صدقة جارية عن المغفور له بإذن الله **عمر عطية** من دفعة 2023 – كلية الطب، الجامعة الأردنية.

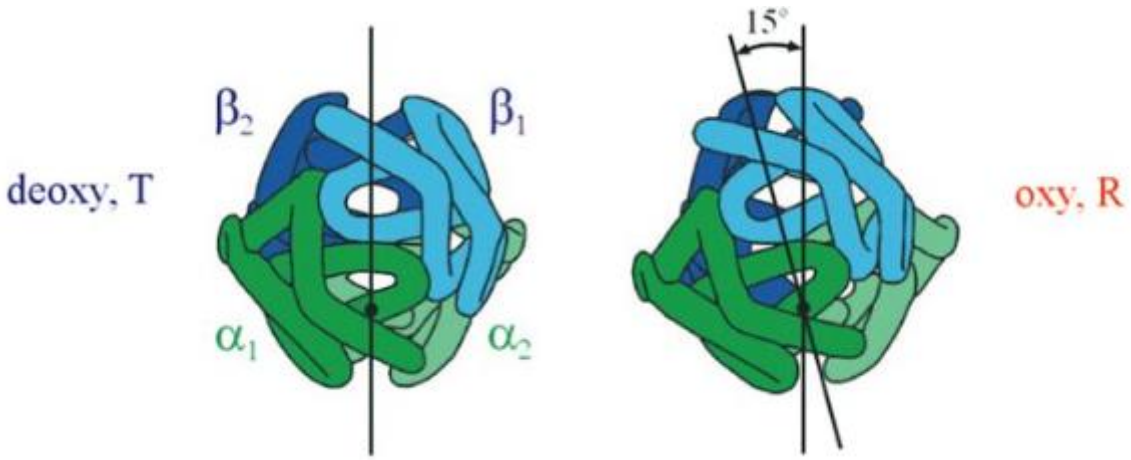
اللهم ارحمه واغفر له وأكرم نزله ووسع مدخله، لا تنسوه من دعائكم، إنا لله وإنا إليه راجعون.

#فريق_دوبامين_العلمي

Respiratory System Physiology

Comprehensive File 9

Dr. Yanal Shafagoj



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Hemoglobin – Recap

Oxygen is transported in the blood in two forms.
The first form is dissolved oxygen, which follows Henry's law, stating that the concentration of dissolved O_2 is proportional to its partial pressure. At a P_aO_2 of 100 mmHg, this equals ≈ 0.3 mL O_2 per dL of blood.

The second and major form is hemoglobin-bound oxygen (oxyhemoglobin), which is ≈ 20 mL O_2 per dL of blood (or 20%) in an individual with 15 g of hemoglobin per dL.

Within the heme group, iron is normally in the ferrous (Fe^{2+}) state, which can bind molecular oxygen. A small fraction (<2%) of hemoglobin contains iron in the ferric (Fe^{3+}) state, forming methemoglobin, which cannot bind O_2. Ferric iron is converted back to ferrous iron by methemoglobin reductase.

Each hemoglobin molecule contains four heme groups and can bind up to four O_2 molecules. Hemoglobin saturation represents the percentage of all heme sites occupied by oxygen and therefore ranges *continuously* from 0–100%, with no oversaturation possible.

Each gram of hemoglobin can bind 1.34 mL of O_2. Thus, with 15 g Hb/dL, oxygen bound to hemoglobin is ≈ 20 mL O_2/dL, whereas dissolved oxygen contributes ≈ 0.3 mL O_2/dL, representing 98.5% and 1.5% of total blood oxygen content, respectively.

Determinants of Blood Oxygen Content

Three points should be kept in mind when confirming normal lung function. Arterial PO_2 is necessary but not sufficient, because it does not indicate whether hemoglobin is adequately saturated with oxygen. Hemoglobin saturation alone is also not sufficient, since a person may be anemic and therefore have reduced oxygen-carrying capacity despite normal saturation.

The sufficient indicator of adequate oxygen content is oxygen concentration [O_2] in blood.

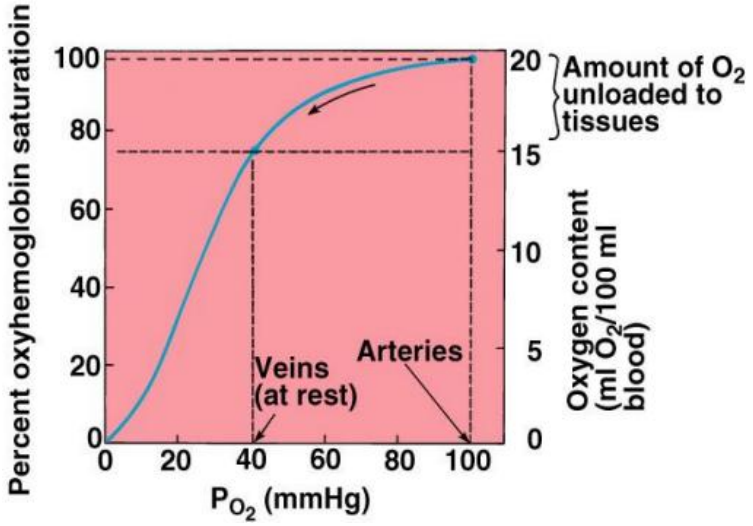
A normal arterial oxygen content of ≈ 20 mL O_2 per dL of blood is achieved when:

- Hemoglobin concentration is ≈ 15 g/dL
- Arterial PO_2 is ≈ 100 mmHg
- Hemoglobin saturation is = 97–98% ≈ 100%

When these conditions are present, blood oxygen concentration is considered normal.

If an anemic patient has a hemoglobin concentration of 7.5 g/dL, their P_aO_2 and O_2 saturation (SaO_2) will be normal, because gas exchange in the lungs is intact and the available hemoglobin becomes fully saturated. However, due to the reduced amount of hemoglobin, the oxygen concentration of blood will be ≈ 10 mL O_2/dL instead of the normal ≈ 20 mL O_2/dL. This makes [O_2] a sensitive indicator of blood oxygen content.

Oxyhemoglobin Dissociation Curve and Oxygen Extraction



PO_2	O_2 Sat
10	25
20	35
25	**50**
30	60
40	**75**
50	85
60	**90**
80	96
100	**98**

When arterial PO_2 is plotted against hemoglobin saturation, we observe that at 100 mmHg, hemoglobin saturation is = 98% ≈ 100%, while at 60 mmHg, saturation is ≈ 90%.

On the venous side, when PO_2 decreases to ≈ 40 mmHg, hemoglobin saturation falls to ≈ 75%, indicating that 25% of the oxygen bound to hemoglobin has been extracted by the tissues, resulting in an oxygen content of ≈ 15 mL O_2 per dL of mixed venous blood.

At a PO_2 of ≈ 26 mmHg, hemoglobin is 50% saturated. This value is known as the P_{50}, which represents the partial pressure of oxygen at which 50% of hemoglobin binding sites are occupied and 50% are unoccupied.

A useful memory aid for the oxyhemoglobin dissociation curve is the "4–5–6 / 7–8–9 rule", which provides approximate values (40 → 75; 50 → 85; 60 → 90).

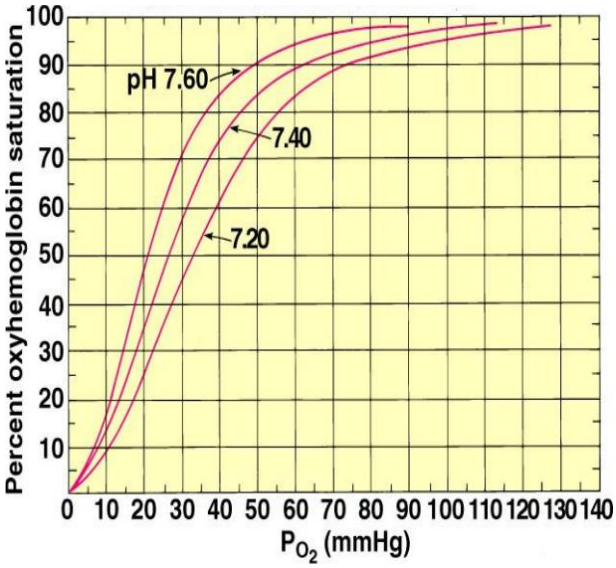
When PO_2 increases above 100 mmHg, hemoglobin is already nearly fully saturated, so no additional oxygen can be bound. Any further increase in PO_2 therefore results only in an increase in the dissolved oxygen fraction. Increasing PO_2 to 600 mmHg raises dissolved oxygen content to ≈ 1.8 mL O_2 per dL of blood, which is still insufficient to meet cellular oxygen requirements (≈ 5 mL O_2/dL) without oxyhemoglobin.

In a theoretical situation where no hemoglobin is present, achieving a dissolved oxygen concentration sufficient for life would require a PO_2 of approximately 3 atm. Such high oxygen pressure is not physiologically tolerable and can lead to oxygen toxicity due to excessive reactive oxygen species (ROS) generation, potentially resulting in death.

Venous PO_2 Changes in Anemia

When comparing an anemic person with a normal person, the key question is the effect on venous PO_2. As discussed before, arterial PO_2 can remain ≈ 100 mmHg in anemia. If hemoglobin concentration is 7.5 g/dL, arterial oxygen content is ≈ 10 mL O_2/dL. If the tissues extract 5 mL O_2/dL, the extraction fraction becomes ≈ 50%. This corresponds to a venous hemoglobin saturation of ≈ 50%, which is associated with a venous PO_2 of ≈ 26 mmHg (the P_{50}), instead of 40 mmHg, on the oxyhemoglobin dissociation curve.

Hemoglobin States



Hemoglobin exists in two conformational states: a high-affinity (R) state, which predominates in the lungs, and a low-affinity (T) state, which predominates in the tissues and facilitates oxygen release. At rest, tissues extract approximately 5 mL O_2 per dL of blood. During exercise, oxygen extraction increases markedly and may reach 10 mL/dL (50% extraction), 15 mL/dL (75% extraction), or even more in extreme cases.

During exercise, to allow increased unloading at the same PO_2 (≈ 40 mmHg in the interstitium), the oxyhemoglobin dissociation curve shifts to the right, reflecting reduced hemoglobin affinity for oxygen and stabilization of the T (tense) state.

This rightward shift is explained by four major mechanisms:

1. Bohr effect: increased H^+ concentration (decreased pH) reduces hemoglobin affinity for O_2.
2. Increased CO_2: CO_2 binding to hemoglobin (carbaminohemoglobin formation) favors O_2 release.
3. Increased temperature: higher temperature promotes oxygen unloading.
4. Increased 2,3-bisphosphoglycerate (2,3-BPG).

Red blood cells rely exclusively on glycolysis for energy. An intermediate of glycolysis, 1,3-bisphosphoglycerate, can be converted to 2,3-BPG via a mutase enzyme present in RBCs. During exercise, increased 2,3-BPG levels raise the P_{50}, indicating a rightward shift of the dissociation curve.

A leftward shift of the curve occurs when these conditions are reversed: alkalosis (↓ H^+), low CO_2, low temperature, and reduced 2,3-BPG, all of which increase hemoglobin affinity for oxygen.

Fetal hemoglobin (HbF) is composed of $\alpha_2\gamma_2$ subunits. 'γ' chains do not bind 2,3-BPG effectively, resulting in a left-shifted dissociation curve. This allows the fetus to extract enough oxygen from maternal blood (via the placenta), where $PO_2 \approx 40$ mmHg, not 100.