Transport of O_2 and CO_2 by the blood

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Lecture Objectives:

1. State the relationship between the partial pressure of oxygen in the blood and the amount of oxygen physically dissolved in the blood.
2. Define oxygen partial pressure (tension), oxygen content, and percent hemoglobin saturation as they pertain to blood.
3. Describe and draw an oxyhemoglobin dissociation curve (hemoglobin oxygen equilibrium curve) showing the relationships between oxygen partial pressure, hemoglobin saturation, and blood oxygen content.
4. On the same axes, draw the relationship between PO_2 and dissolved plasma O_2 content (Henry's Law). Compare the relative amounts of O_2 carried bound to hemoglobin with that carried in the dissolved form.
5. Describe how the shape of the oxyhemoglobin dissociation curve influences the uptake and delivery of oxygen.
6. Define P50.
7. Show how the oxyhemoglobin dissociation curve is affected by changes in blood temperature, pH, PCO_2, and 2,3-DPG, and describe a situation where such changes have important physiological consequences.
8. Describe how anemia and carbon monoxide poisoning affect the shape of the oxyhemoglobin dissociation curve, PaO_2, and SaO_2.
9. List the forms in which carbon dioxide is carried in the blood. Identify the percentage of total CO_2 transported as each form.
10. Describe the importance of the chloride shift in the transport of CO_2 by the blood.
11. Identify the enzyme that is essential to normal carbon dioxide transport by the blood and its location.
12. Draw the carbon dioxide dissociation curves for oxy- and deoxyhemoglobin.
13. Describe the interplay between CO_2 and O2 binding on hemoglobin that causes the Haldane effect.

General Notes:

- If the diffusion coefficient for oxygen is considered as 1, then relative diffusion coefficient for CO_2 is 20.3.
- Normally, the major limitation to the movement of gases in tissues is the diffusion rate through tissue water instead of through the cell membranes (including the alveolocapillary membrane), as both oxygen and CO_2 are highly lipid soluble.
- Hemoglobin (Hb) in the RBC allows blood to transport 30 to 100 times as much oxygen as could be transported in the form of dissolved oxygen in water (230 ml O_2/min at rest).
- PO_2 of the alveolar capillaries is about 104 mmHg. However, PO_2 in the left ventricular blood is about 95 mmHg due to venous admixture of blood.
- Normally, 97% of oxygen transported from the lungs to the tissues is carried combined with the Hb in the RBCs. The remaining 3% is transported in the dissolved state in the water.

The Hemoglobin:

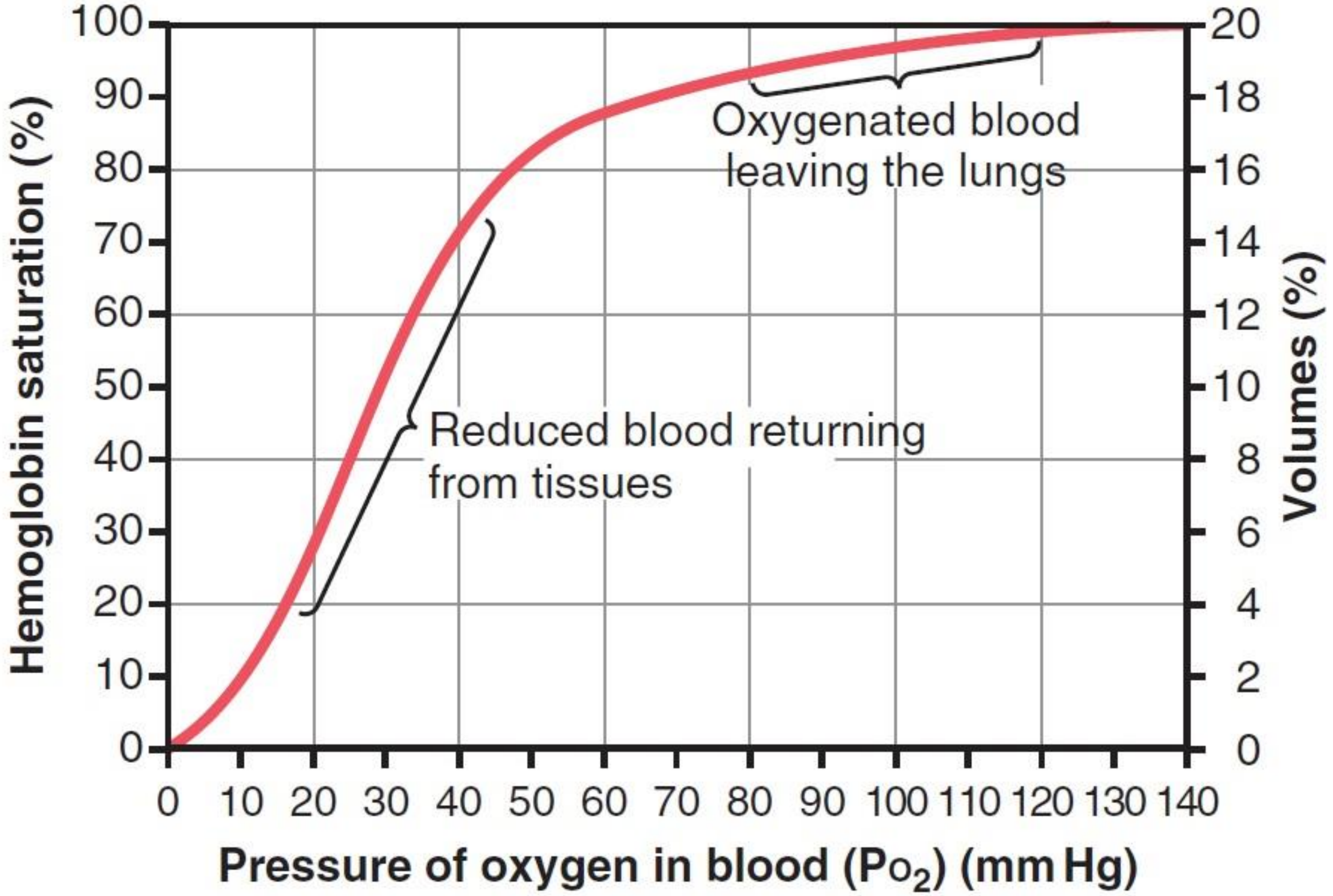
- Hemoglobin is a protein made up of 4 subunits, each of which contains a heme moiety attached to a polypeptide chain. Each heme has one atom of ferrous iron.
- In deoxyhemoglobin, the globin units are said to be in a tense (T) configuration → reduced affinity to O_2 molecules.
- When oxygen is first bound, the bonds holding the globin units are released → relaxed (R) configuration → exposes more O_2 binding sites → ↑ O_2 affinity.
- Hb has 4 functions;
  - Facilitates oxygen transport
  - Facilitates CO_2 transport
  - Acts as a buffer to maintain pH
  - Transports NO that promotes vasodilation

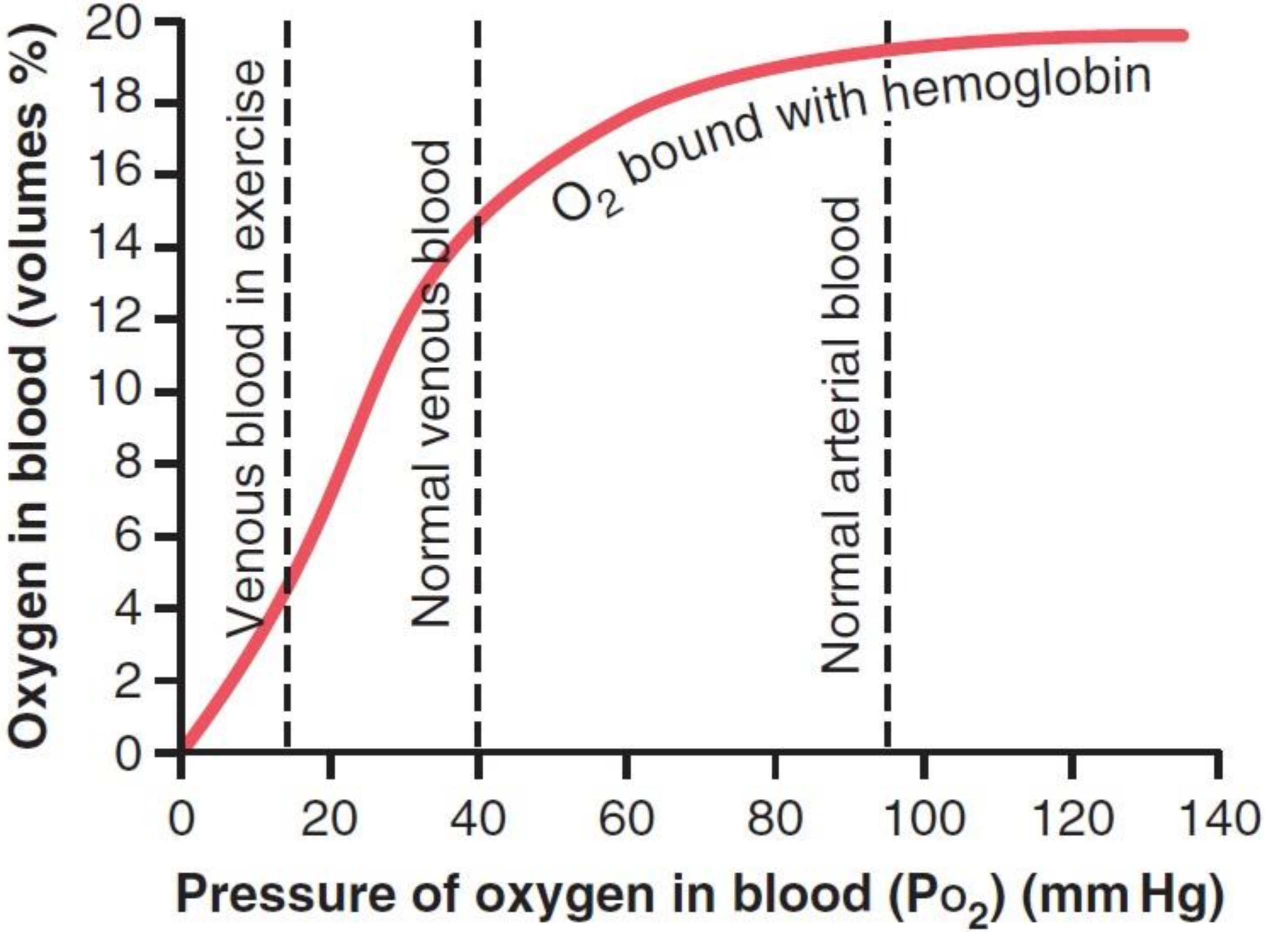
Transport of Oxygen in The Blood

Oxygen-Hemoglobin Dissociation Curve:

This curve demonstrates the relationship between the percentage of Hb saturation with oxygen and PO_2. The curve is sigmoid in shape due to T-R interconversion. The curve shows the following facts;

- The usual oxygen saturation of systemic arterial blood is 97% and that of venous blood is about 75%.
- Each 100 ml of blood carries 20 ml of oxygen at full (100%) saturation considering Hb concentration as 15 g/100 ml of blood.
- Arterial blood carries 19.4 ml O_2/100 ml of blood and 14.4 ml O_2/100 ml of venous blood. Therefore, 5 ml of O_2 are transported from the lungs to the tissues by each 100 ml of blood.
- Hb can buffer marked oxygen concentration changes in atmosphere. Oxygen delivery is almost the same between the range of 60 – over 100 mmHg arterial PO_2.


Hemoglobin saturation (%)
Volumes (%)
Pressure of oxygen in blood (P_{O_2}) (mm Hg)
Oxygenated blood leaving the lungs
Reduced blood returning from tissues
100
90
80
70
60
50
40
30
20
10
0
20
18
16
14
12
10
8
6
4
2
0
0 10 20 30 40 50 60 70 80 90 100 110 120 130 140



Oxygen in blood (volumes %)
20
18
16
14
12
10
8
6
4
2
0
Venous blood in exercise
Normal venous blood
Normal arterial blood
O_2 bound with hemoglobin
0
20
40
60
80
100
120
140
Pressure of oxygen in blood (P_{O_2}) (mm Hg)

Factors that shift the Oxygen-Hemoglobin Dissociation Curve:

Note:

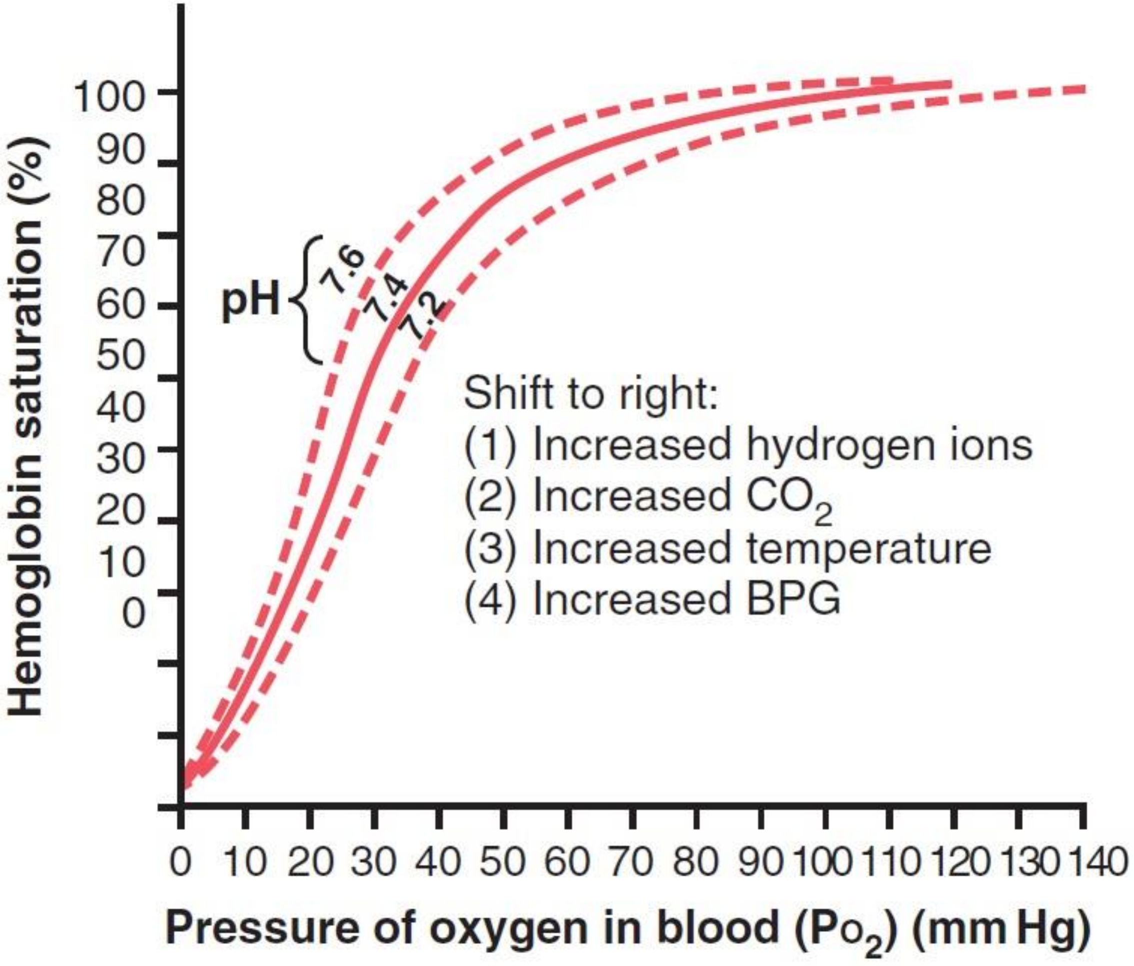
P_{50} is a convenient index to study the shift. The P_{50} is the level of PO_2 where Hb is half saturated with O_2. The higher the P_{50}, the lower the affinity of Hb for oxygen. The normal P_{50} for arterial blood is 26 to 28 mmHg

1. Effect of CO_2 and Hydrogen ion (Bohr effect):

   Bohr effect = the decrease in O_2 affinity of Hb when pH of blood falls.

   ↑ CO_2 and ↑H^+ → shift the curve to the right → ↑ oxygen release from the blood in the tissues.

   Bohr effect causes left shift of the curve in the lungs → ↑ oxygenation of the pulmonary blood.


Hemoglobin saturation (%)
100
90
80
70
60
50
40
30
20
10
0
pH
7.6
7.4
7.2
Shift to right:
(1) Increased hydrogen ions
(2) Increased CO_2
(3) Increased temperature
(4) Increased BPG
0 10 20 30 40 50 60 70 80 90 100 110 120 130 140
Pressure of oxygen in blood (P_{O_2}) (mm Hg)

Factors that shift the Oxygen-Hemoglobin Dissociation Curve:

2. Effect of 2,3 –diphosphoglycerate (**DPG**):
   - DPG is very plentiful in red cells because RBC lack mitochondria. It is a product of glycolysis before forming pyrovate. When 2,3-BPG molecule is then converted to 3-PG, ATP is generated.
   - When 2,3-BPG binds to deoxyhemoglobin, it acts to stabilize the low oxygen affinity state (T state) conformation, making it harder for oxygen to bind hemoglobin and more likely to be released to adjacent tissues. 2,3-BPG acts as such as a part of a feedback loop that can help prevent tissue hypoxia in conditions where it is most likely to occur.
   - It's important to note that the behavior of myoglobin doesn't work in the same way, as 2,3-BPG has no effect on it.
   - In pregnancy, there is a 30% increase in intracellular 2,3-BPG. This lowers the maternal hemoglobin affinity for oxygen, and therefore allows more oxygen to be offloaded to the fetus in the maternal uterine arteries. The fetal hemoglobin (HbF) has a low sensitivity to 2,3-BPG, so HbF has a higher affinity for oxygen. Therefore although the PO_2 in the uterine arteries is low, the fetal umbilical arteries (which are deoxygenated) can still get oxygenated from them.

Factors that shift the Oxygen-Hemoglobin Dissociation Curve:

2. Effect of 2,3 –diphosphoglycerate (**DPG**) cont.:
   - Thyroid hormones, Growth hormone, and androgens increase the concentration of DPG and P50. Ascent to high altitude triggers a substantial rise in DPG concentrations in RBCs. DPG also increases in anemia and in diseases associated with chronic hypoxia (e.g. airway obstruction or congestive heart failure), DPG keeps the oxygen-dissociation curve shifted slightly to the right all the time.
   - In hypoxia, the increased level of DPG →↑ oxygen release. This mechanism adapts for hypoxia caused by poor tissue blood flow and hypoxia due to living in high altitude.

3. Effect of exercise:

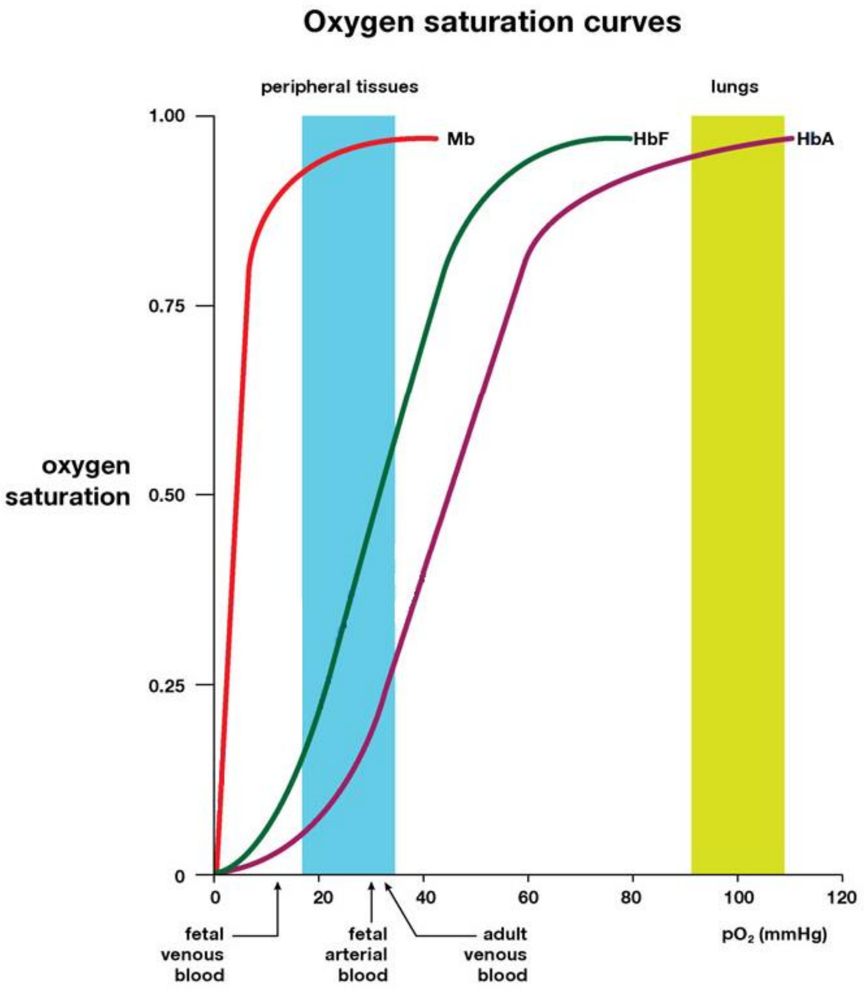
   Several factors cause the curve to shift to the right in exercise. These are ↑ CO_2 release by tissues, acid formation, ↑ DPG production, and increased muscular temperature (2-3° C).

The Myoglobin:

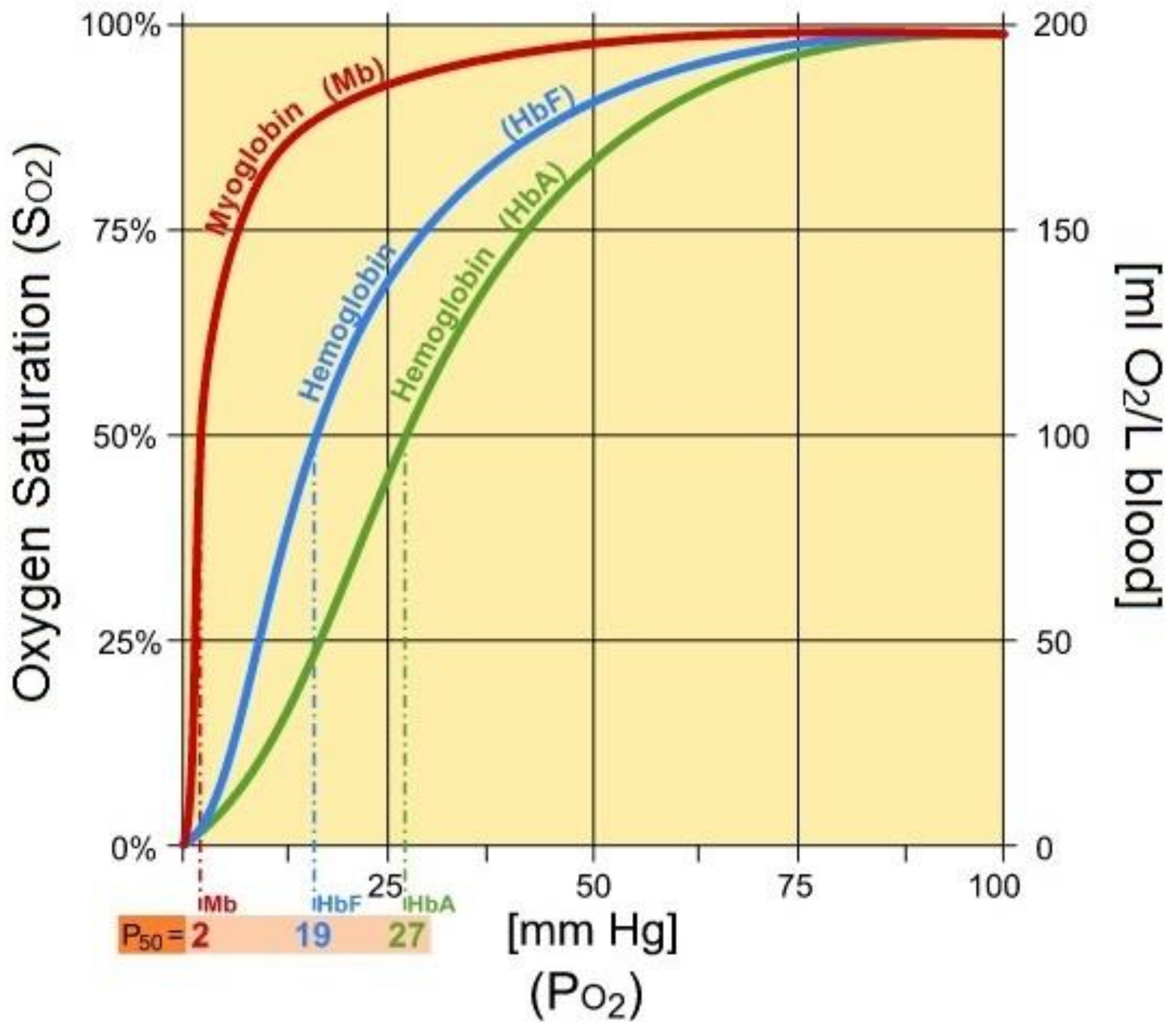
A protein found in skeletal muscle. It resembles Hb but binds 1 rather than 4 mol of oxygen per mole.

Its dissociation curve is a rectangular hyperbolic rather than a sigmoid curve and placed to the left of both fetal and adult oxygen-hemoglobin dissociation curves when plotted together.

As myoglobin has a higher affinity for oxygen it extracts oxygen from the hemoglobin and deliver it later to the skeletal muscle when O_2 is cut off during skeletal muscle contraction.



Oxygen saturation curves
peripheral tissues
lungs
1.00
0.75
0.50
0.25
0
oxygen saturation
Mb
HbF
HbA
0
20
40
60
80
100
120
pO2 (mmHg)
fetal venous blood
fetal arterial blood
adult venous blood



100%
75%
50%
25%
0%
Oxygen Saturation (SO2)
Myoglobin (Mb)
Hemoglobin (HbF)
Hemoglobin (HbA)
200
150
100
50
0
[ml O2/L blood]
25
50
75
100
Mb
HbF
HbA
P50 = 2 19 27
[mm Hg]
(PO2)

Test Question:

A 42-year-old man got an accident and suffered lacerations of his liver and spleen. His hemoglobin concentration was 7 g/dl, and he was given a 2-unit transfusion of packed red blood cells. Which of the following changes would you expect to see as a result of the transfusion?

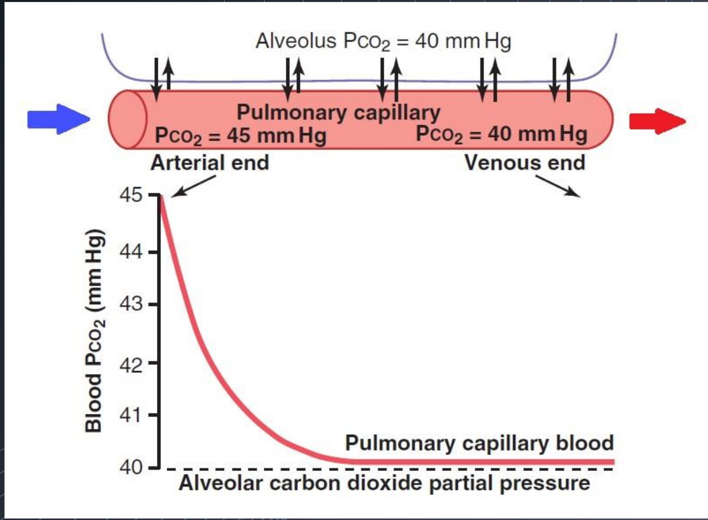
A. Decreased arterial oxygen concentration
B. Increased arterial PO_2
C. Increased oxygen concentration of mixed venous blood
D. Increased arterial oxygen saturation
E. Increased tissue oxygen consumption

Transport of CO_2 in The Blood

Introduction:

- The major difference between diffusion of CO_2 and of O_2 is that CO_2 can diffuse about *20 times as rapidly as O_2*.
- The pressure differences required to cause CO_2 diffusion are far less than the pressure differences required to cause O_2 diffusion. The CO_2 pressure gradients in the body are approximately the following:

1. Only a *1 mmHg* pressure gradient at the cellular level (Intracellular PCO_2 = 46 mmHg; interstitial and venous blood PCO_2 = 45 mmHg).
2. Only a *5 mmHg* pressure gradient causes all the required CO_2 diffusion out of the pulmonary capillaries into the alveoli (Pulmonary arterial PCO_2 = 45 mmHg; PCO_2 of the alveolar air = 40 mmHg).



Introduction (cont.):

- A *decrease* in tissue perfusion (as in hypovolemic shock) *increases* peripheral tissue PCO_2 from the normal value of 45 mmHg to elevated levels and *vice versa*.
- An *increase* in tissue metabolic rate greatly *elevates* the interstitial fluid PCO_2 at all rates of blood flow, whereas *decreasing* the metabolism causes the interstitial fluid PCO_2 to *fall*.
- Under normal resting conditions, an average of **4 ml** of CO_2 is transported from the tissues to the lungs in each 100 ml of blood.

Methods of CO_2 transport:

Upon entering the tissue capillaries, the CO_2 is transported in ***three*** physical and chemical forms. These forms are;

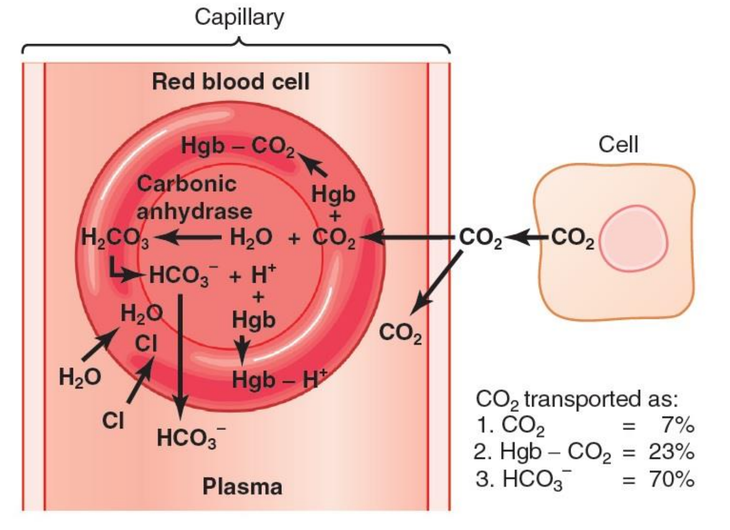
1. Transport of CO_2 in the dissolved state (7%)
2. Transport of CO_2 in the form of bicarbonate ion (70%)
3. Transport of CO_2 in combination with hemoglobin and plasma proteins (23%)

Transport of CO_2 in the dissolved state:

The amount of CO_2 dissolved in the fluid of the venous blood at 45 mmHg is about *2.7 ml/dl*. As *2.4 ml/dl* of CO_2 is dissolved in arterial blood, therefore, only about **0.3 ml/dl** of CO_2 is transported in the dissolved form by each 100 milliliters of blood flow. This is about 7% of all the CO_2 normally transported.

Transport of CO_2 in the form of bicarbonate ion:

- The dissolved CO_2 in the RBC reacts with water to form *carbonic acid*. This reaction is catalyzed by the enzyme *carbonic anhydrase*.
- This phenomenon allows tremendous amounts of CO_2 to react with the red blood cell water even before the blood leaves the tissue capillaries.
- Carbonic acid further dissociates into hydrogen and bicarbonate ions (H^+ and HCO_3^-). Most of the H^+ ions then combine with the hemoglobin.
- Many of the HCO_3^- ions diffuse from the red blood cells into the plasma, while Cl^- ions diffuse into the red blood cells to take their place. This phenomenon is called the ***chloride shift***.



Transport of carbon dioxide in the blood

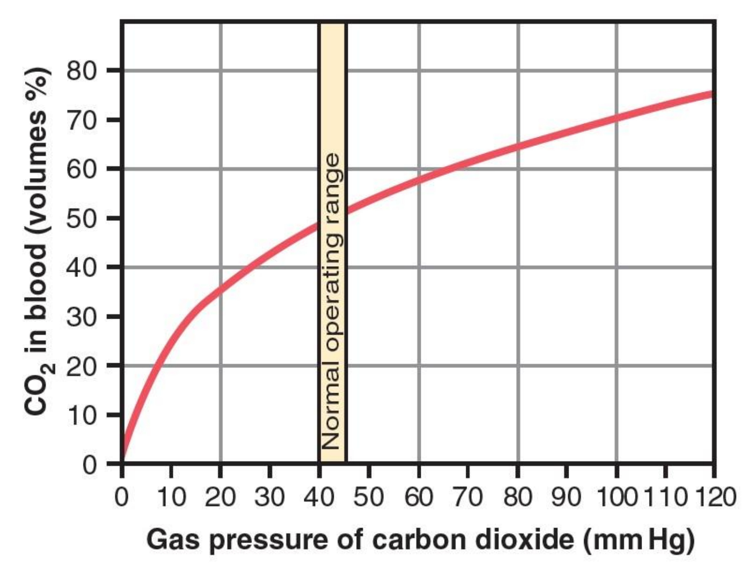
Transport of CO_2 in combination with hemoglobin and plasma proteins:

- CO_2 reacts directly, with a loose bond, with *amine radicals* of the hemoglobin (Hb) molecule to form the compound *carbaminohemoglobin* (CO_2Hb).
- A small amount of CO_2 also reacts in the same way with the plasma proteins in the tissue capillaries. However, this reaction is less significant than Hb transport of CO_2.
- The contribution of the carbaminohemoglobin and plasma proteins in the transport of CO_2 to the lungs is just above **20%** of the total quantity transported.

Carbon dioxide dissociation curve:

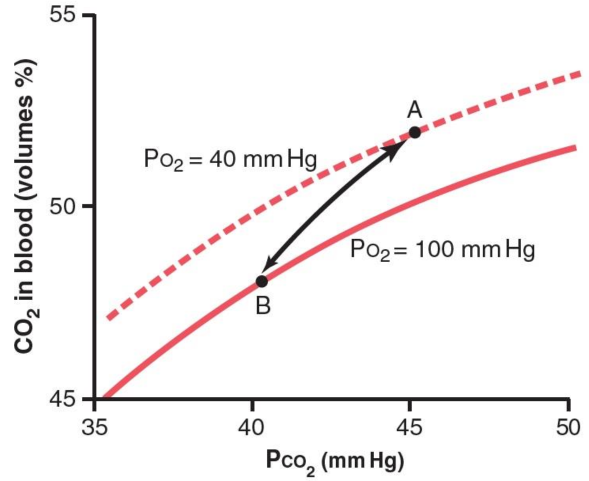
Note:

1. The normal blood PCO_2 ranges between a *narrow range* of 40 mmHg in arterial blood and 45 mmHg in venous blood.
2. The concentration of CO_2 rises to about 52 volumes percent as the blood passes through the tissues and falls to about 48 volumes percent as it passes through the lungs.
3. Only **4 volumes** percent of the CO_2 concentration is exchanged during normal transport of CO_2 from the tissues to the lungs.



The Haldane Effect:

- Binding of oxygen with hemoglobin tends to displace CO_2 from the blood.
- The combination of O_2 with hemoglobin in the lungs causes the hemoglobin to become a stronger acid.
- 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.
- Also the increased acidity of the hemoglobin → ↑release of H^+ ions → ↑binding of H^+ with bicarbonate ions to form H_2CO_3 → dissociation of H_2CO_3 into water and CO_2 → ↑release of CO_2 from the blood into the alveoli.
- The Haldane effect approximately *doubles* the amount of CO_2 released from the blood in the lungs and approximately *doubles* the pickup of CO_2 in the tissues.



Portions of the carbon dioxide dissociation curve when the Po_2 is 100 mm Hg or 40 mm Hg. The *arrow* represents the Haldane effect on the transport of carbon dioxide.

Test Question:

Q. Most of the carbon dioxide transported in the arterial blood is in the form of?

A. Dissolved
B. Bicarbonate
C. Attached to hemoglobin
D. Carbamino compounds
E. Carbonic acid