RIGHT

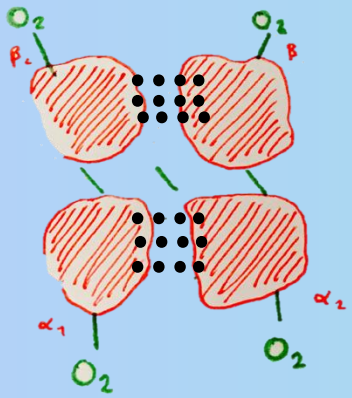
- Dec Hb affinity for O2- inc tissue oxygenation

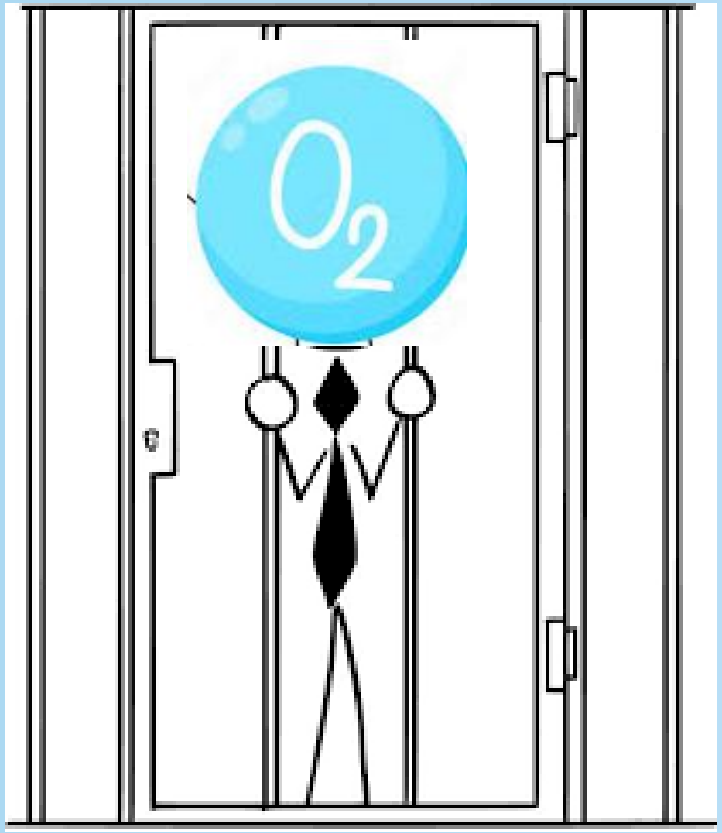
- C= CO2
- A= Acid
- D= 2,3 BPG
- E= Exercise
- T= Temp inc

Left shift= Oxygen is locked up

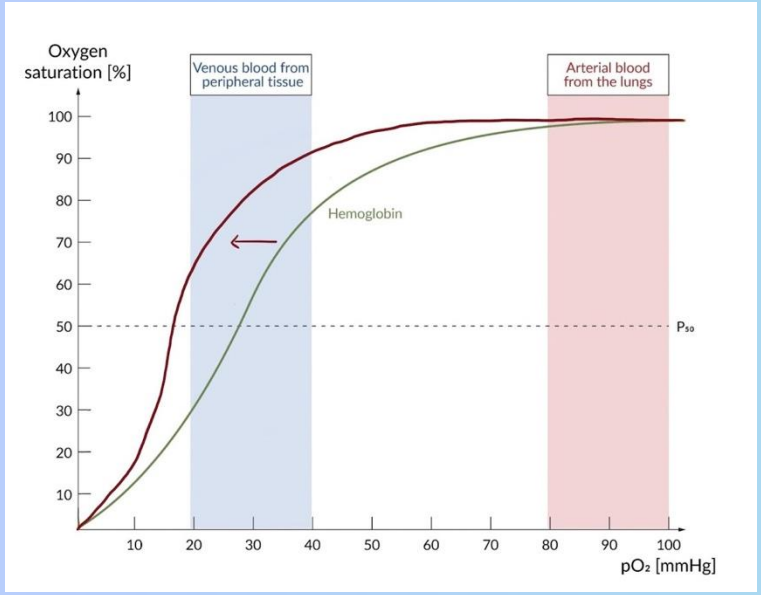
- Inc Hb affinity for O2- dec tissue oxygenation (inc Erythrocytosis)

R form



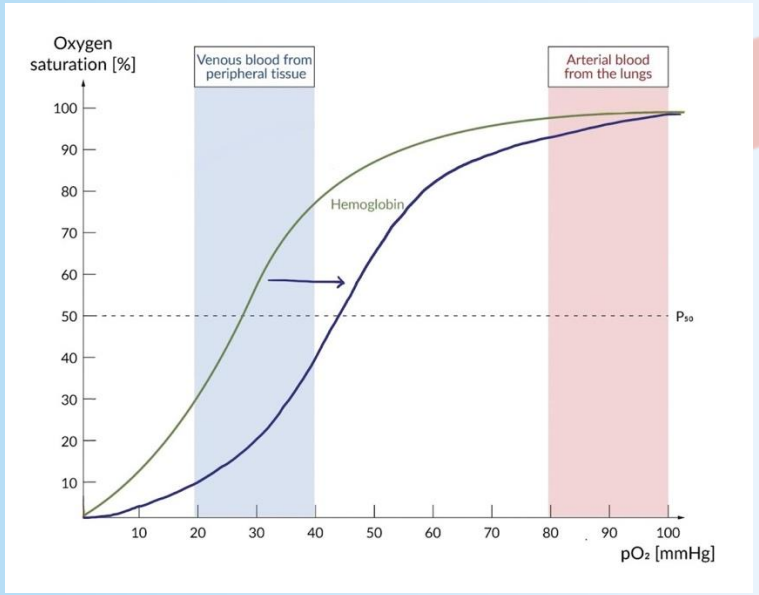


Shift overview



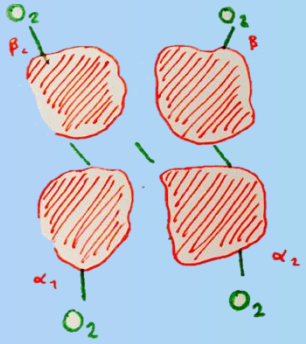
↑ pH (or H^+), ↑ pCO_2, ↑ 2,3-BPG

↓ pH (or H^+), ↓ pCO_2, ↓ 2,3-BPG



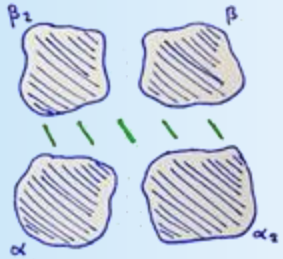
R form

↑ affinity to O_2
(Harder **to unload O_2**)



T form

↓ affinity to O_2
(Easier **to unload O_2**)



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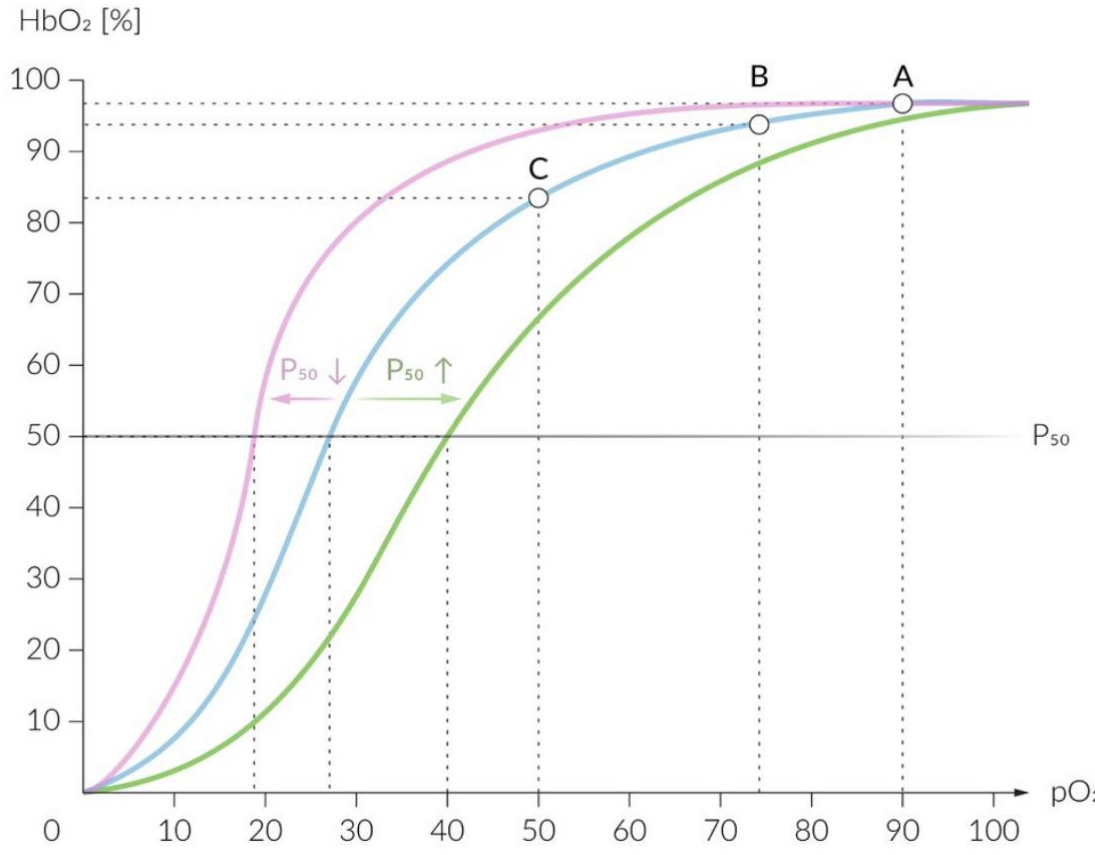
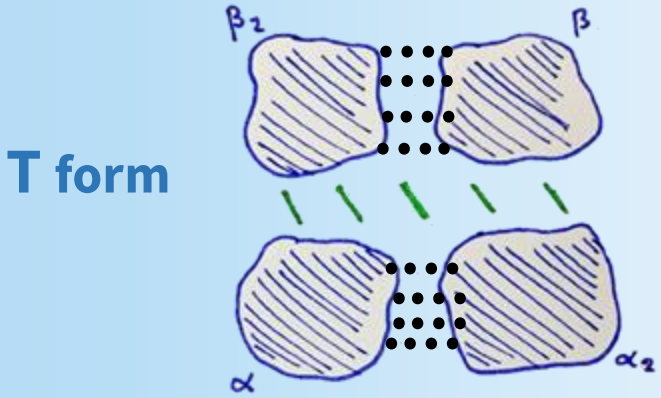
Shifts



- Mean O_2 affinity
- Decreased O_2 affinity (shift to the right)
  - ↑ pCO_2
  - ↑ Body temperature
  - ↑ H^+ (↓pH)
  - ↑ 2,3-Bisphosphoglyceric acid
- Increased O_2 affinity (shift to the left)
  - ↓ pCO_2
  - ↓ Body temperature
  - ↓ H^+ (↑pH)
  - ↓ 2,3-Bisphosphoglyceric acid

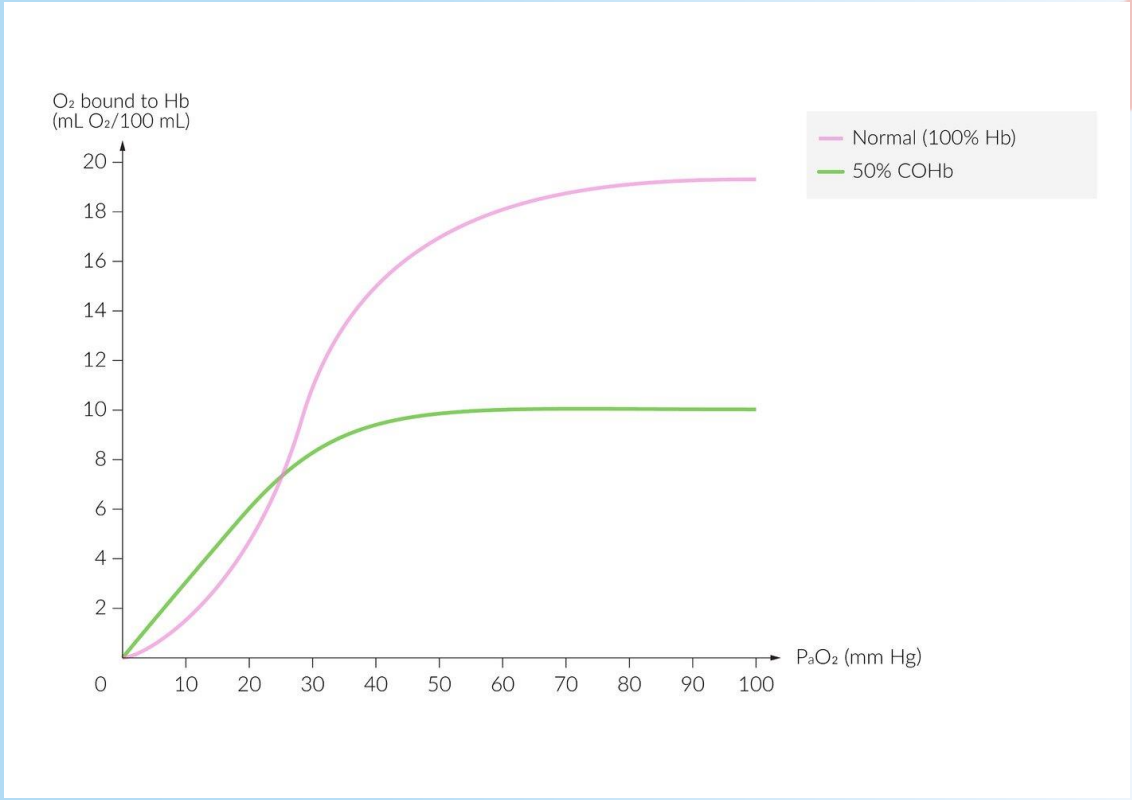
2,3-Bisphosphoglycerate

- 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



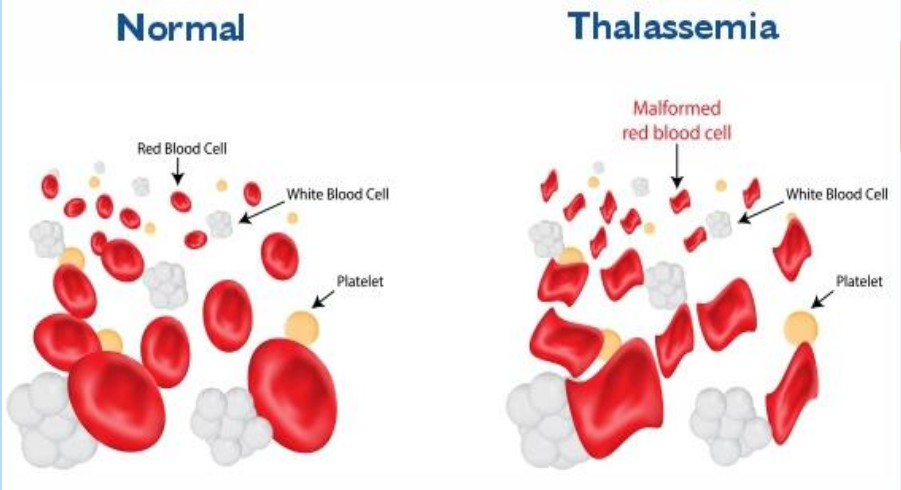
Carbon Monoxide

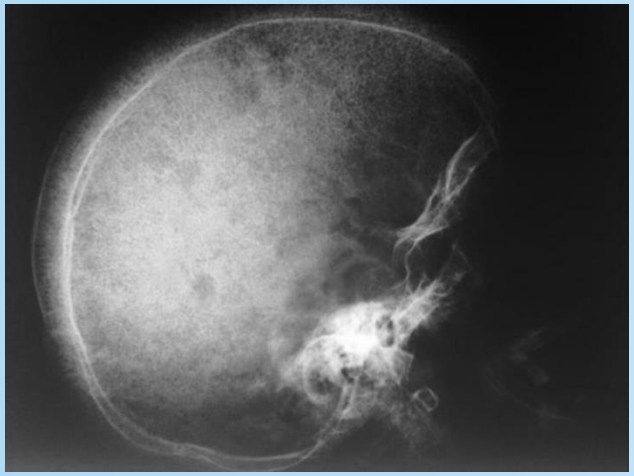
- PATHOLOGICAL- **if >1%**
- **Binds the R form-** stabilizes oxygen form/ binding
- Hb CANNOT release O2
- Symptoms depend on amount of CO in blood
  - 15%= headache
  - 50% = loss of consciousness
  - > 60%= death



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





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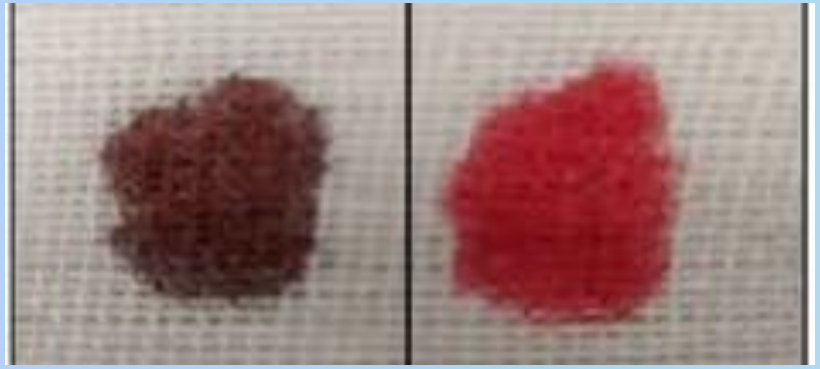
Clinical

- 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 dapsone
D) He is a Smurf

Methemoglobinemia

- **Normally iron is in its Fe2+ (ferrous) form**
  - Here the iron attached to Hb is in its oxidized-Fe 3+ (ferric) form
- > 1% of iron is in Fe3+ form- cannot participate in O2 delivery
- Symptoms appear when methemoglobin (fe3+) is > 10% of total Hb
- Inherited or acquired
  - Acquired via drugs



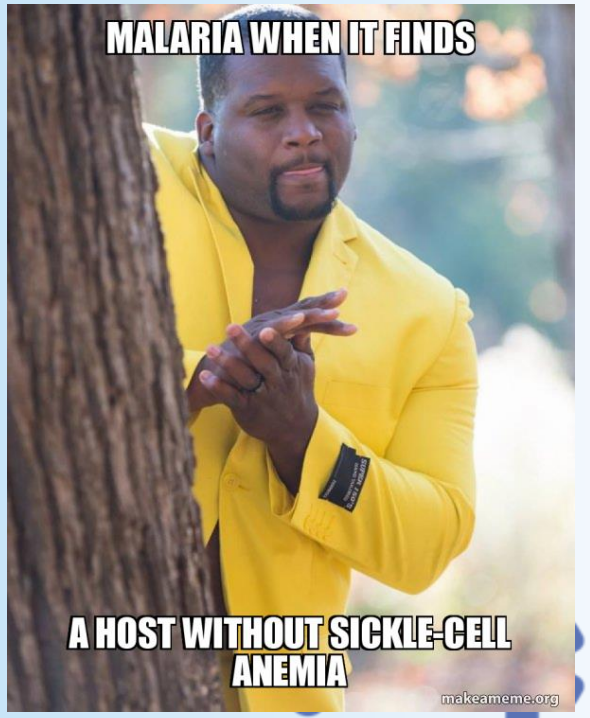
Clinical

- You are doing you're 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 ?

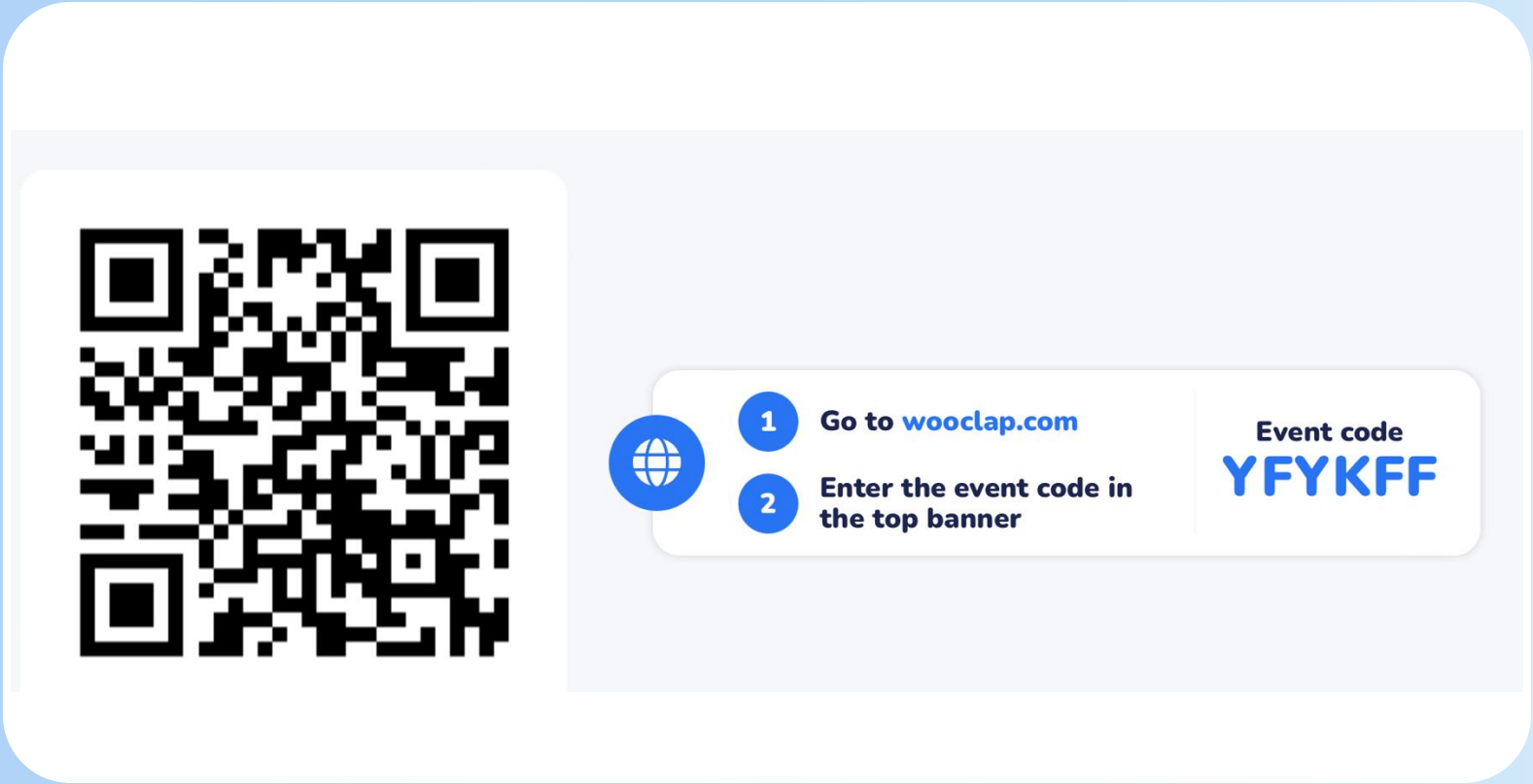
A) Child is normal
B) Thalassemia (subtype)
C) Sickle Cell Anemia
D) Methemglobinemia

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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