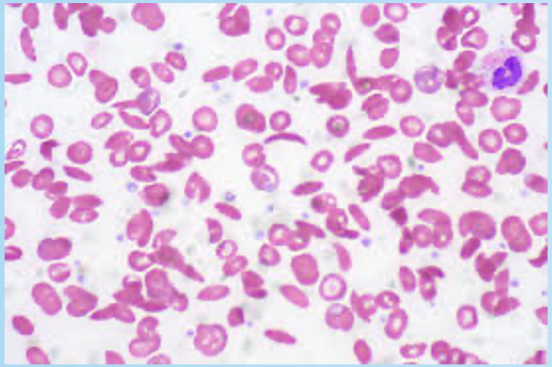
Hemoglobin + Myoglobin Bohr Effect

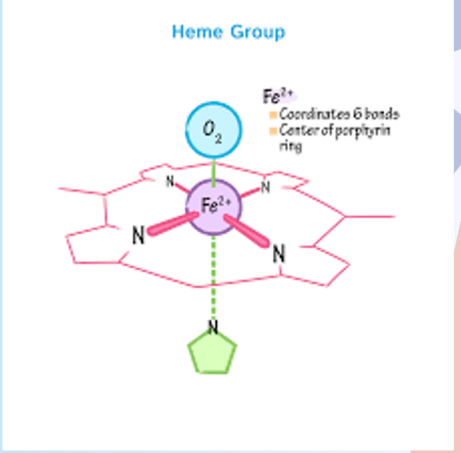
By Katie Skoczen

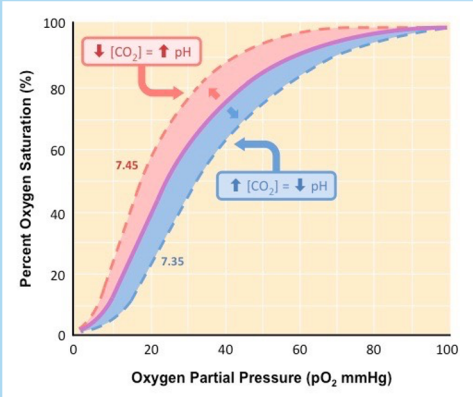
Agenda

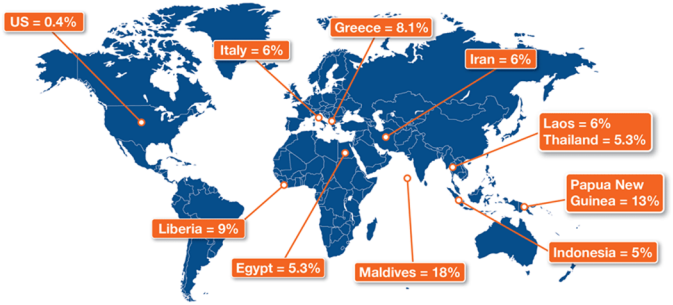
- Summary of the basics
- Structure of Heme
- Hemoglobin vs Myoglobin
- Types of Hemoglobin
- Bohr Effect
- Oxygen dissociation curves
- Pathologies

!! Look out for clinical correlations !!









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Let’s talk the Basics

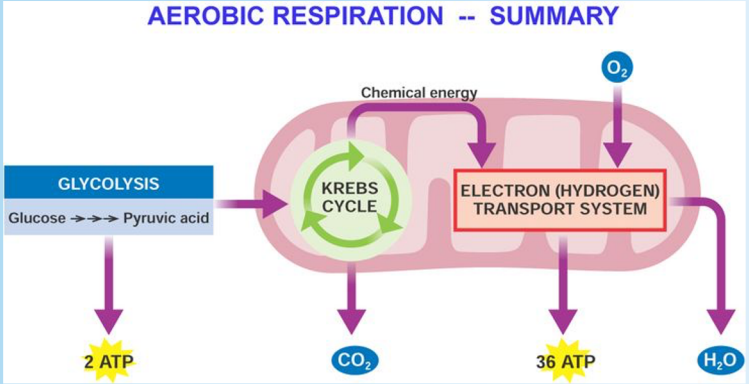
Oxygen is a needed for life!

Why??

Aerobic= 32 ATP

Anaerobic= 2 ATP

1900L/day @ rest



Major problem….

Barely dissolves in blood

Free Oxygen is poisonous to tissues

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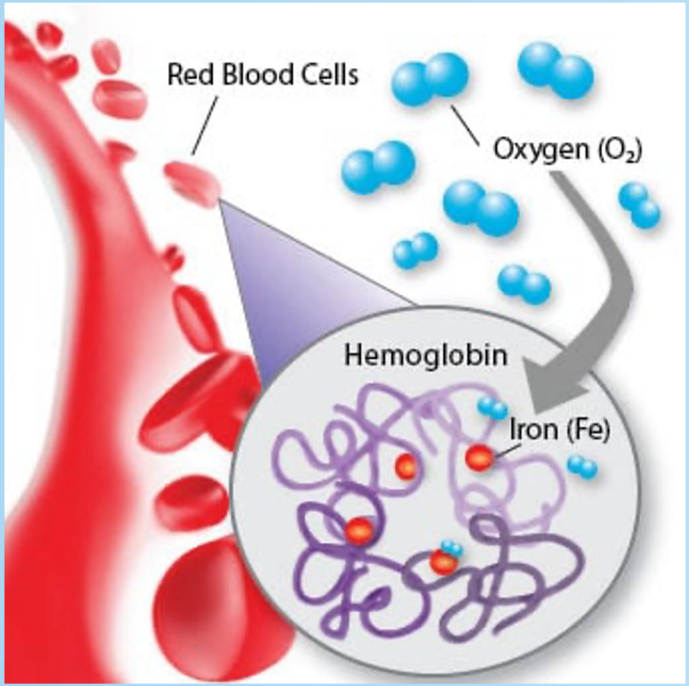
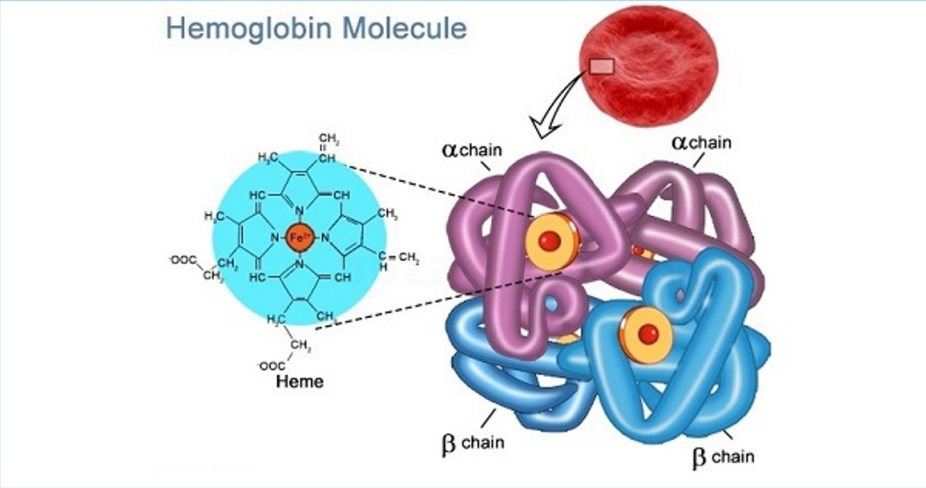
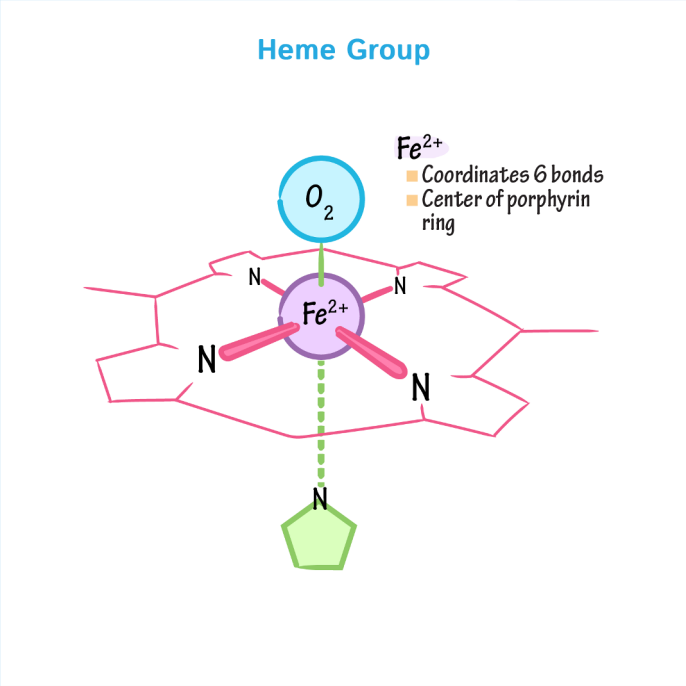
Solution = Heme



Structure of Heme

- Protoporphyrin IV + Fe2+
- Iron in the center with 4 N Bonds
- Histidine binds on the top and/or bottom
  - globin binds the other
- 1 heme= 1 O2 binding ability





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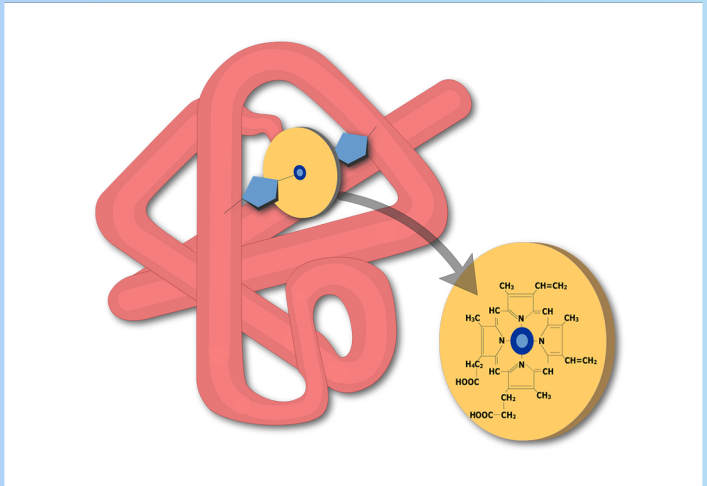
Myoglobin

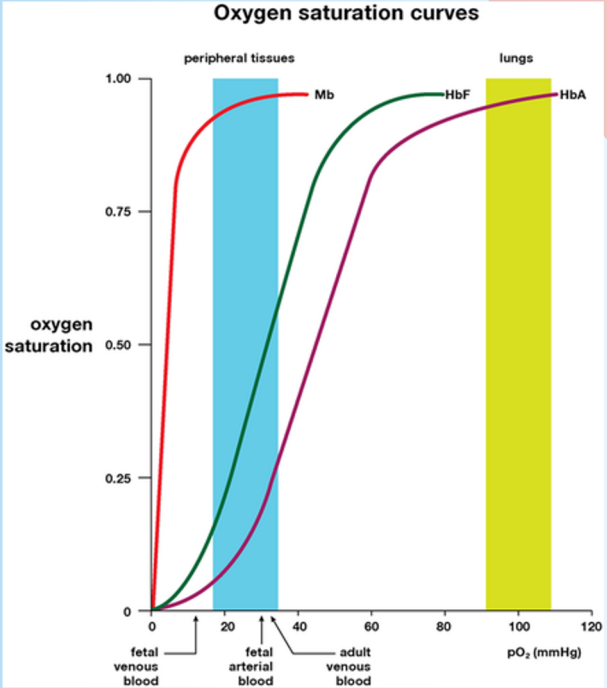
- Functions as a storage site for O2 in heart and skeletal muscles
- 1 polypeptide chain with nonpolar AA
- 1 O2 molecule
- High affinity for Oxygen
    - = O2 CANNOT be released to tissues easily



Clinical Correlation:
↑Myoglobin in blood during skeletal and cardiac muscle injury!
*Myocardial infarction
*Rhabdomyolysis

Hemoglobin

- Found in RBCs
- 4 O2 molecules
- Composed of two dimers (4 total subunits)
  - Alpha
  - Beta
  - Gamma
  - Delta
- There are many subtypes
  - **HbA: ααββ**
  - **HbF:ααγγ**
    - Fetal Hemoglobin with *less* 2,3-BPG
  - **HbS:ααββ**
    - Sickle Cell Anemia



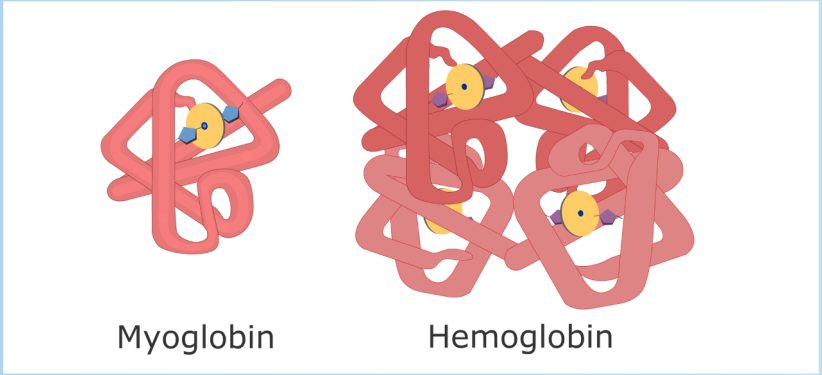
Clinical Correlation

↓Hemoglobin = anemia

Symptoms: Fatigue, Weakness, Pale skin, Irregular heartbeats, Shortness of breath, Dizziness or lightheadedness, Chest pain, Cold hands and feet

Summary: Myoglobin vs Hemoglobin

Differences between the hemoproteins myoglobin and hemoglobin		
	Myoglobin	**Hemoglobin**
Associated with	• 1 Heme (monomeric)	• 4 Hemes (tetrameric)
Binds to	• 1 Oxygen molecule	• 4 Oxygen molecules
Affinity for O_2	• Very high (hyperbolic **oxygen-myoglobin dissociation curve**)	• High (sigmoidal curve)
Function	• **Storage** of O_2 in muscle • Transport of O_2 to mitochondria → aerobic metabolism	• **Transport** of O_2 in blood



Bohr Effect

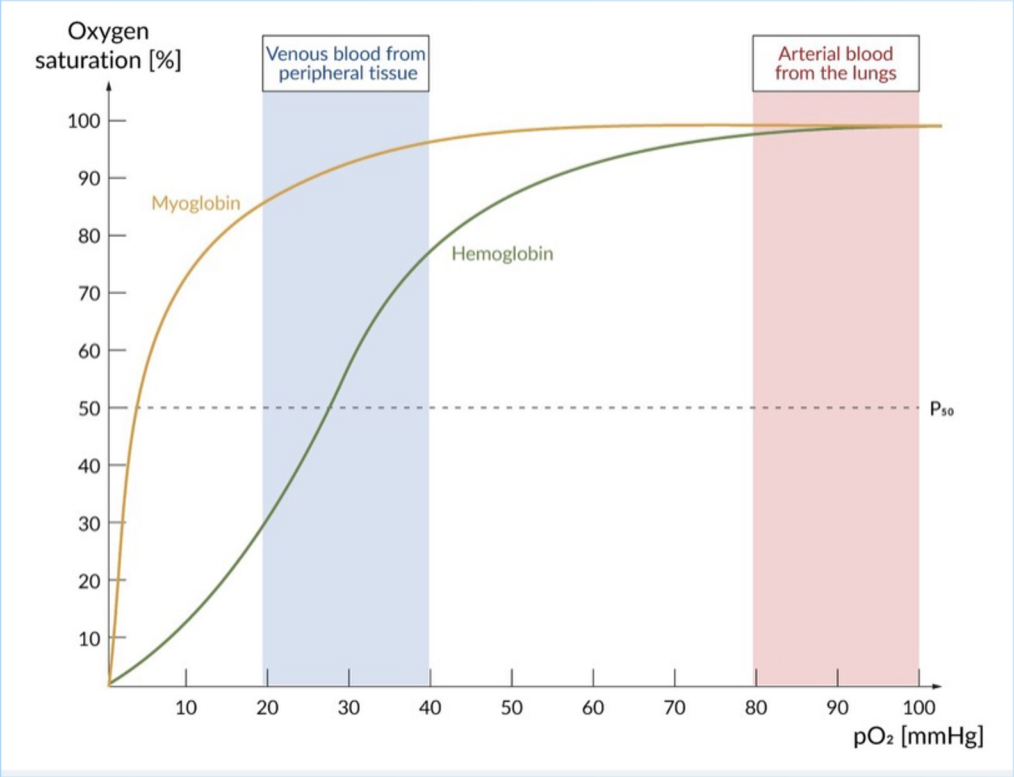
- O2 affinity is inversely proportional to CO2 and H+ concentration of blood
- CO2 and H+ are produced during metabolic processes

$$HbO_2 + H^+ \rightleftarrows H^+Hb + O_2$$

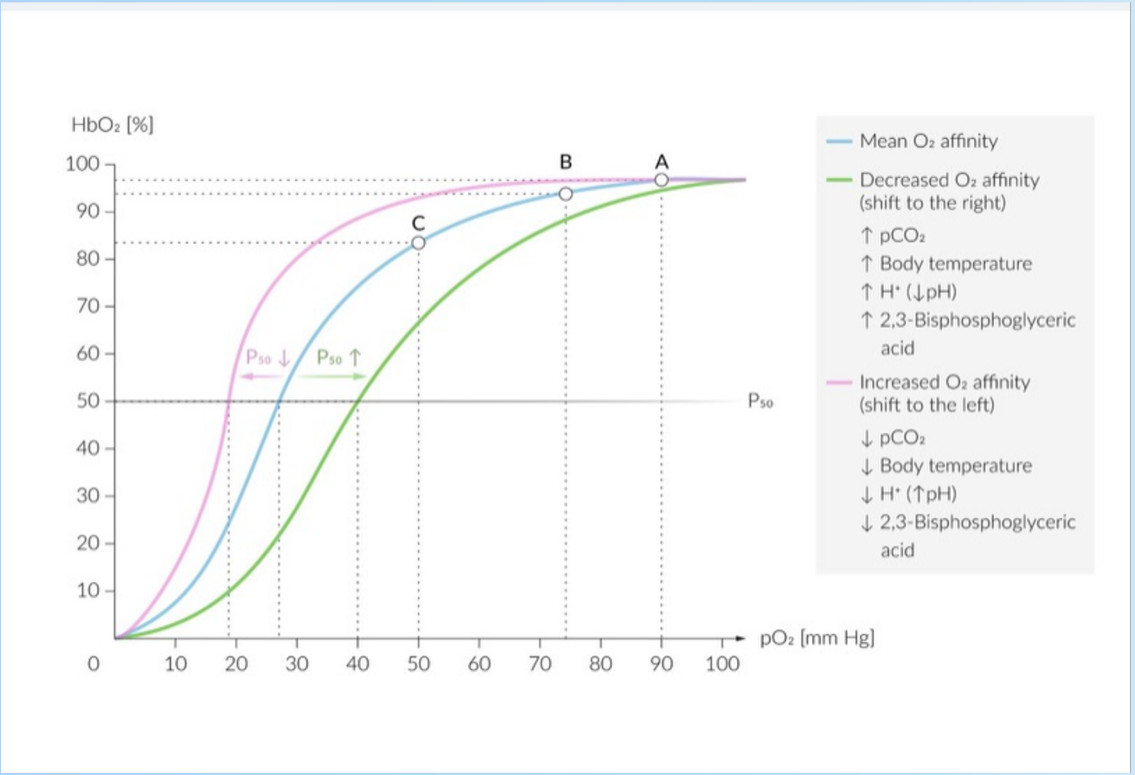
$$HbO_2 + CO_2 \rightleftarrows Hb\text{-}COO^- + H^+ + O_2$$

Clinical Correlation:
pH range= 7.35-7.45
Regulated by kidneys

Hemoglobin Dissociation Curve



Hemoglobin Dissociation Curve: Shifts



Cadet Face RIGHT

C- CO_2

A- Acid (increase H+)

(Altitude)

D- 2,3- DPG

E- Exercise

T-Temperature Inc

Left Shift= Oxygen is LOCKED up

T Form vs R Form Cooperativity

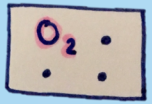
As one subunit binds oxygen… the adjacent subunits affinity for O2 INCREASES

Consequences =

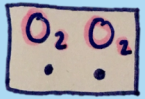
Easier to bind more O2

Harder to Lose

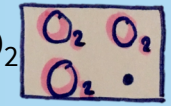
$K_1 : Hb_4(O_2) \Leftrightarrow Hb_4 + O_2$



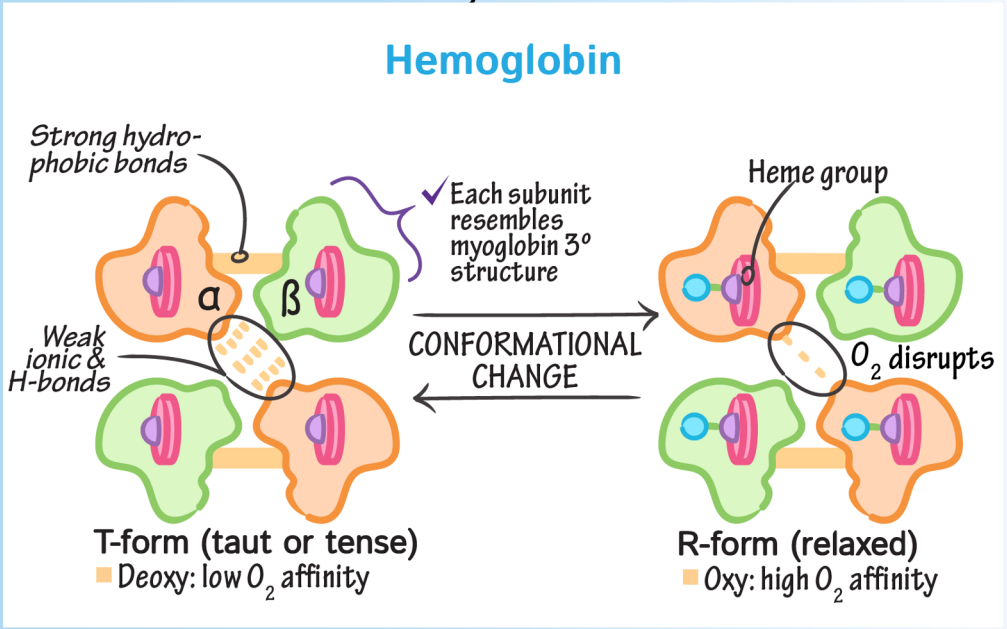
$K_2 : Hb_4(O_2)_2 \Leftrightarrow Hb_4(O_2) + O_2$



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



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



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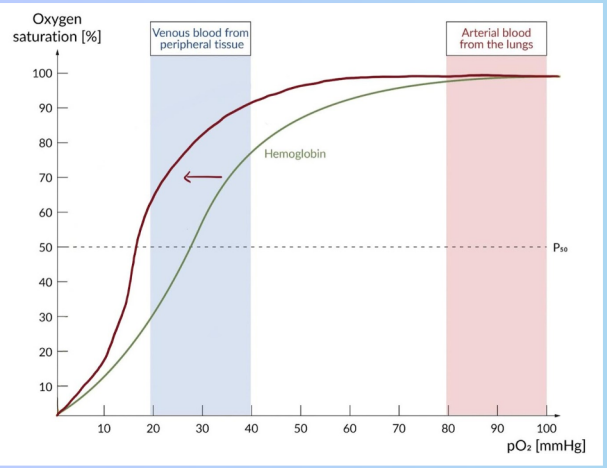
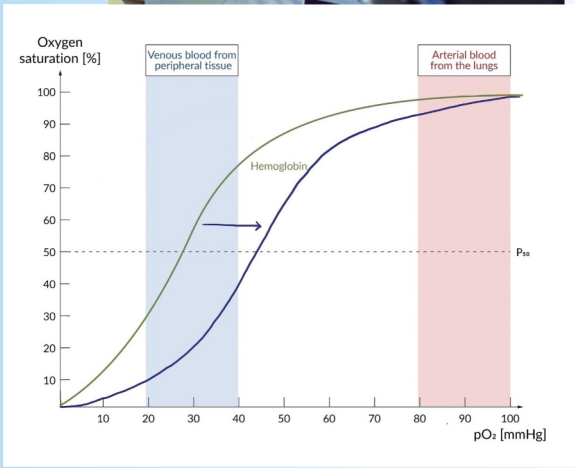
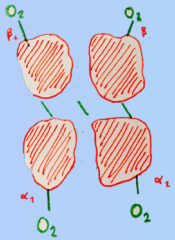
Left and Right Shifts



↓ pH (↑ H^+), ↑ pCO_2, ↑ 2,3-BPG

↑ pH (↓ H^+), ↓ pCO_2, ↓ 2,3-BPG

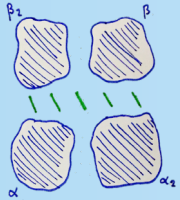




R form

↑ affinity to O_2

(Harder **to unload O_2**)



T form

↓ affinity to O_2

(Easier **to unload O_2**)

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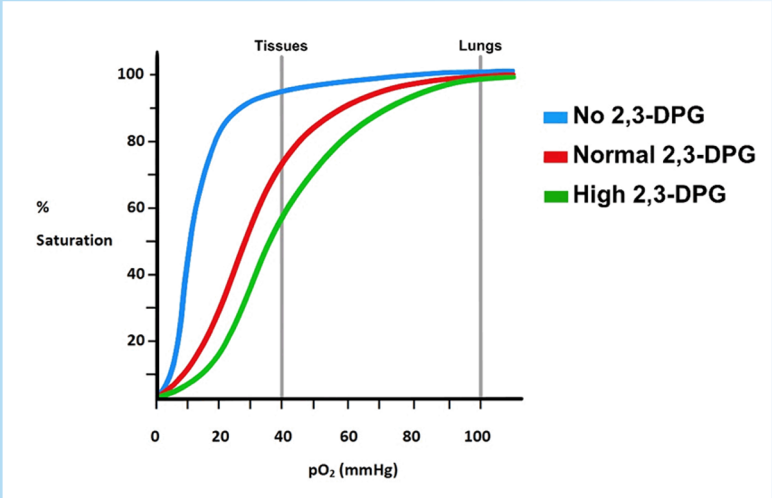
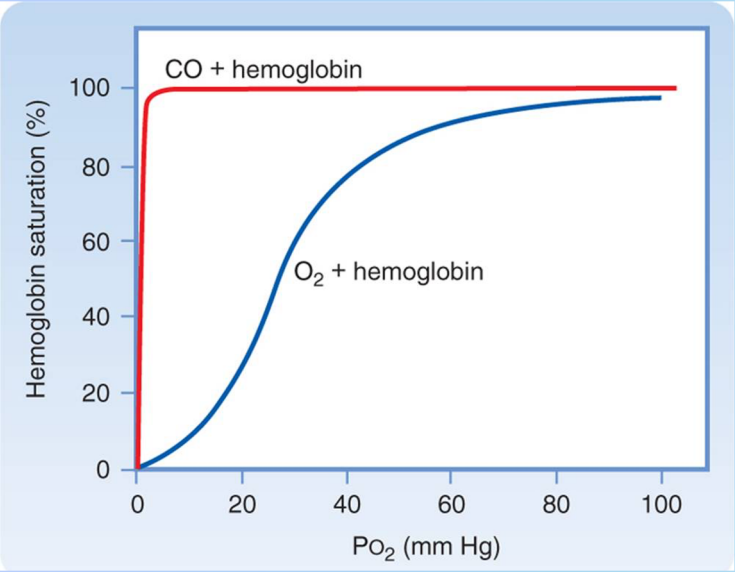
2,3-Bisphosphoglycerate

- Allows for **normal physiology!!**
- Binds T form of Hb… **stabilizes** the deoxygenated form
- More T effect = lower affinity
- Increased in high altitudes



note:DPG=BPG

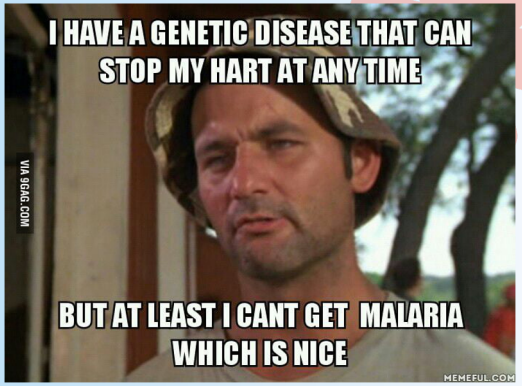
Carbon Monoxide



- **Pathology!!**
  - If more than 1%
- Binds R form of Hb… sabilizes the oxygenated form
- Hemoglobin cannot release O2 in tissues
  INCREASED in smokers
- 15%=headache; 50%=loss of consciousness; >60% = DEATH

Clinical Correlation:
CO Poisoning
Symptoms: headache, dizziness, nausea, sleepiness
Treatment:100% Oxygen

Sickle Cell Trait vs Disease

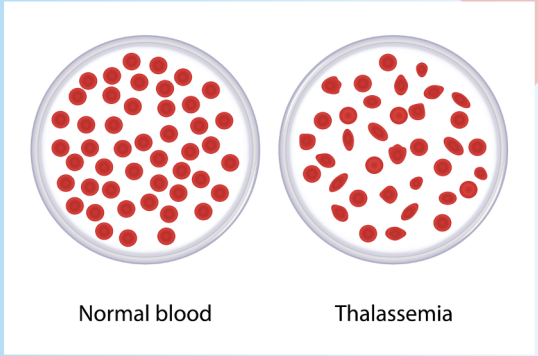


- Single point mutation of beta-globin gene

  resulting in a glutamate being substituted for valine
- **RBC deoxygenation = sickling = symptoms!**
- In sickle cell patients when O2 curve is shifted RIGHT symptoms increase
  - Infection/fever (temperature increases)
  - Acidosis (H+ concentration increases)
  - Stress (increased metabolic processes/wastes)

Hemoglobin	Normal	Sickle cell trait	Sickle cell disease
HbA	95–98%	60%	0%
HbS	0%	40%	75–95%
HbF	< 2%	< 2%	5–25%

Thalassemias



α

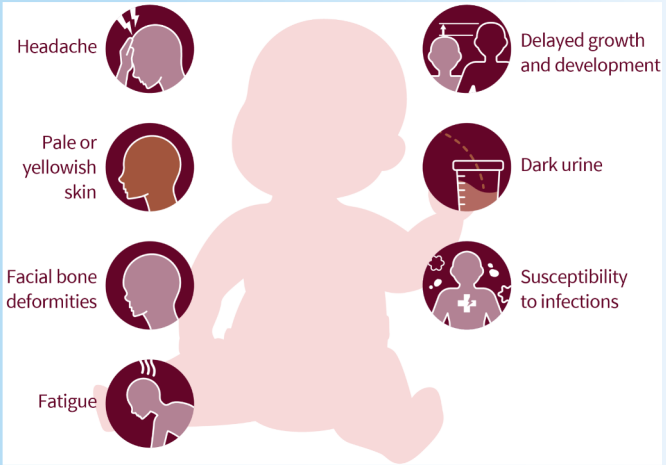
-4 alleles

Mutations: 1= silent, 2=trait, 3=disease, 4=Hydrops Fetalis (Hb Bart)

β

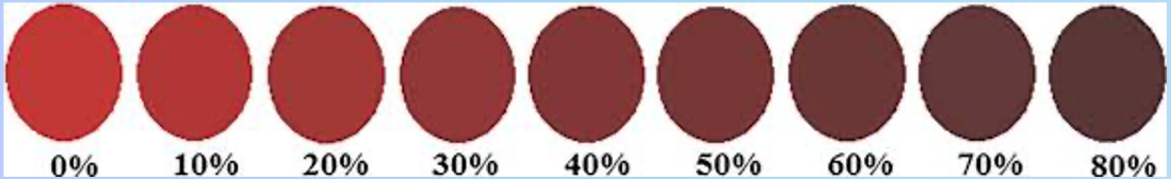
- 2 alleles

Mutations: 1= minor, 2= major



Methemoglobinemia

- Hemoglobin with oxidized iron (Fe3+) instead of reduced (Fe2+)
- Poor O2 binding capability, leading to overall hypoxia
- Can be inherited or caused by drugs (nitrates)
- Similar consequences as thalassemia due to lower baseline O2 levels



Summary

- Myoglobin is 1 polypeptide that binds 1 oxygen molecule TIGHTLY
- Hemoglobin= 2 dimers of heme
- Carries O2 from high to low concentration
- Efficiency of the delivery depends on:
  - pH, CO2, Temp, 2,3-BPG,
  - T form Vs R form contributes to cooperation characteristic
  - Pathology if too much carbon monoxide
  - Left Shift: Increase affinity, decrease dissociation
  - Right Shift: Decreased affinity, increase dissociation
- Pathologies that concern O2 binding affinity
  - Sickle Cell- Right shift causes sickling
  - Thalassemia- Right shift increases symptoms
  - Methemoglobinemia - Right shift increases symptoms

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How to participate?

WEB

1. Connect to www.wooclap.com/DIZLSA
2. You can participate

Thank you!

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