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

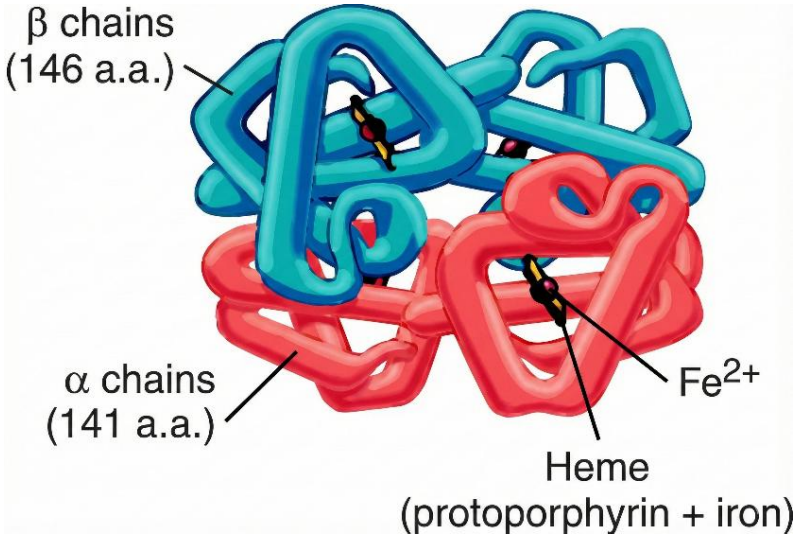
اللهم ارحمه واغفر له وأكرم نزله ووسع مدخله، لا تنسوه من دعائكم، إنا لله وإنا إليه راجعون.

#فريق_دوبامين_العلمي

Respiratory System Physiology

Comprehensive File 8

Dr. Yanal Shafagoj



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Hemoglobin – An Overview

In adults, hemoglobin (HbA) is composed of 4 chains (2 alpha and 2 beta). Each chain has a heme group that can carry one O_2, so each hemoglobin molecule can hold up to 4 oxygen molecules (8 atoms) and not more. Hemoglobin saturation is thus variable between 0-100% but cannot become oversaturated; 4 O_2 is the limit for 1 Hb.

In adult males, hemoglobin concentration in blood is around 14-16 g/dL, while it is 12-14 g/dL in adult females. 15 and 13 are used as average values, respectively.

For a 70-Kg male, total blood volume is about 5 L, which is 5×10^6 µL.
RBC concentration = 5×10^6 cell / µL of blood; **Hb per RBC** = 280×10^6 molecules/RBC.

Oxygen in Blood

Each gram of Hb can reversibly bind 1.34 ml of O_2 as a maximum (100% saturation). Given that, a normal adult male should have about 20 ml of O_2 per deciliter of blood.

$$[O_2] = \frac{15\ g\ of\ Hb}{1\ dl\ of\ blood} \times \frac{1.34\ ml\ of\ O_2}{1\ g\ of\ Hb} \approx 20 \frac{ml\ of\ O_2}{1\ dl\ of\ blood}$$

Oxygen can also be dissolved in plasma, as calculated by **Henry's law**:

$$[\boldsymbol{O_2}] = P_aO_2 * Solubility$$

$$\Rightarrow\ [O_2] = 100 * 0.003 = \mathbf{0.3}\,\boldsymbol{\frac{ml}{dL}}$$

This means that total oxygen in the blood is composed of the dissolved portion (1.5%) and the Hb-bound portion (98.5%). Hb-bound is significant; dissolved O_2 is negligible.

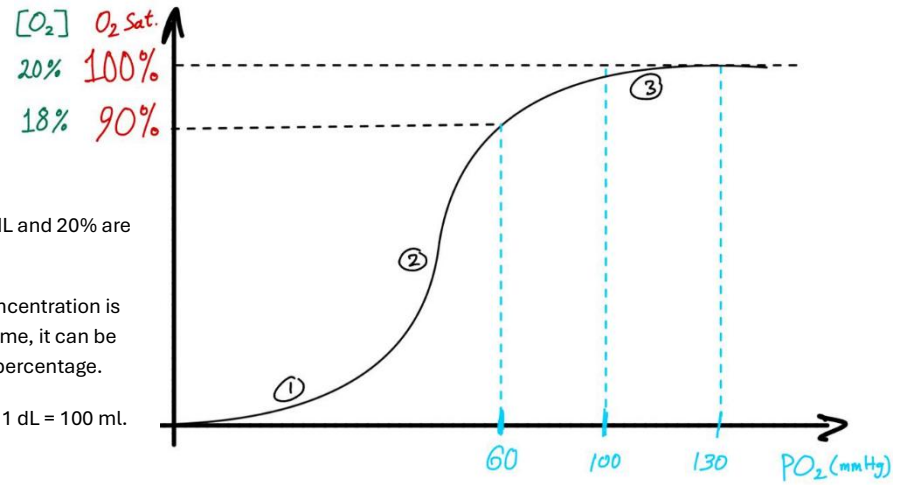
Per deciliter, 5 ml out of the 20 ml are consumed by body cells, yielding an extraction ratio of 25% on average. Given that the cardiac output is 50 dL/min (5 L/min), **oxygen consumption is 250 ml/min** (5 ml/dL * 50 dL/min). In exercise, both the extraction ratio and cardiac output increase, so oxygen consumption greatly increases, reaching 3.5 L/min in an average person and 5 L/min in an athlete.

On the other hand, **CO_2 production is 200 ml/min**, and this is because the respiratory exchange ratio (CO_2 produced per O_2 consumed) is about **0.8 for a mixed diet.** As a matter of fact, the respiratory exchange ratio (R) for pure carbohydrate diet is 1, meaning that 1 CO_2 is produced per consumed O_2 (recall the cellular respiration equation for glucose). For a pure lipid diet, R = 0.7, and for a pure protein diet, R = 0.8 (≈ R_{mixed}).

This fact can be used to calculate the alveolar oxygen partial pressure for a normal person with a balanced (mixed) diet [R = 0.8] as follows:

$$P_AO_2 = P_{inspired}O_2 - \frac{P_ACO_2}{R} = 150 - \frac{40}{0.8} = 100\ mmHg$$

Hemoglobin-Oxygen Dissociation Curve



Note:

For $[O_2]$, 20 ml/dL and 20% are equivalent.

Because the concentration is volume per volume, it can be expressed as a percentage.

Remember that 1 dL = 100 ml.

Notice that the curve is not linear but sigmoidal, meaning that it has 3 regions as shown. Numbers on the Y axis are for an individual with [Hb] = 15 g/dL ➔ 100% ≈ 20 ml O_2/dL.

When PO_2 falls below 100 mmHg, a significant reduction in hemoglobin oxygen saturation (SaO_2) does not occur unless PO_2 drops below 60 mmHg. In other words, the difference between SaO_2 at 100 mmHg (≈ 98%) and at 60 mmHg (≈ 90%) is only 8–10%. However, below 60 mmHg, SaO_2 begins to decrease steeply, compromising oxygen availability to tissues. Interestingly, feedback mechanisms that increase ventilation do not become active unless PO_2 falls below 60 mmHg. Regulatory mechanisms will be discussed in detail in the upcoming lectures.

Why is P_aO_2 = 95 mmHg not 100 mmHg?

Quoting from comprehensive file 7: *"There are more basal alveoli than apical ones (about 3 times more). So, when all oxygenated blood from all parts of the lungs arrives at the left atrium, the mixing gives 95 mmHg as ABG that will be pumped to the whole body for cellular use. Using a weighted average with weights 3 and 1 for basal and apical, respectively, the ABG should be 100 not 95 mmHg. However, the physiologically accurate number is 95. The reason behind this shall be discussed later."* **Later = Now!**

Two phenomena explain the result above: the Hb-O_2 curve and venous admixture.

The Hb-O_2 reaches a plateau after 100 mmHg, where SaO_2 is nearly 100% (98% to be accurate). In apical (hyperventilated) regions, PO_2 = 130 mmHg, but this excess above 100 mmHg cannot be translated to Hb-bound O_2 due to saturation restrictions. This means that these **hyperventilated (apical) regions cannot compensate for hypoventilated (basal) regions**, leading to mixed P_aO_2 that is lower than expected.

Hyperventilated regions compensate for hypoventilated regions in air, **not** blood (Hb).

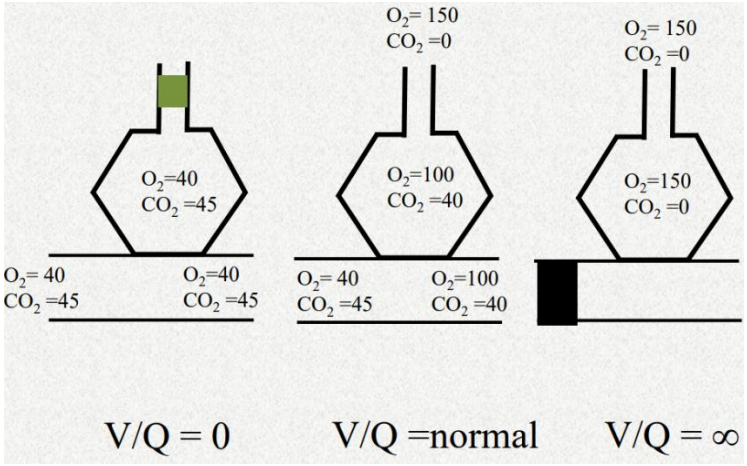
Venous Admixture

The other cause is venous admixture, which is the mixing of deoxygenated venous blood with oxygenated blood and is usually due to either intrapulmonary shunts or deoxygenated venous drainage into the left side of the heart.

In normal lungs, a small fraction (1-2%) of cardiac output bypasses ventilated alveoli, leading to deoxygenated blood mixing with arterial blood in pulmonary veins. Some other veins (like thebesian veins) directly drain into the left atrium or left ventricle, also leading to venous mixing with oxygenated blood coming from the lungs.

Venous admixture lowers P_aO_2 by diluting fully oxygenated pulmonary venous blood with deoxygenated blood after gas exchange has occurred. Well-oxygenated blood cannot compensate for this because hemoglobin is already near maximal saturation, resulting in a persistent alveolar–arterial oxygen gradient even in healthy lungs.

The alveolar–arterial (A–a) PO_2 gradient is normally small and should be equal to or less than 5 mmHg. Therefore, if alveolar PO_2 is 100 mmHg, systemic arterial PO_2 (P_aO_2) would be expected to be ≈ 95 mmHg. Values below 95 mmHg are usually abnormal.



Ventilation–perfusion (V/Q) relationships describe how effectively air reaching the alveoli matches blood flow in pulmonary capillaries. Gas exchange depends on this matching, and deviations from normal V/Q ratios explain many causes of hypoxemia. The two classic extremes are V/Q = 0 and V/Q = ∞, with normal V/Q (0.84) in between.

V/Q = 0

In this case, alveoli are perfused but not ventilated, as occurs with airway obstruction or alveolar collapse. Alveolar gas equilibrates with mixed venous blood, so alveolar PO_2 falls to about 40 mmHg and PCO_2 rises to about 45 mmHg.

V/Q = ∞

In this situation, alveoli are ventilated but not perfused, such as with pulmonary embolism. Alveolar gas approaches inspired air, with high PO_2 (~150 mmHg) and near-zero PCO_2, but no blood is available for gas exchange.

Assessing Pulmonary Function

Consider a marathon runner being tested for eligibility. Three parameters should be tested: red muscle fiber content (biopsy from quadriceps femoris muscle), maximal cardiac output, and lung gas exchange function, which is genetically determined.

Using ABGs to assess the lung function is not enough because normal ABGs is a necessary but not sufficient indicator due to the high reserve (2/3 of the capillaries), meaning that ABGs are insensitive for subthreshold (< 2/3) lung functional loss.

Diffusing Capacity of The Respiratory Membrane

The ability of the respiratory membrane to exchange a gas between the alveoli and the pulmonary blood is expressed in quantitative terms by the **respiratory membrane's diffusing capacity** (**DL**, a measure of permeability (K)), which is defined as the volume of a gas that will diffuse through the membrane each minute for a partial pressure difference of 1 mmHg. All the factors discussed earlier that affect diffusion through the respiratory membrane can affect this diffusing capacity.

$$Flow_x = \Delta P_x * DL_x \; [Ohm's\ law\ for\ gas\ 'x']$$

$$DL = \left(\frac{A}{dx}\right) * \left(\frac{S}{\sqrt{MW}}\right)$$

$(A: Surface\ area;\ dx: Thickness;\ S: Gas\ solubility;\ MW: Gas\ molecular\ weight)$

Gas	O_2	CO_2	CO
Diffusion Coefficient $\left(\frac{S}{\sqrt{MW}}\right)$	1	20	0.8

Diffusing Capacity for Oxygen

In the average young man, the *diffusing capacity for O_2* under resting conditions averages *21 ml/min/mm Hg*. In functional terms, what does this mean? The mean O_2 pressure difference across the respiratory membrane during normal, quiet breathing is about 11 mm Hg. Multiplication of this pressure by the diffusing capacity (11 × 21) gives a total of about 250 ml of oxygen diffusing through the respiratory membrane each minute, which is equal to the rate at which the resting body uses O_2.

$$\text{Flow} = \Delta \text{PO}_2 * DL_{O2} \rightarrow \boldsymbol{DL_{O2}} = \frac{\boldsymbol{Flow}}{\boldsymbol{\Delta PO_2}}$$

Measurement of Diffusing Capacity: The Carbon Monoxide Method

To obviate the difficulties encountered in measuring oxygen diffusing capacity directly, physiologists usually measure carbon monoxide (CO) diffusing capacity instead and then calculate the O_2 diffusing capacity from this. The principle of the CO method is the following: A small amount of CO is breathed into the alveoli, and the partial pressure of the CO in the alveoli is measured from appropriate alveolar air samples. The CO pressure in the blood is essentially zero because hemoglobin combines with this gas so rapidly as the affinity of hemoglobin for CO is 250 times more than its affinity for O_2. This gives no time for CO pressure to build up. Therefore, the pressure difference of CO across the respiratory membrane is equal to its partial pressure in the alveolar air sample. Then, by measuring the volume of CO absorbed in a short period and dividing this by the alveolar CO partial pressure, one can determine accurately the CO diffusing capacity.

To convert CO diffusing capacity to O_2 diffusing capacity, the value is divided by a factor of 0.8 because the diffusion coefficient for CO is 0.8 times that for O_2. Thus, the average diffusing capacity for CO in healthy young men at rest is 17 ml/min/mmHg, and the diffusing capacity for O_2 is 1.23 times this, or 21 ml/min/mmHg.

What exactly is gas partial pressure in blood?

Gas partial pressure in blood refers to the pressure exerted by gas molecules that are freely dissolved in plasma, reflecting their tendency to diffuse and equilibrate with the gas phase. It does not represent total gas content. Operationally, it is the pressure of the gas that would exist if blood were in equilibrium with that gas at the same temperature. Only dissolved gas contributes to partial pressure.

Oxygen in blood exists in two forms:

- **Dissolved O_2**: obeys Henry's law and **solely determines PaO_2**. This fraction is responsible for diffusion across the alveolar–capillary membrane and into tissues.
- **Hemoglobin-bound O_2**: is chemically bound and therefore **does not exert partial pressure**. It contributes to oxygen *content* but not to PaO_2.

Thus, PaO_2 reflects **oxygen tension**, not total oxygen quantity.

Carbon monoxide binds hemoglobin with very high affinity. Once CO enters blood, it is **almost entirely bound to hemoglobin**, leaving an essentially negligible dissolved fraction. Since **partial pressure depends only on dissolved gas**, the partial pressure of CO in blood is effectively zero, even when total CO content is high.