

Minireview Article

Oxygen Dissociation Curve: Reviewing the Its Physiology and Influencing Factors

ABSTRACT: The oxyhemoglobin dissociation curve ~~is a vital tool for comprehending~~ shows how blood transports and releases oxygen. ~~that Oxygen~~ is carried throughout the body both in bound form with protein (hemoglobin present inside **RBC**) and dissolved in **blood** plasma. The oxyhemoglobin dissociation curve ~~helps to describes~~ the relationship of oxygen saturation (SaO₂) ~~i.e. percentage of oxygen bound to oxygen~~ and partial pressure of oxygen in the blood (PaO₂).¹

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Keywords: Oxygen dissociation curve, oxygen binding affinity, Bohr effect

INTRODUCTION:

Oxygen saturation is essential for medical care and is closely regulated within the body.² Most oxygen (98%) ~~is transported within the body is attached to the hemoglobin,~~ whereas a small fraction (2%) is in dissolved form in the blood [17-19]. At atmospheric pressure, oxygen in dissolved form is only 3ml per liter per Henry's law, whereas approximately 197 ml of O₂ per liter is transported in protein-bound form. That means the dissolved fraction contributes a minor portion to the total amount of oxygen carried in the bloodstream.^{3, 4, 20, 21.}

Comment [H1]: What means the author with this?

Comment [H2]: Other option is using de active voice: "Hemoglobin transports 98% of oxygen, the rest is dissolved in plasma"

~~Concerning oxygen transport in the bloodstream, we need to understand two terms, Clarifying terms: -(i)~~ Oxygen saturation (SaO₂) means the percentage of hemoglobin bound to Oxygen, and Partial pressure of oxygen in the blood (PaO₂) ~~and this~~ determines the amount of Oxygen dissolved ~~in blood~~.

DISCUSSION:

Hemoglobin has two parts: ~~namely~~ a protein part (Globin) and a non-protein part (haem). This haem is composed of 4 subunits (2 alpha and 2 beta) bound to an iron atom which is in ferrous form (Fe⁺⁺). This hemoglobin tetramer binds to 4 Oxygen molecules.⁵

~~In general, t~~The Oxygen dissociation curve is a sigmoid curve, ~~and it~~. ~~The curve~~ is obtained by plotting oxygen tension on the X-axis and hemoglobin saturation on the Y-axis. It ~~gives a shows graphically visual impression of~~ how oxygen binds to hemoglobin.

Many ~~p~~ physiologic factors ~~can~~ shifts the oxygen dissociation curve either to the right or the left. Shift to the right causes hemoglobin to have a lesser affinity for oxygen and ~~to causes easier unloading release of~~ oxygen from hemoglobin. The shift to the left increases the affinity of hemoglobin for oxygen and causes hemoglobin to take up and retain oxygen more readily. ~~Factors that shifts the curve rightwards are An increase in~~ carbon dioxide, ~~increase in~~ hydrogen ion (i.e. decreased pH or acidity), ~~increase in~~ 2,3-DPG, and ~~an increase in~~ temperature ~~shifts the curve rightwards~~.

Hemoglobin exists in two states: the T state (tense, low affinity, deoxygenated) and the R state (relaxed, high affinity, oxygenated). These two states differ in their oxygen-binding affinity. In the unbound form, hemoglobin subunits exist in the T state. In lung alveoli, where there is a higher partial pressure of oxygen (pO_2), a hemoglobin subunit in the T state binds oxygen causing a conformational change in the other hemoglobin subunits, changing them to high-affinity R state. This causes oxygen ~~binding to occur with binds~~ ease. This process, in which one hemoglobin subunit helps others to gain more affinity for oxygen is ~~termed called as~~ positive cooperativity.^{6, 7.}

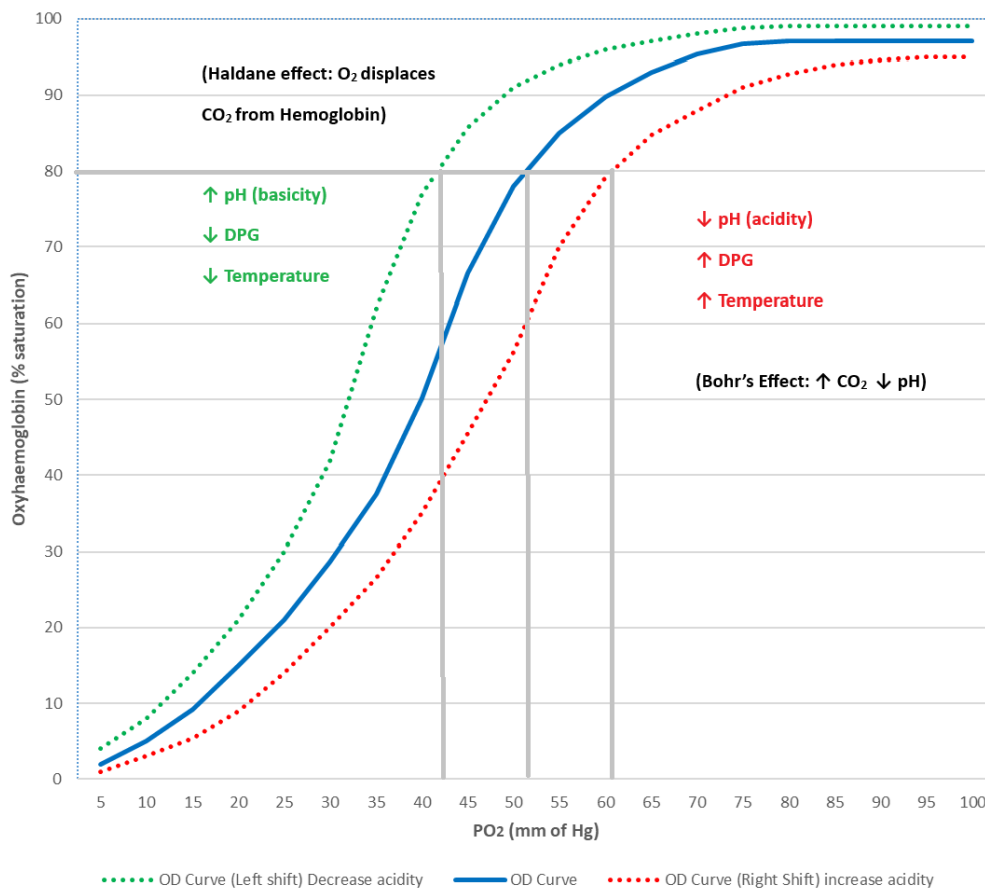


Figure 1: Hemoglobin Dissociation Curve: The dotted line corresponds with the shift to the right caused by Bohr effect. The figure can have the name of who elaborate it

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Parameters affecting Oxygen dissociation curve.

pH: With the increase of hydrogen ions acidity increases ~~and/or pH decrease~~. So, a decrease in pH (acidity) shifts the dissociation curve rightwards. The opposite is also true. An increase in pH (alkalinity) shifts the dissociation curve to the left.⁸

Carbon Dioxide: The effect of carbon dioxide and H⁺ ions on the oxygen dissociation curve is ~~quite closely~~ related. Carbon dioxide is mostly transported in the blood bloodstream in the bicarbonate buffer system, with a small portion being transported in carbaminohemoglobin form. Carbon dioxide on entering the red blood cells quickly converts to carbonic acid with the help of the enzyme carbonic anhydrase. This acid immediately dissociates into bicarbonate and hydrogen ion (H⁺ ion). The increase in hydrogen ion shifts the dissociation curve to the right by stabilizing the hemoglobin in the T-state, weakening its binding capacity, and increasing the likelihood of dissociation thus promoting the oxygen unloading. Hemoglobin's lower affinity for oxygen secondary to increases in the partial pressure of carbon dioxide is called the Bohr effect.^{9, 10, 11.}

2, 3-Diphosphoglycerate (DPG): ~~It is produced as a counter mechanism; the red blood cells produce more 2, 3-DPG which leads to the shifting of the curve to its normal position i.e. rightwards - and establish a respiratory compensation state - in conditions. At high altitudes where the oxygen level is low and hyperventilation occurs causing CO₂ washout, less pCO₂, and less hydrogen ion concentration leading to leftward shifting of oxygen-hemoglobin dissociation curve, as in the altitude. As a counter mechanism, the red blood cells produce more 2, 3 DPG which leads to the shifting of the curve to its normal position i.e. rightwards and establish a respiratory compensation state. That means under the stress of chronic hypoxic conditions at high altitudes, more 2,3-DPG is produced, which shifts the oxy-hemoglobin dissociation curve to the right in favor of oxygen unloading.~~ The relationship of hydrogen ions is inversely proportionate with levels of 2, 3 DPG.^{12, 13, 14.}

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Comment [H3]: I think it is redundant

Temperature: Oxygen unloading is favored with a rightward shift of the curve as the temperature increases. ~~Exercise is an example. As example, -~~ Muscular temperature increases ~~during exercise with increased exercise~~, shifting the curve to the right, and creating an environment where more and more oxygen is available for utilization as per the tissue demand.¹⁵

Carbon monoxide: Carbon monoxide has 240 times more affinity for hemoglobin than oxygen. Therefore, during carbon monoxide poisoning, CO attaches tightly with hemoglobin (carboxyhemoglobin), causing structural changes in the other oxygen binding sites of hemoglobin to relax (R) stage, and causing more affinity for oxygen and a leftward shift of curve. Therefore, the unloading of oxygen in the peripheral tissue is hampered. Despite maintaining normal paO₂, the person faces a state of tissue hypoxia. As the pulse oximeter is unable to differentiate carboxyhemoglobin from oxyhemoglobin, the ~~reading of person oxygen saturation~~ seems to be normal as per the reading of this machine.¹

Comment [H4]: Maybe it could be explained that in a blood gas analysis we can see the changes in SO₂

Fetal Hemoglobin: Fetal hemoglobin (HbF) is composed of 2 alpha and 2 gamma chain proteins in contrast to the adult hemoglobin (HbA) which is made up of 2 alpha and 2 beta chain. Due to this structural difference, fetal hemoglobin has a higher affinity for oxygen. The partial pressure at which HbF is half saturated with oxygen (P50) is 19 mm Hg, compared to 27 mm Hg for HbA. This helps the easier extraction of oxygen from maternal circulation for the fetus.¹⁶

CONCLUSION:

The oxyhemoglobin dissociation curve is ~~a vital~~ tool for comprehending how blood transports and releases oxygen. Detail knowledge of various factors involved in the right and the left shift of the oxygen-hemoglobin dissociation curve is essential for understanding the different physiological processes that occur at the tissue level and the level of the alveoli.

CONFLICT OF INTEREST: None

DISCLOSURE STATEMENT

Author Arijit Sil is an employee of IQVIA, a leading global provider of advanced analytics, technology solutions, and clinical research services to the life sciences industry but the views in the article are the author's own. Other than this, the author declares no professional, academic, competitive, or financial conflicts of interest related to this article. No funding was used in the preparation of this article.

COMPETING INTERESTS DISCLAIMER:

Authors have declared that they have no known competing financial interests OR non-financial interests OR personal relationships that could have appeared to influence the work reported in this paper.

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