Hemoglobin (Hb)

Hemoglobin

- A **hemeprotein** found only in red blood cells
- Oxygen transport function
- Contains heme as prosthetic group
- Heme reversibly binds to oxygen

The heme group

- A complex of **protoporphyrin IX and ferrous iron (Fe^{2+})**
- Fe^{2+} is present in the center of the heme
- Fe^{2+} binds to four nitrogen atoms of the porphyrin ring
- Forms two additional bonds with:
  - Histidine residue of globin chain
  - Oxygen

Types of Hb

Normal

Hemoglobin A (HbA) (97%)

- Major Hb in adults
- Composed of four polypetide chains:
  - Two α and two β chains
- Contains two dimers of $\alpha\beta$ subunits
- Held together by non-covalent interactions
- Each chain is a subunit with a heme group in the center that carries oxygen
- A Hb molecule contains 4 heme groups and carries 4 moelcules of O_2

Fetal Hemoglobin (HbF) (1%)

- Major hemoglobin found in the fetus and newborn
- Tetramer with two α and two γ chains
- Higher affinity for O_2 than HbA
- Transfers O_2 from maternal to fetal circulation across placenta

HbA_2 (2%)

- Appears ~12 weeks after birth
- Constitutes ~2% of total Hb
- Composed of two α and two δ globin chains

HbA_{1c}

- HbA **undergoes non-enzymatic** glycosylation
- Glycosylation depends on plasma glucose levels
- HbA1c levels are high in patients with diabetes mellitus

Forms of HbA

T-form of Hb

- The deoxy form of Hb
- Taut form
- The movement of dimers is constrained
- **Low-oxygen-affinity form**

R-form of Hb

- The oxygenated form of Hb
- **Relaxed** form
- The dimers have more freedom of movement
- **High-oxygen-affinity form**

Abnormal

Carboxy-Hb	Met-Hb	Sulf-HB
CO replaces O_2 and binds 220X tighter than O_2 (in smokers)	Contains **oxidized Fe^{3+}** (~2%) that cannot carry O_2	Forms due to high sulfur levels in blood (**irreversible reaction**)

Hemoglobin function

- Carries oxygen from the lungs to tissues
- Carries carbon dioxide from tissues back to the lungs
- Normal level (g/dL):
  - Males: 14-16
  - Females: 13-15

Oxygen Dissociation Curve

- The curve is **sigmoidal**
- Indicates **cooperation** of subunits in O_2 binding
- Binding of O_2 to one heme group increases O_2 affinity of others
- Heme-heme interaction

Factors affecting oxygen binding (Three allosteric effectors) :		
pO2 (partial oxygen pressure)	❖ **pH of the environment** ❖ **pCO2 (partial carbon dioxide pressure)**	**Availability of 2,3-bisphosphoglycerate**
P_{50}	**The Bohr effect**	■ Binds to deoxy-Hb and stabilizes the **T-form** ■ When oxygen binds to Hb, BPG is released At high altitudes: - RBC number increases - Hb conc. increases - BPG increases **BPG reduce O2 affinity of Hb → fast unloading of O_2 → shift to the right in Oxygen Dissociation Curve**
■ Indicates affinity of Hb to O_2 ■ P_{50}(mm Hg): the pressure at which Hb is 50% saturated with O_2 ■ **High affinity → slow unloading of O_2** ■ **Low affinity → fast unloading of O_2** ■ Lung pO_2 is 100 mm → Hb saturation 100% ■ Tissue pO_2 is 40 mm → Hb saturation reduces ■ Hence O_2 is delivered to tissues	• Effect of pH and pCO2 on: ○ Oxygenation of Hb in the lungs ○ Deoxygenation in tissues • Tissues have lower pH (acidic) than lungs • Due to proton generation (two reactions): ○ CO2 + H20 → $HCO3^-$ + H+ • Protons reduce O2 affinity of Hb **DR'S NOTE :** Protons reduce O2 affinity of Hb **→ fast unloading of O_2 → shift to the right in Oxygen Dissociation Curve** **The Bohr effect** • Causing easier O2 release into the tissues • **The free Hb binds to two protons** • Protons are released and react with $HCO3^-$ to form CO2 gas ($HCO3^-$ + H+→CO2 + H20) • The proton-poor Hb now has greater affinity for O2 (in lungs) • The Bohr effect removes insoluble CO2 from blood stream and Produces soluble bicarbonate	**High altitude and O_2 affinity** • In hypoxia and high altitude ○ 2,3 BPG levels rise ○ This decreases O_2 affinity of Hb ○ Thus increases O_2 delivery to tissues **High O_2 affinity** High O_2 affinity is due to: ■ Alkalosis ■ High levels of **Hb F** ■ Multiple transfusion of 2,3 DPG-depleted blood

DR'S NOTE : increase CADET shift the curve to the right
C: CO2 , A: Acidity , D:DPG , E: Exercise , T : Temperature