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# Oxygen Dissociation Curve: Reviewing the Physiology and Influencing Factors

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***Author's contribution***

*The sole author designed, analysed, interpreted and prepared the manuscript.*

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## ABSTRACT

The oxyhemoglobin dissociation curve is a vital tool for comprehending how blood transports and releases oxygen, that is carried throughout the body both in bound form with protein (hemoglobin) and dissolved in plasma. The oxyhemoglobin dissociation curve describes the relationship of oxygen saturation ($SaO_2$) and partial pressure of oxygen in the blood ($PaO_2$) (Patel & Jose 2024).
The oxygen dissociation is affected by factors like pH, $CO_2$, 2,3-DPG, CO. This paper discusses the significance of factors like pH, $CO_2$, 2,3-DPG, CO, and structurally different haemoglobin which have a considerable effect on the affinity of haemoglobin for oxygen and determine how efficiently oxygen is supplied to the body cells.

*Keywords: Oxygen dissociation curve; oxygen binding affinity; Bohr effect.*

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## 1. INTRODUCTION

Oxygen saturation is essential for medical care and is closely regulated within the body (Abraham et al. 2023). Most oxygen (98%) transported within the body is attached to the hemoglobin, whereas a small fraction (2%) is in dissolved form in the blood (Boening et al. 2021, Rengasamy et al. 2021, Balcerek et al. 2020). At atmospheric pressure, oxygen in dissolved form is only 3ml per liter per Henry's law, whereas approximately 197 ml of $O_2$ 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 (Kaufman et al. 2024, Hess 1987, Sun et al. 2021, Ishihara et al. 2014).

Concerning oxygen transport in the bloodstream, we need to understand two terms, (i) Oxygen saturation ($SaO_2$) means the percentage of hemoglobin bound to Oxygen and Partial pressure of oxygen in the blood ($PaO_2$) and this determines the amount of Oxygen dissolved in blood.

The oxygen dissociation curve is important for understanding oxygen delivery to tissues under various physiological conditions. Body adaptation to different environments is reflected by the changes in the curve. The manuscript highlights the significance of factors like pH, $CO_2$, 2, 3-DPG, CO and structurally different haemoglobin which have a considerable effect on the affinity of haemoglobin for oxygen and determine how efficiently oxygen is supplied to the body cells.

## 2. FINDINGS

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 (Thom et al. 2013).

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

Many physiologic factors can shift 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 causes easier unloading 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. 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.

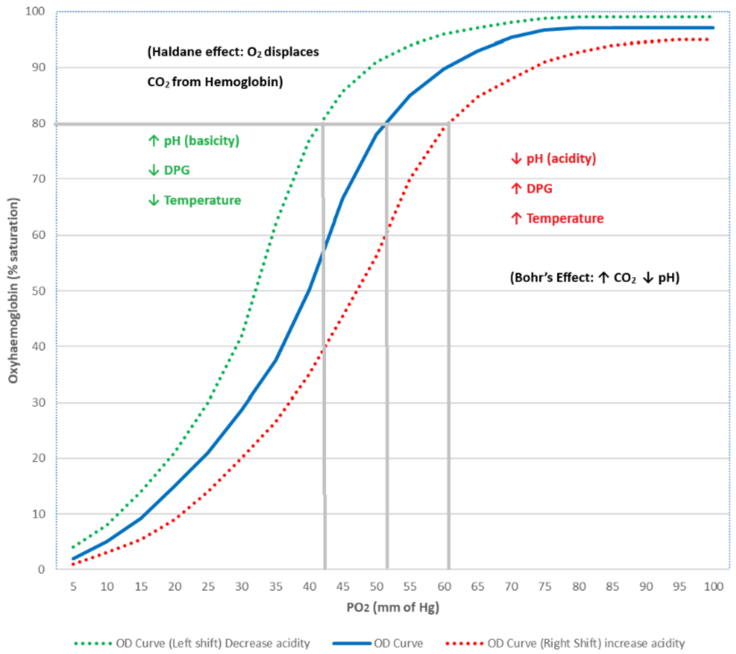


**Fig. 1. Hemoglobin dissociation curve: The dotted line corresponds with the shift to the right caused by Bohr effect. The figure was created by the author using MS Excel**

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 ease. This process, in which one hemoglobin subunit helps others to gain more affinity for oxygen is termed as positive cooperativity (Cambronero 2001, Mihailescu & Russu 2001).

## 3. PARAMETERS AFFECTING OXYGEN DISSOCIATION CURVE

### 3.1 pH

With the increase of hydrogen ions acidity increases (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 (Sharan & Popel 1989).

### 3.2 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 (Malte & Lykkeboe 2018, Benner et al. 2023, Malte et al. 2021).

### 3.3 2, 3-Diphosphoglycerate (DPG)

At high altitudes where the oxygen level is low, hyperventilation occurs causing $CO_2$ washout, less $pCO_2$, and less hydrogen ion concentration leading to leftward shifting of oxygen-hemoglobin dissociation curve. 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 (Sohmer & Dawson 1979, Scott et al. 2016, Mairbäurl et al. 1986).

### 3.4 Temperature

Oxygen unloading is favored with a rightward shift of the curve as the temperature increases. Exercise is an example. Muscular temperature increases 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 (Woyke et al. 2022).

### 3.5 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 $paO_2$, the person faces a state of tissue hypoxia. As the pulse oximeter is unable to differentiate carboxyhemoglobin from oxyhemoglobin, the person seems to be normal as per the reading of this machine (Patel & Jose 2024).

### 3.6 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 (Kaufman et al. 2024).

## 4. 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.

## DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author hereby declares that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.) and text-to-image generators have been used during the writing or editing of this manuscript.

## CONSENT

It is not applicable.

## ETHICAL APPROVAL

It is not applicable.

## 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

Author has 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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