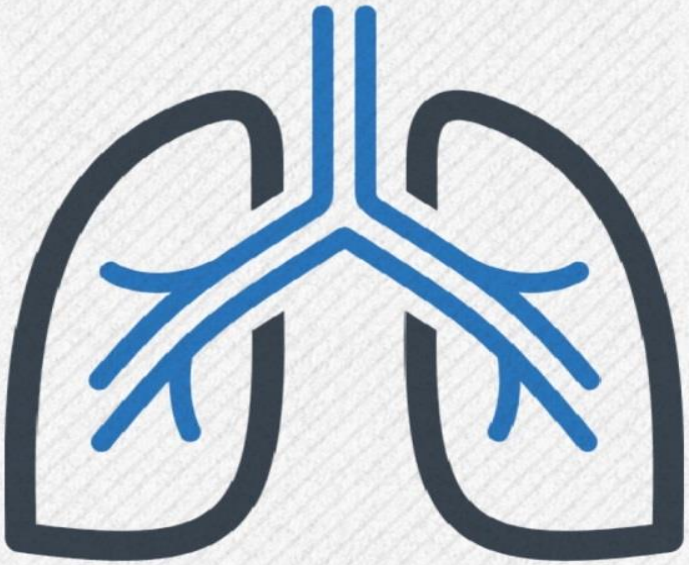


Respiratory system physiology

sheet handout slides

Number	10
Doctor	Yanal Shafagoj
Done by	Abdullah AlZibdeh
corrected by	Omayma Hassanin

Introduction

In this sheet, the discussed topics include transport of oxygen and carbon dioxide by the blood, hemoglobin-oxygen dissociation curve and the factors that affect it, in addition to answering questions on the past lectures. The doctor also discussed a question from the midterm exam (mentioned at the end of the sheet).

Transport; amounts

[Discussed at 15:00]

We said in previous lectures that O_2 consumption is 250 ml/minute, and CO_2 production is 200 ml/minute. In other words, the amount of O_2 transported and the amount of CO_2 transported are 5 ml/dl and 4 ml/dl, respectively (200/250 = 4/5 = 0.8). (Note: CO = 5 L/min; so 200 ml/min = 200 ml/ 5L = 40 ml/L = 4 ml/dl.)

This means that for each 100 ml of blood that reaches the lung, 5 ml of oxygen diffuses towards the blood, and 4 ml of CO_2 diffuses towards the alveoli. So, the transport of CO_2 in terms of amount equals to 4 ml/dl.

Oxygen Transport in Blood

Forms of oxygen in blood

Oxygen is carried in blood in two forms: dissolved and hemoglobin-bound.

Dissolved oxygen

According to Henry's law, the concentration of dissolved O_2 is proportional to the partial pressure of O_2; the proportionality constant is simply the solubility of O_2 in blood, 0.003 mL O_2/100 mL blood/mm Hg.

$$[O2] = Partial\ Pressure\ of\ O2 \times solubility\ of\ O2$$

Oxygen bound to hemoglobin

Oxyhemoglobin dissociation curve is affected by many factors, which include:

- PCO_2: increasing PCO_2 shifts the curve to the right
- Temperature: increasing the temperature shifts the curve to the right
- PH; $[H^+]$: decreasing the PH and increasing [H+] shifts the curve to the right
- 2,3-DPG: increasing the concentration of 2,3-DPG shifts the curve to the right

According to that, exercise shifts the hemoglobin curve to the right; because during exercise, CO_2 is produced faster, temperature increases, pH falls [increased hydrogen ion concentration], and 2,3-DPG concentration increases. Consequently, the bound oxygen decreases, and oxygen tends to dissociate from the hemoglobin. So, the oxygen released increases to be utilized by muscles. So, in these settings, extraction ratio increases.

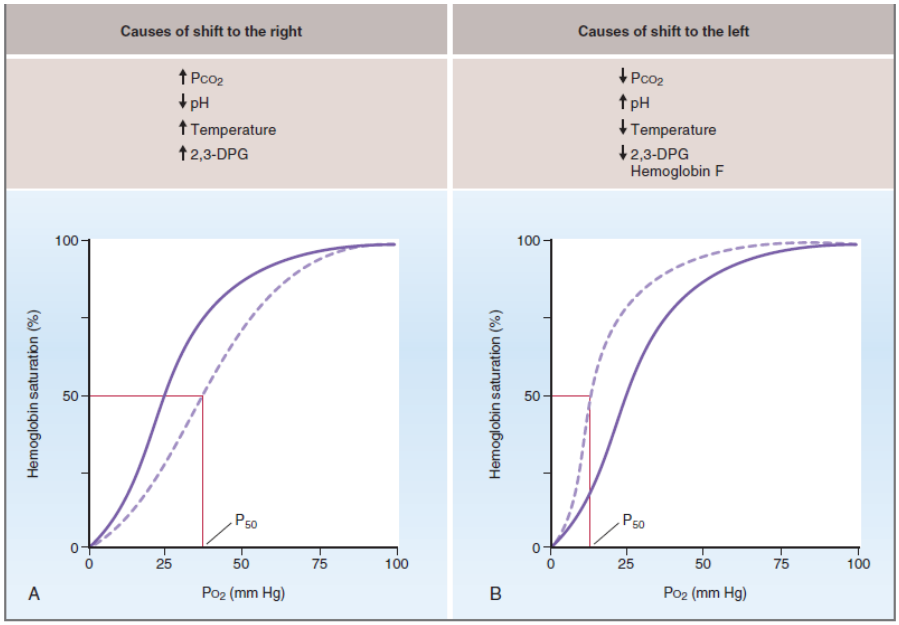


Figure 5–22 **Shifts of the O_2-hemoglobin dissociation curve. A**, Shifts to the right are associated with increased P_{50} and decreased affinity. **B**, Shifts to the left are associated with decreased P_{50} and increased affinity.

Effects of 2,3-diphosphoglycerate on oxygen transport

2,3-DPG production

RBC's do not have mitochondria; they cannot utilize oxygen in energy production. So, in order to produce energy, glucose is broken down anaerobically. And since anaerobic glucose breakdown yields less energy than aerobic respiration, glucose amounts utilized by RBD's are high.

Glucose breakdown results with 1,3-DPG, which is transformed into 2,3-DPG by the action of *mutase* enzyme.

2,3-DPG and hemoglobin; high altitude

2,3-DPG binds the β chain of HbA, reducing hemoglobin's affinity to oxygen (and shifting the dissociation curve to the right).

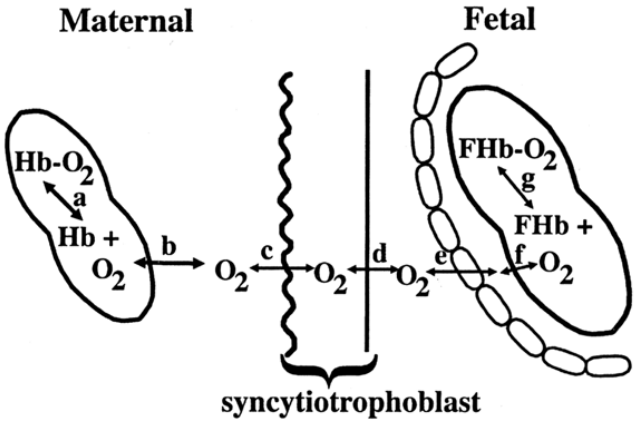
At *higher altitudes*, oxygen partial pressure decreases, so hyperventilation ensues. Hyperventilation decreases P_aCO_2; resulting in shifting Hb-O_2 dissociation curve to the left. This effect is good and bad at the same time: it is good because it enables the blood to carry more oxygen from the alveoli; it is bad because it becomes harder to extract the oxygen from the blood. Now, what corrects this situation is the accompanying increase in 2,3-DPG, which shifts the curve back to normal.

Fetal Blood Oxygenation

The fetus breathes through the placenta; it is the "lung" of the fetus (no external respiration with air). When fetal blood reaches the placenta, PO_2 of the interstitium there is only 40mmHg (vs. 100mmHg in alveoli in external respiration).

00:00 – 10:00

So, in order to grab the oxygen from the interstitium despite the low PO_2, fetal blood contains HbF instead of HbA. HbF has γ chains instead of β chains; so HbF does not bind to 2,3-DPG as avidly as does HbA; so the dissociation curve is shifted to the left, resulting with saturation of hemoglobin at lower PO_2.



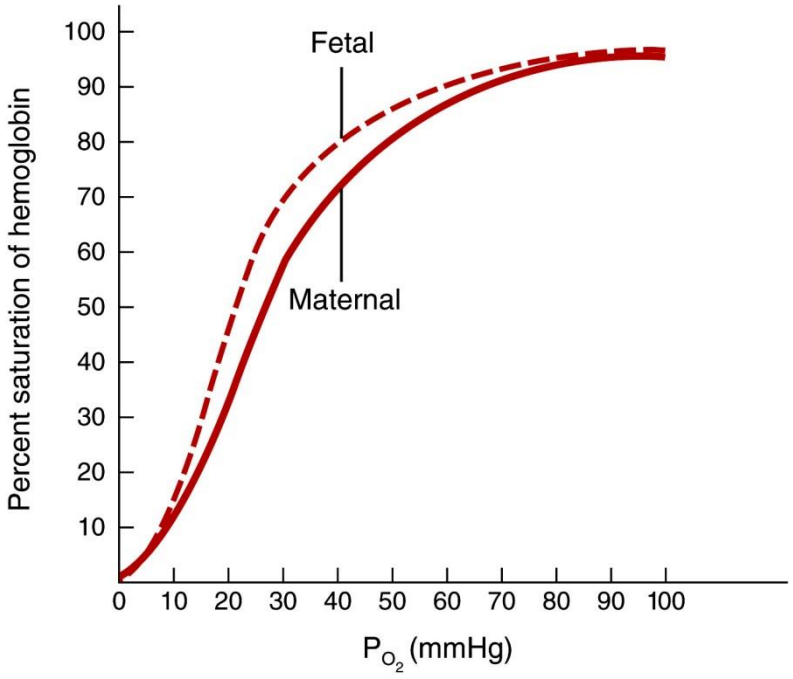


Figure 23.22 Tortora - PAP 12/e

After birth, the baby's respiration starts, and so, HbF production from the bone marrow decreases, shifting the production towards HbA (shifting the curve back to normal). Normally, HbF levels should be ≤2% of total hemoglobin (more than that may be associated with problems).

Carbon Dioxide Transport in Blood

Forms of CO_2 in blood

CO_2 is produced by cells, so the PCO_2 in the interstitium is 45mmHg. This CO_2 diffuses to the capillaries, which contain RBC's (Hb-bound CO_2; carbon anhydrase enzyme) and plasma (dissolved CO_2). These forms are discussed in the following sections.

Dissolved CO_2

Again, according to Henry's law, the concentration of dissolved CO_2 is proportional to the partial pressure of CO_2; the proportionality

constant is simply the solubility of CO_2 in blood, which is 20-folds the solubility of O_2.

According to that:

$$[CO2] = Partial\ Pressure\ of\ CO2 \times solubility\ of\ CO2$$

$[CO_2]_{arterial\ blood}$ = 40 X 0.06

= 2.4 ml/dl

$[CO_2]_{venous\ blood}$ = 45 X 0.06

= 2.8 ml/dl

Remember that the transport of CO_2 in terms of amount equals to 4 ml/dl (refer to the first section in this sheet; "transport; amounts"). Thus, dissolved CO_2 makes up 10% of transported CO_2.

CO_2 in the RBC's

- In tissue capillaries:
  CO_2 can bind hemoglobin, resulting with carbaminohemoglobin. Moreover, when CO_2 enters the RBC, it reacts with H_2O to give off H_2CO_3. This reaction is catalyzed by the enzyme carbonic anhydrase. This scheme of catalyzing this reaction is important, to enable the blood to take up CO_2 at the capillaries in a fast manner, since it does not have much time to do so.

  H_2CO_3 dissociates into HCO_3^- and H^+. After that, HCO_3^- ions that get out of the cell are substituted with Cl^- ions from the plasma (chlorine shift).

- In the lungs: HCO_3^- ions get back to the RBC's, replacing Cl ions that get back to the plasma. HCO_3^- reacts with H^+ to form H_2CO_3 all over again. After that, H_2CO_3 gives off CO_2 and H_2O (catalyzed by carbonic anhydrase). Then, CO_2 diffuses towards the alveoli.

CO_2 Transport; amounts summary:

CO_2	Arterial	Venous	A-V Difference	Percentage (of 4 ml/dl)
Dissolved	**2.4**	2.8	0.4	**10%**
Hb-CO_2	2.4	3.6	1.2	30%
Bicarbonate	43.2	45.6	2.4	**60%**
Total	48	52	**4**	100%

- Dissolved form is the least contributor.
- Bicarbonate ion form is the most important contributor.
- Significant numbers are in bold; the rest are not for memorization.
- Remember: dissolved CO_2 > dissolved O_2.

10:00 – 20:00

Insights into Previous Topics

What determines VO_{2max}?

VO_{2max} is the maximal O_2 consumption during maximal exercise. It is a genetically determined value that is not significantly affected by training (may only increase in 10%). But what is the determinant of VO_{2max}?

- Is it the mitochondria?
  To measure VO_{2max}, the person is asked to do an exercise while having their breath monitored. During exercise, VO_{2max} is reached even if the person did not use all of his muscles and used only part of his total mitochondria. And using more muscles does not affect VO_{2max} value. So, it is not the mitochondria.

- Is it the lung?

The lungs are good ventilators. Normally, they provide as much oxygen as the blood needs (in a perfusion-limited manner). Removing a part of the lung does not change VO_{2max}. So, it is not the lung that determines VO_{2max}.

- Is it the cardiovascular system?
  The cardiovascular system is the determinant of VO_{2max}. Giving a person inotropic agents (increasing calcium availability) results with increased the contractility and increased cardiac output. This increases VO_{2max}. Remember that contractility is the behavior of the heart at fixed afterload and preload (fixed sarcomere length).

20:00 – 30:00

Why is arterial PO_2 95mmHg, while alveolar PO_2 is 100mmHg?

$P_aCO_2 = P_ACO_2$; but $P_aO_2 < P_AO_2$

In other words,→

For O_2

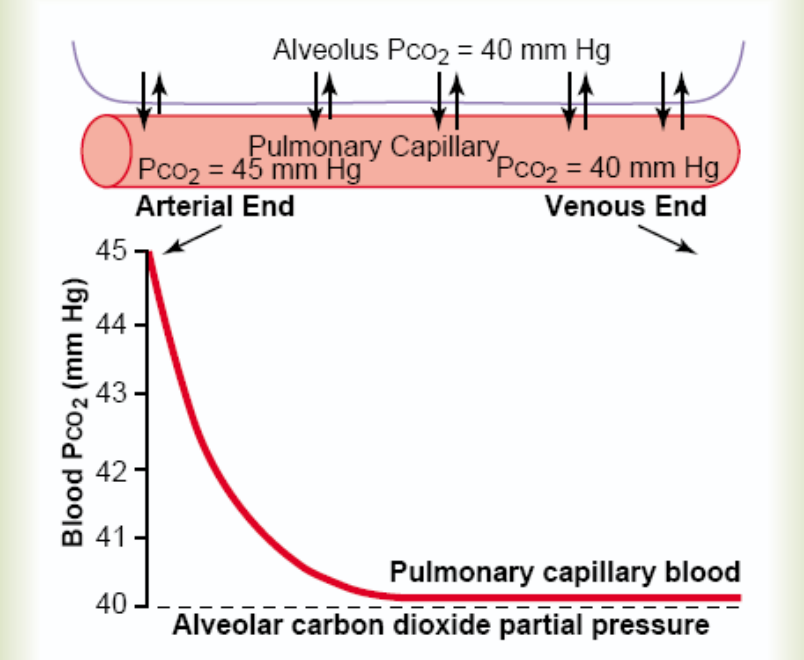
1- Venous admixture:
   Venous admixture is the result of mixing of non-reoxygenated blood with reoxygenated blood. This "pollution" has three sources:
   - Bronchial veins
   - Cardiac veins (that empty in the left heart/ atrium)
   - Physiologic A-V shunt (right to left): some blood from the pulmonary artery bypasses the alveoli without undergoing gas exchange. Approximately, 2% of the cardiac output is shunted.

2- Inequality in V/Q ratio:
   In the base of the lung, PO_2 is 90mmHg, while in the apex, PO_2 is 130mmHg. This 130mmHg does not compensate for the 90mmHg. This is a result of the S-shaped Hb-O_2 dissociation curve. At PO_2 of 130mmHg, saturation is 100%, and at PO_2 of 90mmHg, saturation is nearly 100%, too. So, for oxygen, the hyperventilated area does

not compensate for the hypoventilated area, because of the S-shaped Hb-O_2 dissociation curve.
(If the curve was linear, then 30% increase in the x-axis is accompanied with a 30% increase in the y-axis.)

30:00 – 40:00

For CO_2



Notice that the curve in the figure is "linear". CO_2 is self-compensatory; if one lung is hypoventilated and the other lung is hyperventilated, the hyperventilated one would not compensate for the hypoventilated in terms of oxygen. However, CO_2 levels would be compensated for.

Oxygen does not activate the respiratory centers in the medulla oblongata unless PO_2 is less than 60mmHg. Yet for CO_2, respiratory centers are affected with any change in PCO_2 (increase in PCO_2 increases respiration, and vice versa). So, the main effector on respiratory centers is PCO_2 and not PO_2. (an increase in PO_2 over 100mmHg does not affect oxygen levels; hemoglobin is already saturated.)

40:00 – 45:00

Midterm; Question revision

The doctor added this note at the beginning of the lecture on a question in the midterm exam:

Respiration through a tube – more ADS – less alveolar ventilation; because vital volume is constant—so, end respiratory CO_2 decreases.