صدقة جارية عن المغفور له بإذن الله **عمر عطية** من دفعة 2023 – كلية الطب، الجامعة الأردنية.

اللهم ارحمه واغفر له وأكرم نزله ووسع مدخله، لا تنسوه من دعائكم، إنا لله وإنا إليه راجعون.

#فريق_دوبامين_العلمي

Respiratory System Physiology

Comprehensive File 10

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In this lecture, a great deal of the topics discussed have been covered previously, so we will focus on some notes that are worth mentioning and discuss some questions and cases as explained during the lecture… Good Luck!

During exercise the diffusing capacity of oxygen increases, facilitating more oxygen entry into the blood and thus more oxygen availability for tissues. The increase in DL_{O2} is primarily due to recruitment of more capillaries (at rest only 1/3 are open), which makes for a 3-fold increase in total area in maximal exercise. Recall that $DL \propto A$.

QUESTIONS:

Arterial PO_2 is 100 mmHg and content is 20 ml O_2/dl. What is arterial PO_2 if ½ of all of the red cells are removed?

A. PO_2 = 0 mmHg
B. PO_2 =30 mmHg
C. PO_2 =50 mmHg
D. PO_2 =60 mmHg
E. PO_2 =100 mmHg

ANS = E

½ RBCs → Hb ≈ 7.5 g/dL → *no effect* on arterial PO_2 since lungs are functioning well, however $[O_2]$ is decreased because it represents total oxygen content.

Systemic arterial PO_2 is 100 mmHg and hematocrit is 40%. What is systemic arterial PO_2 if blood is added to increase hematocrit to 50?
A. PO_2 = 50 mmHg
B. PO_2 =70 mmHg
C. PO_2 =100 mmHg
D. PO_2 =120 mmHg
E. PO_2 =149 mmHg

ANS = C

The lungs will need more time to fully oxygenate the blood, but PO_2 will still be the same.

A person is breathing from a gas tank containing 45% oxygen. What is the alveolar PO_2?

A. 149 mmHg
B. 250 mmHg
C. 270 mmHg
D. 320 mmHg
E. 340 mmHg

ANS = C

Using the equation below after finding inspired PO_2 (45% * (760 – 47)):

$$P_AO_2 = P_{inspired}O_2 - \frac{P_ACO_2}{R} = 321 - \frac{40}{0.8} \approx 270\ mmHg$$

A person has a hemoglobin concentration of 10 gm/dl. The arterial oxygen content is 6.5 ml O_2/dl. What is the saturation?

A. 25%
B. 50%
C. 75%
D 100%

ANS = B

$$[O_2] = [Hb] * 1.34\ \frac{ml\ O_2}{g\ Hb} * \boldsymbol{SaO_2} = 20\frac{ml\ O_2}{dL}\ normally$$

$$6.5\frac{ml\ O_2}{dL} = 10\frac{g\ Hb}{dL} * 1.34\ \frac{ml\ O_2}{g\ Hb} * \boldsymbol{SaO_2} \rightarrow \boldsymbol{SaO_2} = \frac{6.5}{1.34 * 10} \approx 0.5 = \mathbf{50}\%$$

In carbon monoxide (CO) poisoning, the apparent paradox—marked reduction in SaO_2 and arterial O_2 content with a *normal* PaO_2—is explained by how CO interacts with hemoglobin rather than with dissolved oxygen.

P_aO_2 is unaffected

P_aO_2 reflects the partial pressure of dissolved O_2 in plasma, determined by alveolar ventilation and diffusion across the alveolar–capillary membrane. CO does not significantly alter alveolar PO_2 or the diffusion of O_2 into plasma. Therefore, arterial P_aO_2 remains normal.

SaO_2 is reduced

SaO_2 represents the fraction of hemoglobin binding sites occupied by O_2. CO binds hemoglobin with 250 times the affinity of O_2, forming carboxyhemoglobin (HbCO). If, for example, PCO = 0.4 mmHg → SaCO = 0.5, then 50% of hemoglobin binding sites are occupied by CO, leaving only the remaining fraction available for O_2. Consequently, SaO_2 falls, even though P_aO_2 is normal.

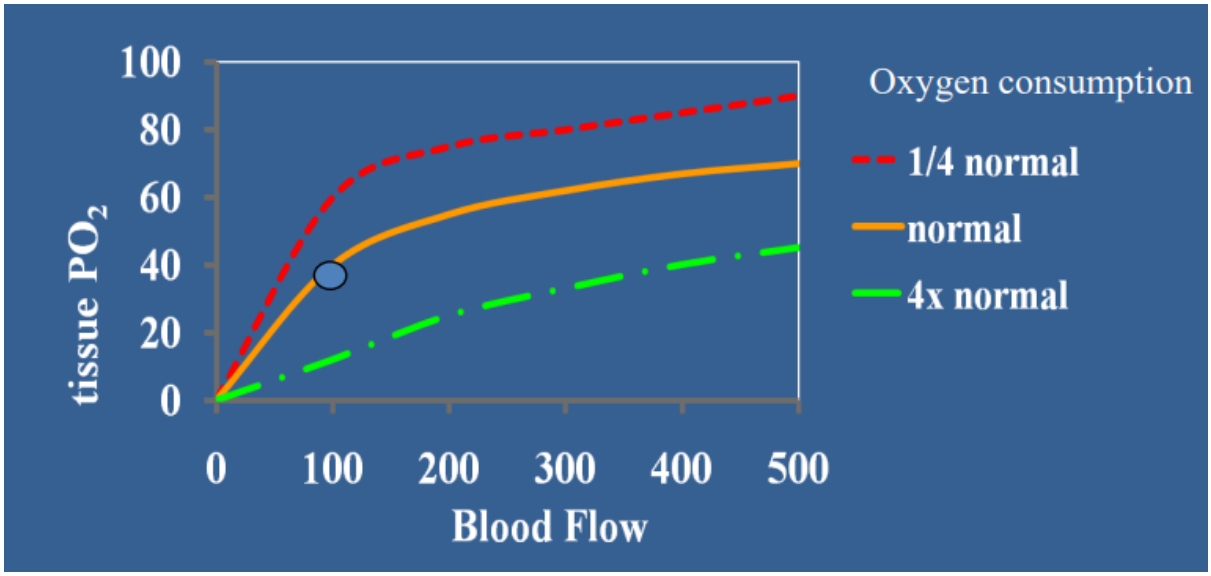
Arterial O_2 content is reduced

Arterial O_2 content depends primarily on hemoglobin-bound O_2:

$$[O_2] \approx (1.34 * [Hb] * SaO_2) + (0.003 * P_aO_2)$$

Because the dissolved O_2 term is negligible, the CO-induced reduction in functional hemoglobin and SaO_2 leads to a marked decrease in total O_2 content.

Effect of Metabolic Activity and Blood Flow on Venous Oxygen Tension



The figure is explained on the next page.

Considering the effect of (1) tissue blood flow and (2) metabolic activity on P_vO_2, which are represented by the x-axis and the 3 different curves on the previous page, respectively, the following can be inferred:

1. With increasing blood flow, P_vO_2 increases, explained by more oxygen delivery and thus lower extraction ratio (also known as utilization coefficient), given that the metabolic activity of the tissue is constant.
2. With increasing metabolic activity, P_vO_2 decreases, explained by higher oxygen intake and thus higher extraction ratio, given that oxygen delivery is constant.

Red vs White Muscle Fibers (from MSS):

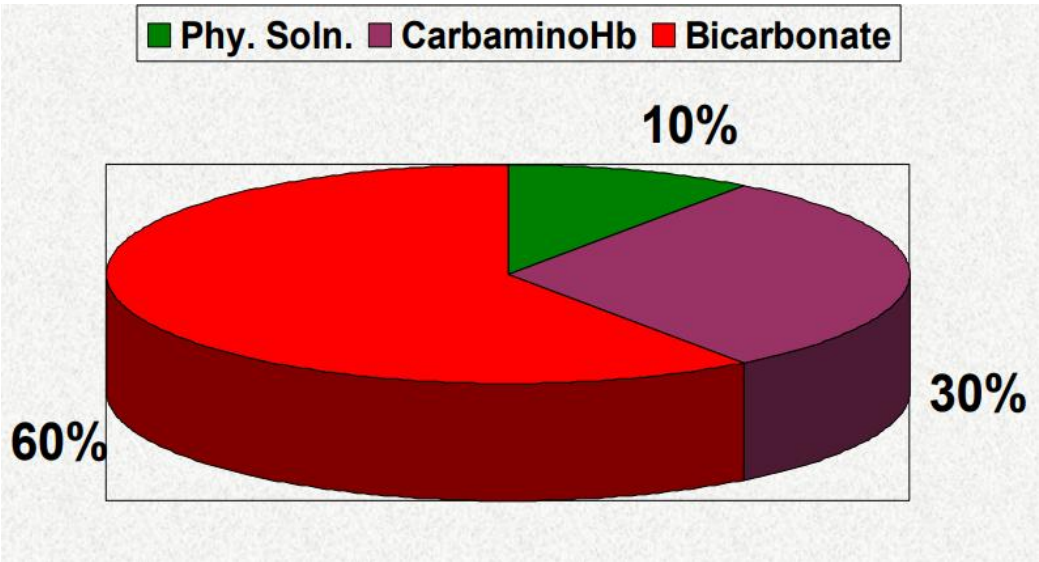
Red muscle fibers contain a high density of myoglobin (O_2 storage) and mitochondria, supporting sustained aerobic ATP production and explaining their specialization for endurance activities. In contrast, white muscle fibers have a low mitochondrial content, are bulky, and rely predominantly on glycolytic metabolism, allowing rapid ATP generation and high force output over short durations.

Maximal Oxygen Consumption During Intense Exercise – $VO_{2,\,max}$

VO_2 max, or maximal oxygen uptake, is the highest rate at which the body can consume oxygen during intense exercise, reflecting the integrated capacity of the lungs, heart, blood, and muscles to deliver and use oxygen. It represents the upper limit of aerobic metabolism and is a key measure of cardiovascular fitness.

Oxygen delivery and utilization during exercise depends on three main factors: pulmonary function, cardiovascular output, and muscle mitochondrial capacity. The lungs load oxygen into the blood, hemoglobin carries it to the tissues, and mitochondria in muscles consume it to produce ATP. Experimental evidence shows that the lungs are not normally limiting, because even after a lobectomy, VO_2 max is maintained, and mitochondrial capacity is not limiting, because VO_2 max can be achieved even without recruiting all muscles.

Of the three factors, cardiac output is the primary limiting factor. Even if hemoglobin is fully saturated and mitochondria are abundant, the total oxygen delivered per minute cannot exceed what the heart can pump. Cardiac output is largely genetically determined, explaining why some individuals naturally reach higher VO_2 max than others. VO_2 max can be modestly increased by interventions that raise oxygen-carrying capacity, such as red blood cell transfusion or altitude-induced erythropoiesis, but the maximal cardiac output ultimately sets the upper limit.



CO_2 is carried in blood in three forms. The majority, about 60%, is bicarbonate, formed when CO_2 enters red blood cells and is converted to HCO_3^- by carbonic anhydrase; it exits the cell via the chloride shift. About 30% is carbamino compounds, where CO_2 binds hemoglobin; binding is stronger to deoxygenated hemoglobin, and oxygenation in the lungs releases it (the Haldane effect, also known as the reverse Bohr effect). The remaining ~10% is dissolved CO_2, which, although small, determines blood PCO_2 and drives diffusion into alveoli. Together, these forms allow rapid, efficient CO_2 transport and elimination.

For oxygen, the solubility coefficient is about 0.003 mL/dL per mmHg. CO_2 is about 20 times more soluble than O_2, so its effective coefficient is:

$$0.003 \times 20 = 0.06 \text{ ml/dL per mmHg}$$

For **arterial blood**, the CO_2 partial pressure (P_aCO_2) is ~40 mmHg. Using Henry's law:

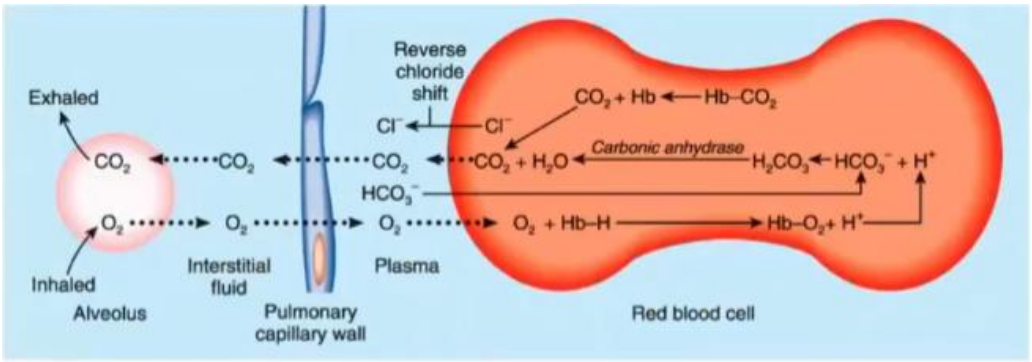
$$\text{Dissolved } CO_2 = 0.06 \times 40 = 2.4 \text{ ml/dL}$$

For **venous blood**, the PCO_2 rises to ~46 mmHg because CO_2 is picked up from tissues:

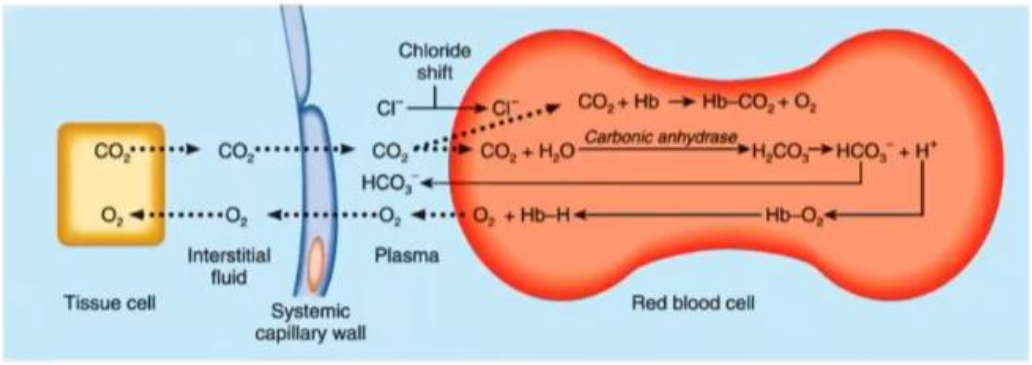
$$\text{Dissolved } CO_2 = 0.06 \times 46 \approx 2.8 \text{ ml/dL}$$

The arterio-venous difference is important – it is the part of the dissolved that is exhaled – contributing to nearly 10% of all exhaled CO_2.

At rest, the body produces and eliminates approximately **4 ml of CO_2 per dL of blood per minute** as blood traverses the pulmonary circulation, representing the arteriovenous difference in CO_2 content generated by tissue metabolism. Venous blood arriving at the lungs therefore contains this excess CO_2, which must be removed continuously and rapidly to prevent CO_2 accumulation and acid–base disturbance and maintain the gradient necessary to extract CO_2 from the cells into blood.



(a) Exchange of O_2 and CO_2 in pulmonary capillaries (external respiration)



(b) Exchange of O_2 and CO_2 in systemic capillaries (internal respiration)

How is this amount (4 ml/dL) removed every minute?

During its transit through systemic capillaries, CO_2 diffuses into red blood cells and is rapidly converted, within fractions of a second, into carbonic acid by carbonic anhydrase. This immediately dissociates into hydrogen ions and bicarbonate; hydrogen ions are buffered by deoxygenated hemoglobin, while bicarbonate exits the red blood cell into plasma via the chloride shift.

By the time venous blood leaves the tissues, about **2.4 ml/dL (60% of the 4 ml/dL)** CO_2 is being carried as bicarbonate and **about 1.2 ml/dL (30% of the 4 ml/dL)** is bound to hemoglobin as carbamino compounds, with only a small amount **(0.4 ml/dL; 10% of the 4 ml/dL)** remaining dissolved.

As this venous blood enters pulmonary capillaries, the timing of events becomes critical. Oxygen uptake occurs early during capillary transit and alters hemoglobin's binding properties, promoting the release of hydrogen ions and carbamino-bound CO_2 (the Haldane effect). Almost immediately, bicarbonate re-enters the red blood cell as chloride leaves, and carbonic anhydrase rapidly converts carbonic acid back into CO_2 and water. These reactions occur fast enough to be complete before the blood exits the pulmonary capillary. **By this, 4 ml CO_2 from each dL blood is cleared per minute.**

Throughout this process, the slight but crucial drop in PCO_2 from venous to alveolar blood maintains the diffusion gradient that drives CO_2 out of the blood. Thus, within a single pass and within seconds, the CO_2 produced in the tissues—mainly stored as bicarbonate and carbamino compounds—is reconverted to gaseous CO_2 and eliminated, ensuring tight minute-to-minute control of arterial PCO_2 and pH.