Blood Gas Transport

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Required Reading: Respiratory Physiology: A Clinical Approach, Shwarrtzstein & Parker, Ch. 5 (p.105-111).

Objectives

1. State the physical and chemical forms of oxygen transported by the blood and specify the relative proportion of each form.
2. Define oxygen content, hemoglobin saturation and the oxygen-carrying capacity of blood.
3. State the physiological consequences of the shape of the oxygen-hemoglobin dissociation curve on loading of oxygen at the lungs and unloading of oxygen at the tissues.
4. Identify the factors that shift the position of the oxyhemoglobin curve to the right & explain the result of such a rightward shift on P_{50} , the affinity of hemoglobin for oxygen and tissue oxygenation.
5. Specify the effect of carbon monoxide on the oxygen content and oxygen carrying capacity of blood.
6. Identify the colour of hemoglobin in the following forms: 1) oxyhemoglobin, 2) deoxyhemoglobin 3) caboxyhemoglobin.
7. State the physical and chemical forms of carbon dioxide transported by the blood and specify the relative proportion of each form.
8. State the role of carbonic anhydrase in the transport of carbon dioxide.
9. Describe the carbon dioxide dissociation curve for whole blood and explain how the conformational changes in hemoglobin (Hb) associated with binding with oxygen molecules affects transport of carbon dioxide by the blood [the *Haldane effect*].

1-2 Transport of Oxygen By Blood

Oxygen is transported in two forms in the blood:

1. Physically dissolved in plasma (2 %)
   - Compared to carbon dioxide, oxygen is relatively insoluble in plasma
   - 100 ml blood contains 0.3 ml of oxygen at PO_2 = 100 mmHg

2. Chemically bound to the hemoglobin molecule (Hb) in the red blood cells (98 %) Hb can combine rapidly and reversibly with oxygen. The reversibility of this reaction allows oxygen to be released to the tissues.

$$\underset{\substack{\text{deoxyhemoglobin}\\ \text{a.k.a reduced Hb}}}{Hb} + O_2 \leftrightarrow \underset{\text{oxyhemoglobin}}{HbO_2}$$

- Each gram of Hb can combine with 1.34 ml of oxygen. Normally, blood contains ≈ 15g Hb/100ml of blood [or 150g/L]. Hence the **oxygen carrying capacity of Hb** is 15 X 1.34 = 20 ml oxygen/100 ml blood.

The amount of oxygen in the blood (sum of both forms, dissolved and bound to hemoglobin) is called the **oxygen content of blood** and is described in ml O_2 per 100 ml blood (or volume %).

The O_2 content of arterial blood (C_aO_2) is ≈ 20 vol% ; the O_2 content of venous blood (C_vO_2) ≈ 15 vol%.
Therefore, each time blood circulates through the circulation, 5 vol% of oxygen is taken up by the tissues.

The proportion of hemoglobin that is bound to oxygen is called percent saturation and written as **% Hb saturation** or often clinically for arterial blood as **S_aO_2**:

$$S_aO_2\ (\%) = \frac{\text{oxygen combined with Hb}}{\text{oxygen carrying capacity of Hb}} \times 100$$

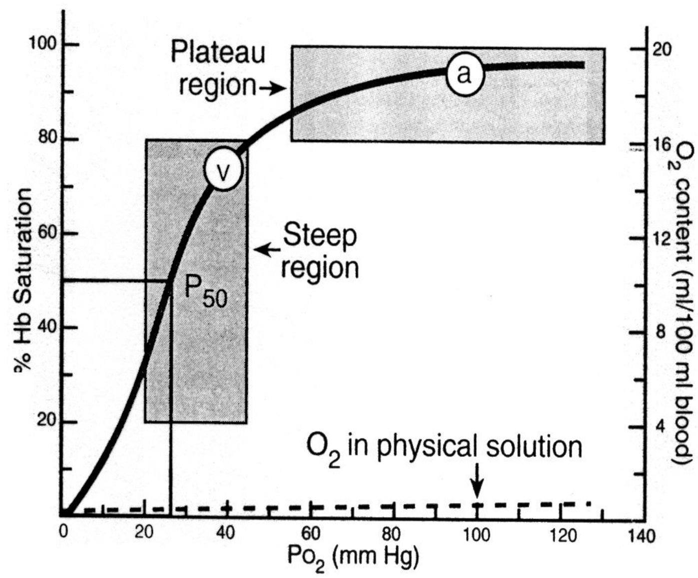
<u>It is important to note that</u> both **oxygen carrying capacity** and **oxygen content** depend on the amount of hemoglobin in an individual's blood and are expressed as volume of oxygen present per unit volume of blood. Whereas, the **S_aO_2** expresses a percentage and not a unit volume of oxygen. Therefore **S_aO_2** and oxygen content are not interchangeable. For example, two patients may have the same **S_aO_2** but if one has a low blood hemoglobin concentration because of anemia, she will have lower oxygen content.

3. The Oxyhemoglobin Dissociation Curve

Loading oxygen in the lungs

- Venous blood entering the pulmonary capillaries has a PO_2 of 40 mm Hg; Hb is 75% saturated with oxygen. As the blood passes through the pulmonary capillaries, it equilibrates with the alveolar PO_2 of about 100 mmHg and Hb becomes about 97% saturated with oxygen.

- In the plateau region, at PO_2 60-100 mm Hg, there is little change in amount of O_2 bound to Hb. Therefore, if arterial PO_2 decreases within this plateau range, either due to a low inspired level of oxygen or due to disease, the Hb is still almost maximally saturated. This feature provides a safety margin for the exchange of oxygen in the lungs. In addition, increasing PO_2 beyond 100 mmHg does not improve oxygen carriage by Hb significantly.



A normal adult oxy-hemoglobin dissociation curve for blood at 37°C, pH= 7.4, PCO_2= 40mmHg. A, arterial; v, venous; P_{50}, partial pressure of O_2 required to saturated 50% of the hemoglobin with oxygen.

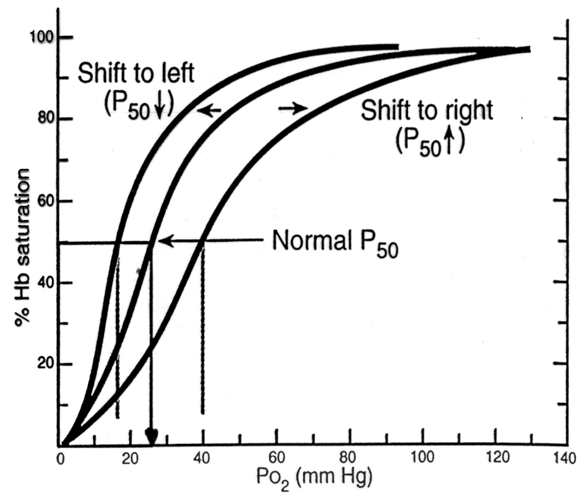
Unloading oxygen at the tissues:

- As blood passes from the systemic arteries into the capillaries, it is exposed to lower PO_2; oxygen is released from Hb, leaving the blood and entering the tissue. The PO_2 in the systemic capillaries varies from tissue to tissue. The oxyhemoglobin dissociation curve is very steep between PO_2 = 60-20 mm Hg. Therefore, within this steep range, a small decrease in PO_2 in the tissues will result in great unloading of oxygen to the tissues.

Key points to memorize:

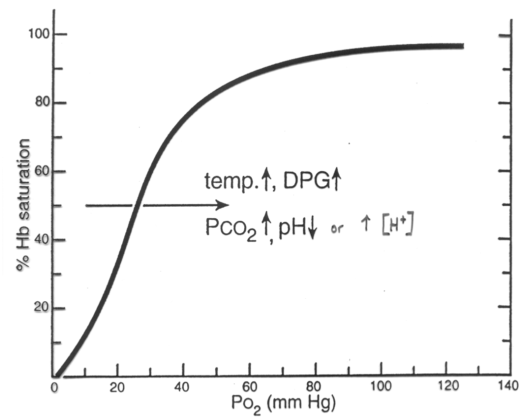
P_aO_2 (mmHg)	SaO2 (%) a.k.a. %Hb Saturation
100	99
60	90
27	50

4. The position of the oxy-hemoglobin dissociation curve is not fixed & can vary by a few factors. These variations in the position of the curved are described as changes in the affinity of hemoglobin for O_2.



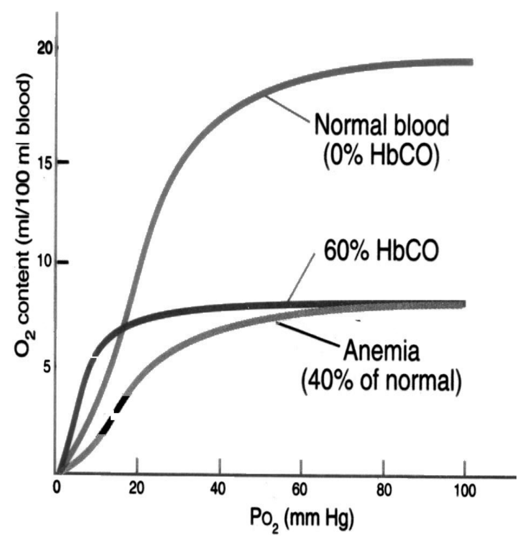
The position of the curve can be defined by the PO_2 at which 50% of Hb is bound to oxygen, P_{50}. At normal body temperature of 37°C, arterial blood with a pH of 7.4, a PCO_2 of 40 mmHg, $P_{50} \approx 27$ mmHg. When the affinity of hemoglobin for oxygen decreases (P_{50} increases) the curve is shifted to the right & unloading of oxygen to the tissues is enhanced.

Factors that enhance the unloading of the oxygen at the tissues and shift the curve to the right:



1) ↑ [H+], ↓ pH
2) ↑ PCO_2 ***(Bohr Shift)***
3) ↑ temperature
4) ↑ 2,3 DPG (2,3 DPG=2,3 diphosphoglycerate, or more accurately 2,3 BPG=2,3 bisphoshoglycerate)
   - an organic phosphate; a byproduct of anaerobic metabolism of glucose in the red blood cell
   - levels increase with chronic hypoxia [e.g. high altitude, chronic lung disease].

<u>5. Other Factors That Affect Oxygen Transport in The Blood</u>



1) Anemia
- The association of oxygen and Hb expressed as % Hb saturation is not affected, but the association of oxygen and Hb expressed as arterial content of blood is reduced [see figure on the right] because the decreased amount of hemoglobin per 100 ml blood decreases the oxygen carrying capacity of the blood

2) Carbon Monoxide (CO)

a. The affinity of Hb for carbon monoxide is 240 times that for O_2. CO competitively blocks the combination of oxygen with Hb.CO bound Hb is called **carboxyhemoglobin** (HbCO).

b. CO also shifts the oxyhemoglobin dissociation curve to the left (interferes with the unloading of O_2 at the tissues).

Together these characteristics of CO can lead to severe tissue hypoxia. A person breathing CO can slowly reach life-threatening levels of carboxyhemoglobin. Carbon monoxide is colorless, odorless, tasteless and does not elicit reflexes such as coughing or sneezing. It does not increase ventilation nor results in a sensation of shortness of breath (dyspnea)._Small amounts of carboxyhemoglobin are present in normal individuals due to urban pollution or smoking. A non- smoker living in a rural area may have only 1% COHb in the blood; whereas a heavy smoker living in urban area can have 5-8% COHb in the blood.

Self directed study of hemoglobins other than the adult Hb such as fetal hemoglobin and hemoglobinopathies would be useful in this context.

6. The Colours Of Hemoglobin

Oxygenated Hb, HbO_2 - bright red [e.g. normal arterial blood]
Deoxygenated Hb, Hb- blue [same as the color of systemic veins carrying venous blood]
Carboxyhemoglobin, COHb – cherry red [e.g. patient with CO poisoning]

Cyanosis is defined as arterial blood with > 5g Hb/100ml in deoxygenated state and results in a bluish / purple discoloration of nail beds and mucous membranes. The presence of cyanosis can be a sign of poor transport of oxygen. However, the absence of cyanosis does not indicate normal oxygen transport. For example, an anemic patient with low oxygen in the blood may not appear cyanotic because he may not have sufficient deoxygenated Hb to appear cyanotic. Also patients with abnormally high levels of Hb, such as those with polycythemia may appear cyanotic.

7-8 Transport Of Carbon Dioxide By The Blood

Carbon dioxide is transported in blood more readily than oxygen because carbon dioxide is 20 times more soluble than oxygen in plasma. The amount of carbon dioxide in the blood (carbon dioxide content) is described as ml CO_2 per 100 ml blood (or volume %).

The CO_2 content of arterial blood (C_aCO_2) is 48 vol%; the CO_2 content of venous blood (C_vCO_2) is 52 vol%.

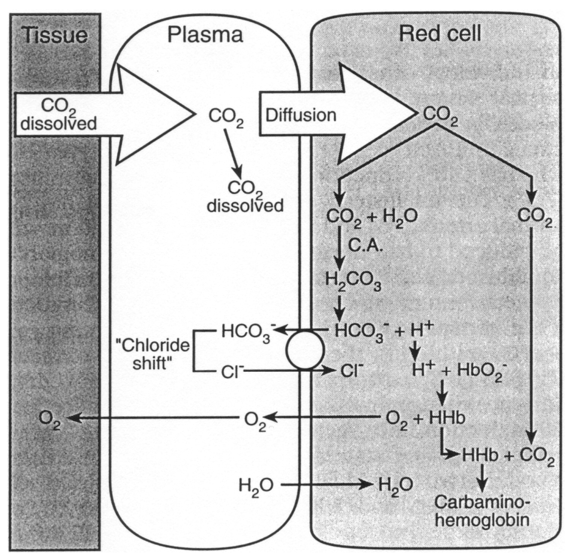
Therefore, each time blood circulates through the body, 4 vol% of carbon dioxide is removed from the tissues and delivered to the lungs to be exhaled.

Carbon dioxide is transported in 3 forms in the blood:

1. physically dissolved [5 %*]
2. physically dissolved as bicarbonate ion [90%]*
3. combined with Hb as carbamino-compound [5%]*

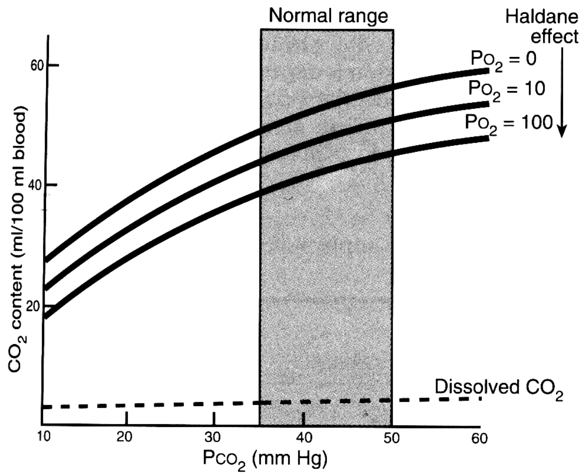
- C.A.= carbonic anhydrase, an enzyme present in red blood cells but not in plasma that accelerates the formation of carbonic acid from water and CO_2 over 1000 times.

**in arterial blood*



10. The Carbon Dioxide Dissociation Curve

The relationship between the PCO_2 & the whole blood CO_2 content (in all 3 forms mentioned above) is known as the **carbon dioxide dissociation curve**. Within the range of normal blood PCO_2, the curve is nearly a straight line.



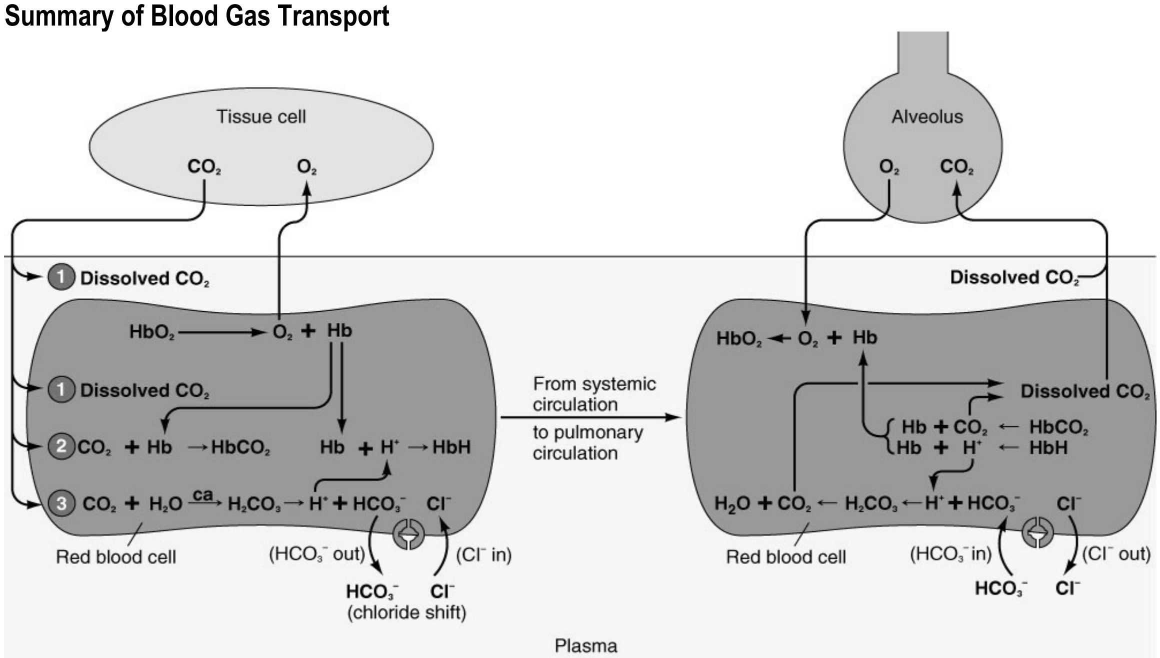
Transport of CO_2 is dependent on O_2 release.

The CO_2 dissociation curve is influence by the state of oxygenation of the Hb (***Haldane effect***). The Haldane effect can be explained by the fact that deoxygenated Hb is better than oxygenated Hb in:

1) combining with hydrogen ions and in turn assisting the blood to load more CO_2 from the tissues.

2) combining with carbon dioxide to form carbamino compounds and in turn assisting the blood to load more CO_2 from the tissues for removal at the lungs.

Summary of Blood Gas Transport



<u>Gas exchange at the tissues</u>: As CO_2 leaves the tissue cells and enters the red blood cell, it causes more O_2 to dissociate from Hb (Bohr shift); thus more CO_2 combines with Hb and more HCO_3^- is produced.

<u>Gas exchange at the lungs</u>: As O_2 passes from the alveoli into the red blood cells, Hb becomes saturated with O_2 and becomes a stronger acid. The more acidic Hb releases more H^+ that binds to more HCO_3^- to form carbonic acid. The carbonic acid dissociates into CO_2 and water. The CO_2 diffuses from the blood into the alveoli.