O2 and CO2 Transport in the Blood

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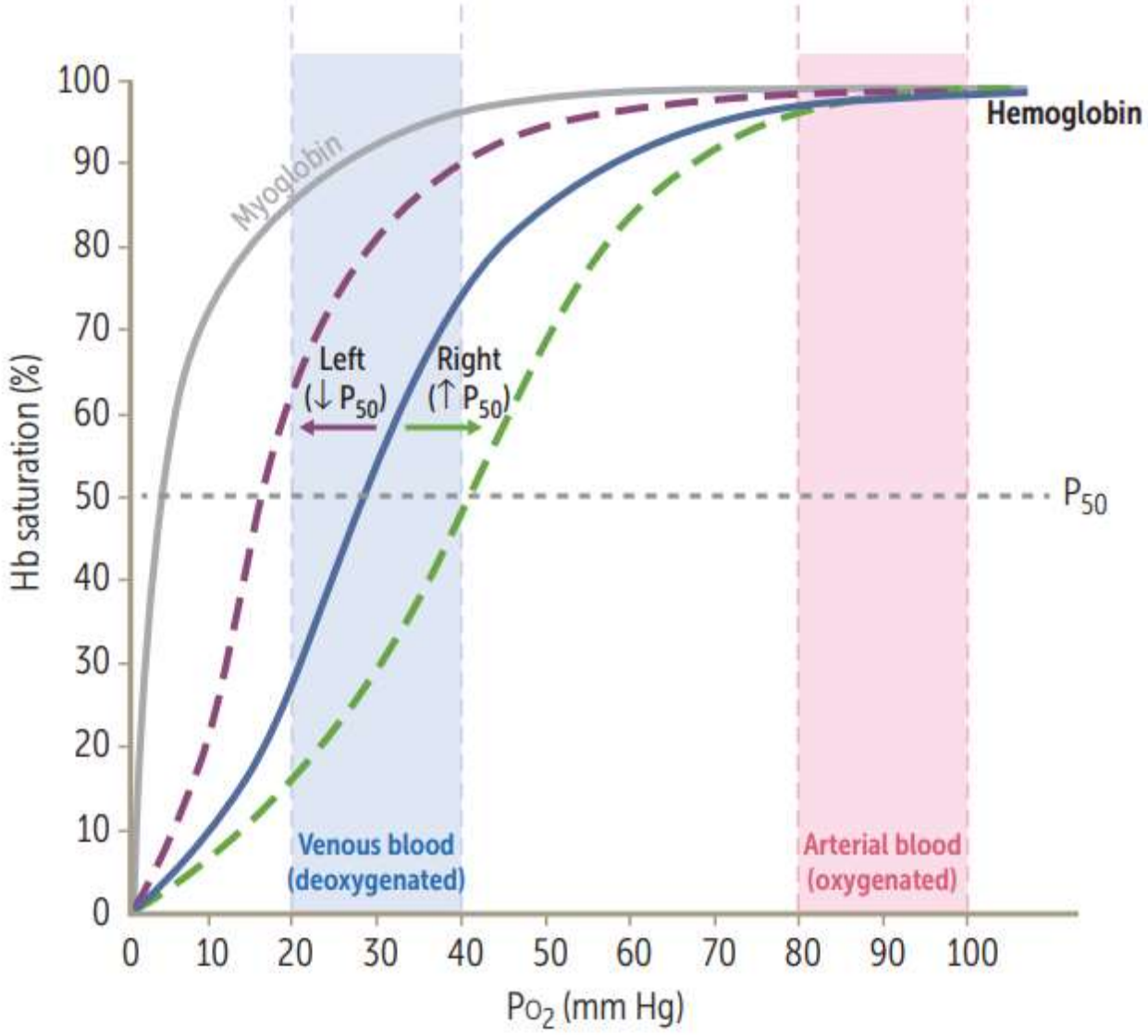

Hb saturation (%)
100
90
80
70
60
50
40
30
20
10
0
Myoglobin
Hemoglobin
Left
(↓ P50)
Right
(↑ P50)
P50
Venous blood
(deoxygenated)
Arterial blood
(oxygenated)
0
10
20
30
40
50
60
70
80
90
100
PO2 (mm Hg)

Utilization coefficient

- The percentage of the blood that gives up its O2 as it passes through the tissue capillaries is called the **utilization coefficient**.

- The normal value is about 25%, i.e. 25% of the oxygenated hemoglobin gives its O2 to the tissues.

- During strenuous exercise, the utilization coefficient in the entire body can increase to 75% to 85%.

PO2, O2 sat, O2 content

- O2 saturation (although clinically useful, does not always reflect the oxygen content of blood. For example, if a patient is anemic (low hemoglobin), but breathing well (normal pO2), then oxygen saturation may be close to 100%, but total oxygen content may be low.)

- differentiate between pO2 (mm Hg, the dissolved fraction), oxygen saturation (% of hemoglobin occupied), and O2 content (expressed as a volume percentage).

- Arterial oxygen content is approximately 20 g/dL, the venous oxygen content is 15 g/dL, and dissolved oxygen contributes 0.1 g/dL in each case.

Hemoglobin

- Entering the systemic circulation, oxygen-rich hemoglobin is in the R form. At the lower pO2 in the peripheral tissues, oxygen begins to unbind. With less oxygen bound, and at a lower pO2, the T state becomes more favorable, which facilitates unloading oxygen atoms two through four.

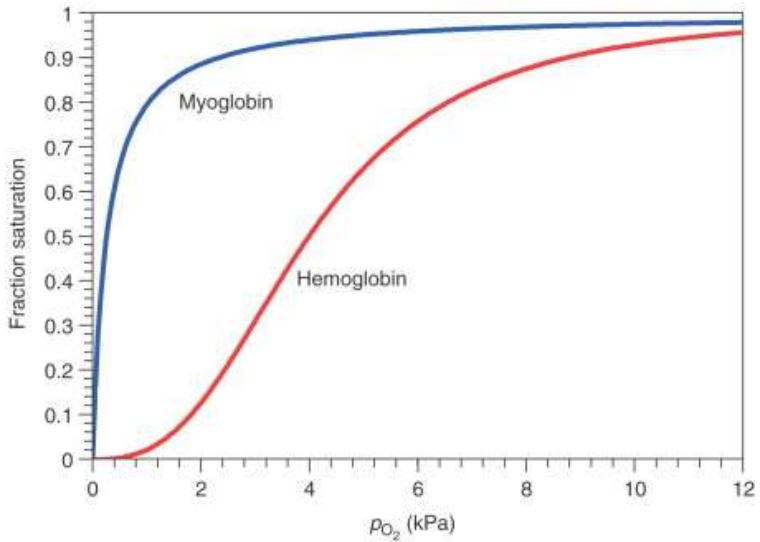
- Throughout the bloodstream, at different pO2 levels, there is a continuum between the T state (unloading, requiring high O2 to bind) and the R state (loading, requiring low O2 to unbind).

O2- Hb dissociation curve

- At higher oxygen tension, for example during pulmonary circulation, the oxygen dissociation curve plateaus.
- At lower oxygen tension, the slope of the oxygen dissociation curve is steeper.
- A rightward shift favors unloading oxygen compared to the original curve at the same oxygen tension.
- Conversely, oxygen loading is favored with a leftward shift with the oxygen dissociation curve.

Myoglobin

- myoglobin, as a single subunit oxygen-carrying protein, does not exhibit cooperativity. This helps pull oxygen into skeletal muscle



https://www.sciencedirect.com/topics/neuroscience/myoglobin

Rt shift

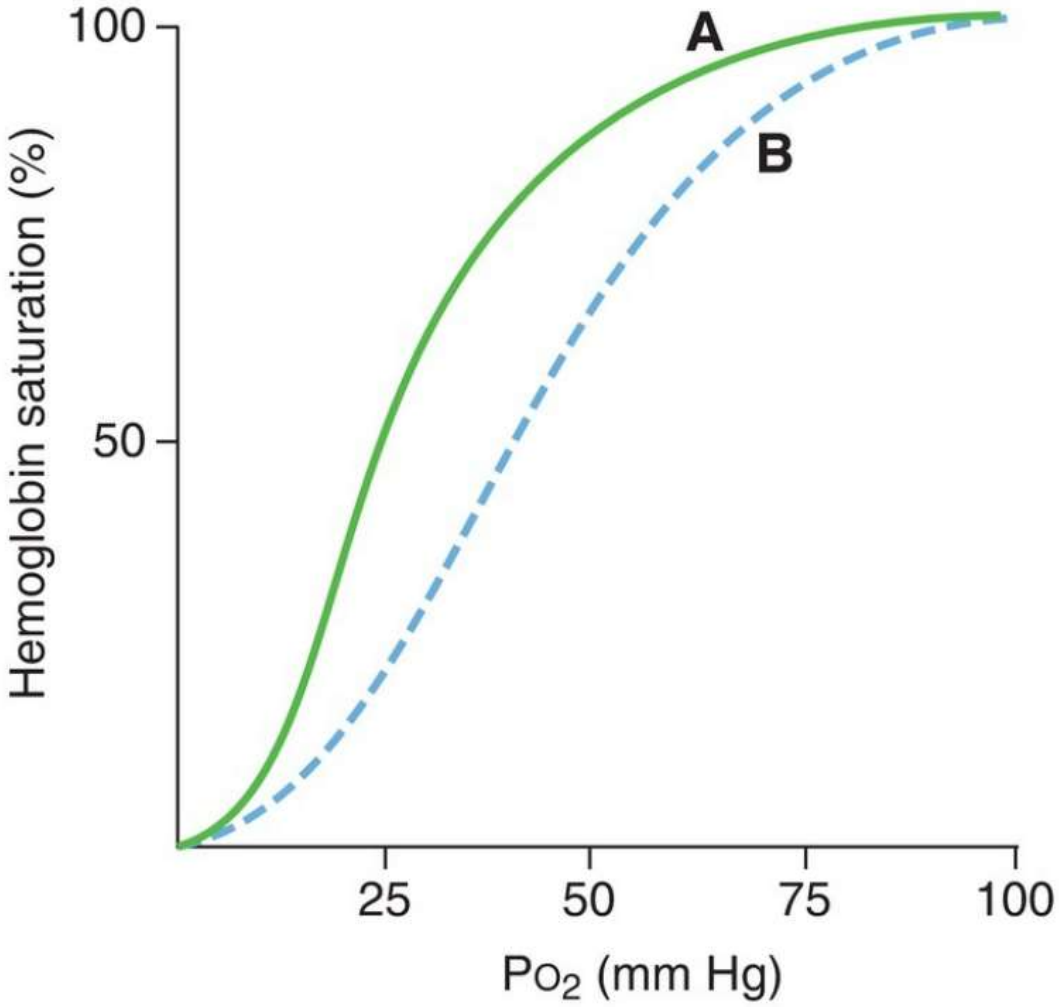
- helpful in delivering oxygen to metabolically active tissues

- The relationship between acidity, CO2, and hemoglobin O2 affinity is called the **Bohr effect**. An increase in CO2 will decrease the pH and induce oxygen unloading.
- in a high acid state 2,3 BPG binds specifically to deoxy Hb in the central cavity thus stabilizing the deoxygenated state of Hb and decreasing O2 affinity.
- At higher temperatures, unloading is favored.

Lt shift

- Fetal Hb introduces a leftward shift of the curve, favoring O2 binding to hemoglobin at lower oxygen tension. This is favorable in the womb, to allow the growing fetus to pull O2 from the maternal circulation.

- In the treatment of sickle cell disease, treatment with hydroxyurea has been shown to increase levels of circulating fetal hemoglobin. These patients will have higher oxygen tension, which favors the O2 bound form, which helps prevent the hemoglobin from sickling and causing an acute crisis.


100
50
Hemoglobin saturation (%)
A
B
25
50
75
100
P_{O_2} (mm Hg)

Question

- In the hemoglobin–O2 dissociation curves shown above, the shift from curve A to curve B could be caused by:

- (A) increased pH
- (B) decreased 2,3-diphosphoglycerate (DPG) concentration
- (C) strenuous exercise
- (D) fetal hemoglobin (HbF)
- (E) carbon monoxide (CO) poisoning

Question

- The shift from curve A to curve B is associated with

- (A) increased P50
- (B) increased affinity of hemoglobin for O2
- (C) impaired ability to unload O2 in the tissues
- (D) increased O2-carrying capacity of hemoglobin
- (E) decreased O2-carrying capacity of hemoglobin

CO poisoning

- The dissociation curve undergoes a leftward shift in carbon monoxide poisoning.
- CO has a 240-fold greater affinity for hemoglobin than oxygen and will displace oxygen.
- Despite a greater proportion of saturated hemoglobin molecules, total O2 content is decreased because of the high affinity of CO for hemoglobin.

CO poisoning

- two effects of CO on O2 binding to hemoglobin are catastrophic for O2 delivery to tissues.

- Reduced O2-binding capacity of hemoglobin.
- The remaining heme sites bind O2 more tightly.

CO poisoning

- Even though the O2 content of blood is greatly reduced in CO poisoning, the Po2 of the blood may be normal.

- This situation makes exposure to CO especially dangerous because the blood is bright red, and there are no obvious signs of hypoxemia, such as a bluish color of the fingertips or lips (cyanosis).

- Po2 is not reduced, and the feedback mechanism that usually stimulates an increased respiration rate in response to lack of O2 (usually reflected by a low Po2) is absent.

CO poisoning

- Because the brain is one of the first organs affected by lack of oxygen, the person may become disoriented and unconscious before becoming aware of the danger.
- A patient severely poisoned with CO can be treated by administering pure O2 because O2 at high alveolar pressure can displace CO rapidly from its combination with hemoglobin.
- The patient can also benefit from simultaneous administration of 5% CO2 because this strongly stimulates the respiratory center, which increases alveolar ventilation and reduces alveolar CO.
- With intensive therapy, CO can be removed from the blood as much as 10 times as rapidly as without therapy.

DESCRIPTION OF CASE. On a cold February morning in Boston, a 55-year-old man decides to warm his car in the garage. While the car is warming, he waits in a workshop adjoining the garage. About 30 minutes later, his wife finds him tinkering at his workbench, confused and breathing rapidly. He is taken to a nearby emergency department and given 100% O_2 to breathe. The following arterial blood values are measured:

Pa_{O_2}, 660 mm Hg

Pa_{CO_2}, 36 mm Hg

pH, 7.43

% O_2 saturation of hemoglobin, 60%

EXPLANATION OF CASE. The man inhaled the exhaust fumes from his automobile and is suffering from acute CO poisoning. The arterial blood values obtained can be explained by the effects of CO-binding to hemoglobin.

CO binds avidly to hemoglobin, with an affinity that is 250 times that of O_2-binding to hemoglobin. Thus heme groups that normally are bound to O_2 now are bound to CO. The percent saturation of hemoglobin with O_2 is measured as 60%, so 40% of the sites must be occupied by CO. Because O_2-hemoglobin is the major form of O_2 transport to the tissues, the first detrimental effect of CO poisoning is the decreased O_2-carrying capacity of blood. The second detrimental effect of CO poisoning is a shift of the O_2-hemoglobin dissociation curve to the left, which reduces P_{50} and increases the affinity of hemoglobin for what little O_2 is bound. As a result, it is more difficult to unload O_2 to the tissues. Together, these two effects of CO poisoning can result in death caused by a failure to deliver sufficient O_2 to critical tissues such as the brain.

TREATMENT. Treatment of this patient consists of having him breathe 100% O_2 in an effort to rapidly displace as much CO from hemoglobin as possible.

Notice the strikingly high value of Pa_{O_2} at 660 mm Hg. *Is this value plausible?* Assuming that there is no $\dot{V}/\dot{Q}$ defect, Pa_{O_2} should be equal to PA_{O_2} because there is equilibration of pulmonary capillary blood with alveolar gas. Therefore a better question is *Why is* PA_{O_2} *660 mm Hg?* The expected value for PA_{O_2} can be calculated from the alveolar gas equation, if values are known for the PO_2 of inspired air, PA_{CO_2}, and the respiratory quotient. PI_{O_2} can be calculated from the barometric pressure (corrected for water vapor) and the percent of O_2 in inspired air (100%). PA_{CO_2} is equal to Pa_{CO_2}, which is given. The respiratory quotient is assumed to be 0.8. Thus

$$P_{I_{O_2}} = (P_B - P_{H_2O}) \times F_{O_2}$$
$$= (760 \text{ mm Hg} - 47 \text{ mm Hg}) \times 1.0$$
$$= 713 \text{ mm Hg}$$

$$P_{A_{O_2}} = P_{I_{O_2}} - \frac{P_{A_{CO_2}}}{R}$$
$$= 713 \text{ mm Hg} - \frac{36 \text{ mm Hg}}{0.8}$$
$$= 668 \text{ mm Hg}$$

Again, assuming that systemic arterial blood has the same P_{O_2} as alveolar gas, and assuming that $\dot{V}/\dot{Q}$ ratios are normal, the *measured* value for Pa_{O_2} of 660 mm Hg is consistent with the *expected* $P_{A_{O_2}}$ value of 668 mm Hg, calculated with the alveolar gas equation. This extremely high Pa_{O_2} does little to improve O_2 delivery to the tissues because the solubility of O_2 in blood is so low (0.003 mL O_2/100 mL blood per mm Hg). Thus at a Pa_{O_2} of 660 mm Hg, the dissolved O_2 content is only 1.98 mL O_2/100 mL blood.

Respiratory exchange ratio

- normal transport of O2 from the lungs to the tissues by each 100 ml of blood is about 5 ml, whereas normal transport of CO2 from the tissues to the lungs is about 4 ml.
- Thus, under normal resting conditions, only about 82% as much CO2 is expired from the lungs as O2 is taken up by the lungs.

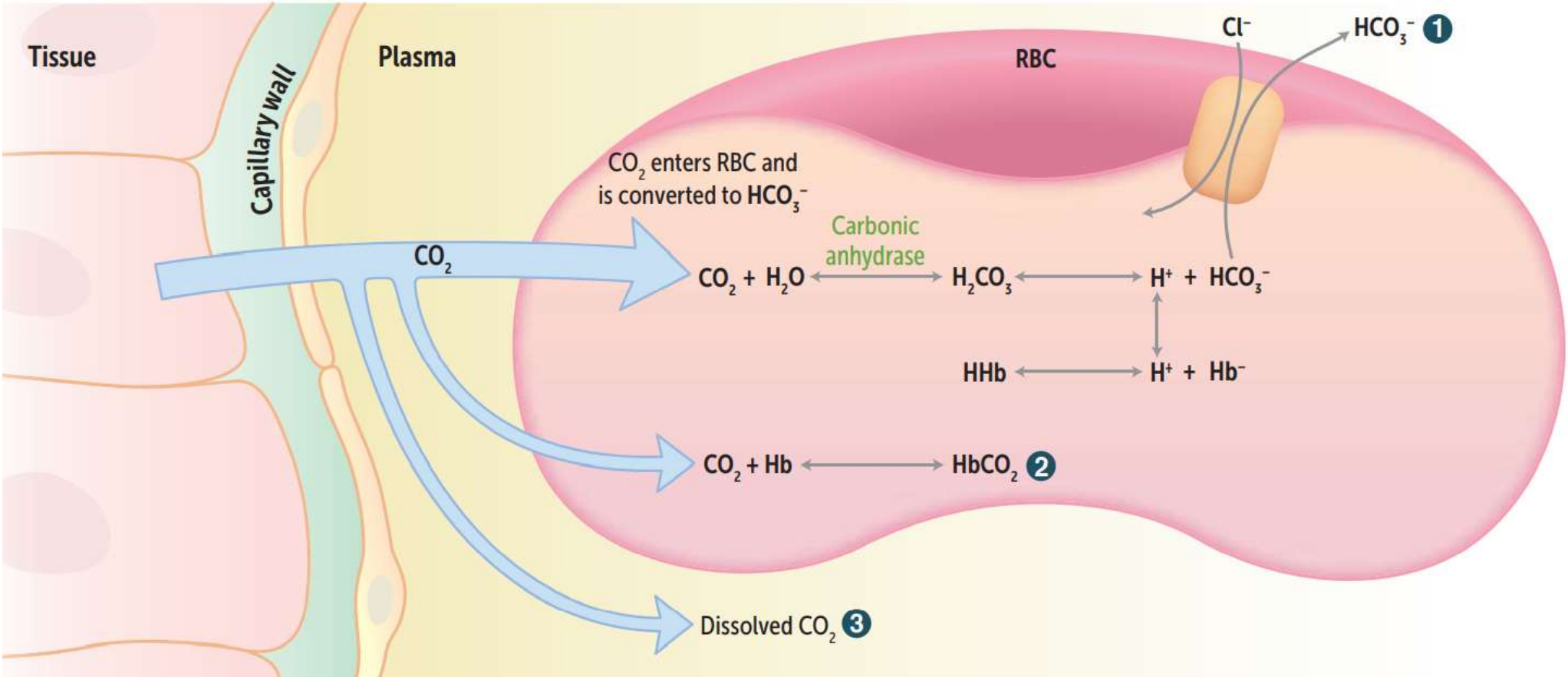
- The ratio of CO2 output to O2 uptake is called the respiratory exchange ratio (R).
- R = Rate of carbon dioxide output / Rate of oxygen uptake

Respiratory exchange ratio

- The value for R changes under different metabolic conditions.
- When a person is using carbohydrates exclusively for body metabolism, R rises to 1.00.
- Conversely, when a person is using fats exclusively for metabolic energy, the R level falls to as low as 0.7.

Dissolved CO_2

- As with O_2, a portion of the CO_2 in blood is in the dissolved form.
- The concentration of CO_2 in solution is given by Henry's law, which states that the concentration of CO_2 in blood is the partial pressure multiplied by the solubility of CO_2.
- The solubility of CO_2 is 0.07 mL CO_2/100 mL blood per mm Hg; thus the concentration of dissolved CO_2 in arterial blood, as calculated by Henry's law, is 2.8 mL CO_2/100 mL blood (40 mm Hg × 0.07 mL CO_2/100 mL blood per mm Hg), which is approximately 5% of the total CO_2 content of blood.


Tissue
Capillary wall
Plasma
RBC
Cl⁻
HCO3⁻ 1
CO2 enters RBC and is converted to HCO3⁻
Carbonic anhydrase
CO2
CO2 + H2O
H2CO3
H+ + HCO3⁻
HHb
H+ + Hb⁻
CO2 + Hb
HbCO2 2
Dissolved CO2 3

CO2

- Carbonic anhydrase inside the red blood cells catalyzes the reaction between CO2 and water and accelerates its reaction rate by about 5000-fold.

- Therefore, instead of requiring many seconds or minutes to occur, as is true in the plasma, the reaction occurs so rapidly in red blood cells that it reaches almost complete equilibrium within a small fraction of a second.

- This phenomenon allows tremendous amounts of CO2 to react with the red blood cell water, even before the blood leaves the tissue capillaries.

Carbaminohemoglobin

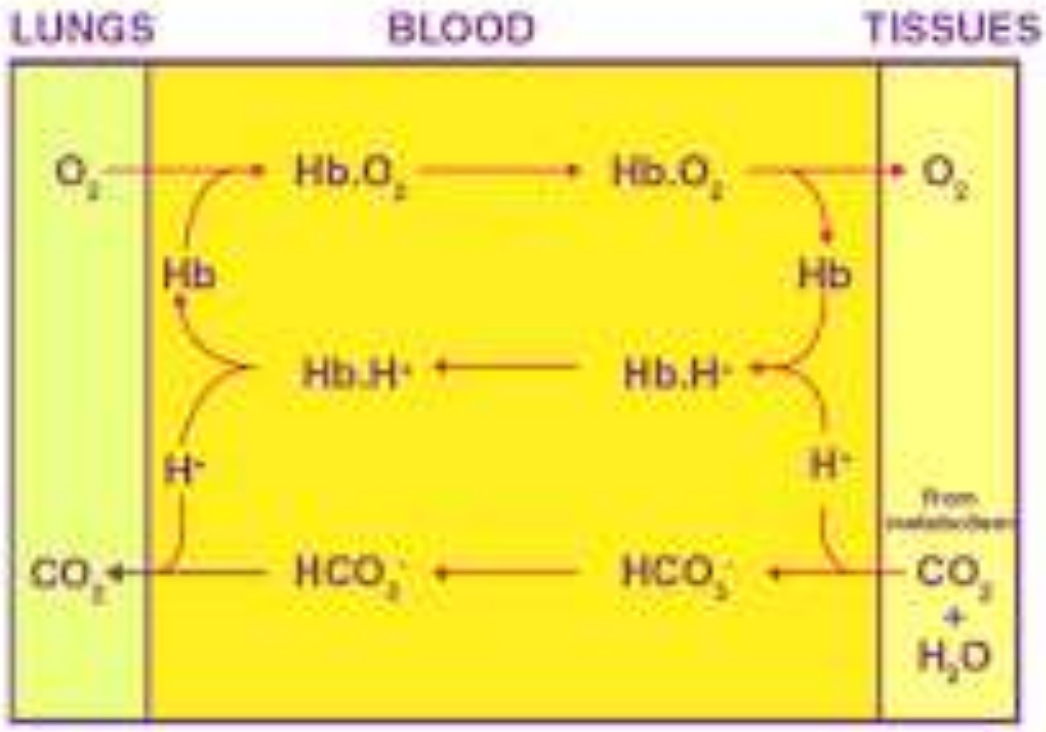
- CO_2 binds to terminal amino groups on proteins (e.g., hemoglobin and plasma proteins such as albumin).
- When CO_2 is bound to hemoglobin, it is called carbaminohemoglobin.
- CO_2 binds to hemoglobin at a different site than O_2 binds to hemoglobin.
- CO_2 binding to hemoglobin reduces its affinity for O_2 and causes a right shift of the O_2-hemoglobin dissociation curve (**Bohr effect**).

CO_2

- All of the reactions illustrated in the figure occur in reverse in the lungs.

- H^+ is released from its buffering sites on deoxyhemoglobin, HCO_3^- enters the red blood cells in exchange for Cl^-, H^+ and HCO_3^- combine to form H_2CO_3, and H_2CO_3 dissociates into CO_2 and H_2O.

- The regenerated CO_2 and H_2O are expired by the lungs.


LUNGS
BLOOD
TISSUES
O_2
$Hb.O_2$
$Hb.O_2$
O_2
Hb
Hb
$Hb.H^+$
$Hb.H^+$
H^+
H^+
from metabolism
CO_2
HCO_3^-
HCO_3^-
CO_2 + H_2O

Haldane effect

- In lungs, oxygenation of Hb promotes dissociation of H+ from Hb.
- This shifts equilibrium toward CO2 formation; therefore, CO2 is released from RBCs.

The Haldane effect

- The Haldane effect results from the simple fact that the combination of O_2 with hemoglobin in the lungs causes the hemoglobin to displace CO_2 from the blood and into the alveoli in two ways.

- First, the more highly acidic hemoglobin has less tendency to combine with CO_2 to form carbaminohemoglobin, thus displacing much of the CO_2 that is present in the carbamino form from the blood.

- Second, the increased acidity of the hemoglobin also causes it to release an excess of H^+, and these ions bind with HCO_3^- to form carbonic acid, which then dissociates into water and CO_2, and the CO_2 is released from the blood into the alveoli and, finally, into the air.

Haldane effect

- drops in pH promote oxygen unloading, but the venous blood is not appreciably more acidic than arterial blood due to the Haldane effect.

- Deoxygenation in the periphery promotes carbaminohemoglobin (CO_2-Hgb) formation, binding up of H^+, and release of bicarbonate. This allows for effective buffering between the arterial and venous ends of the circulation, and for efficient carriage of a significant portion of the CO_2 pool.

Question

- In the transport of CO_2 from the tissues to the lungs, which of the following occurs in venous blood?

- (A) Conversion of CO_2 and H_2O to H^+ and HCO_3^- in the red blood cells (RBCs)
- (B) Buffering of H^+ by oxyhemoglobin
- (C) Shifting of HCO_3^- into the RBCs from plasma in exchange for Cl^-
- (D) Binding of HCO_3^- to hemoglobin
- (E) Alkalinization of the RBCs

Question

- The pH of venous blood is only slightly more acidic than the pH of arterial blood because

- (A) CO_2 is a weak base
- (B) there is no carbonic anhydrase in venous blood
- (C) the H^+ generated from CO_2 and H_2O is buffered by HCO_3^- in venous blood
- (D) the H^+ generated from CO_2 and H_2O is buffered by deoxyhemoglobin in venous blood
- (E) oxyhemoglobin is a better buffer for H^+ than is deoxyhemoglobin

Additional references

- Kaufman DP, Kandle PF, Murray I, et al. Physiology, Oxyhemoglobin Dissociation Curve. [Updated 2022 Aug 1]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK499818/

Thank you