DIFFUSIVE TRANSFER OF RESPIRATORY GASES

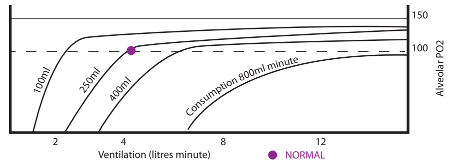
The Oxygen Cascade

1. Inspired Gas

Barometric pressure (normally 760mm Hg)
Oxygen Concentration (21%)

2. Humidified Gas results in a decrease in oxygen of around 10mmHg
At body temperature, H2O = 47mmHg Therefore: ((760-47) 0.21)= 150

3. Alveolar Air is influenced by the oxygen consumption (in that higher consumption leads to lower O2 levels) and the alveolar ventilation which increases O2 levels up towards the humidified gas level. The combination of these factors is shown below graphically. The cardiac output and third gas effect are both transient although the later important in off gassing from NO anaesthesia.

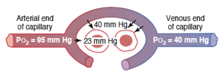


4. Arterial Blood This step in the oxygen cascade is often the most important clinically. In normal patients the decrease here is usually around 5mmHg usually due to V/Q mismatch, the physiological shunt caused by the thebsian and bronchial venous systems. In disease states however the drop may be more profound and is usually due to marked ventilation perfusion inequality although pathological shunts such as congenital heart disease may also result in significant O2 decreases. Rarely impaired diffusion may cause a drop in O2 as well.

5. Capillary Bed The amount of oxygen delivered to the capillary bed is dependent on the cardiac output (or regional blood flow for a specific organ) arterial oxygen saturation and the haemoglobin concentration. Impairment of any of these leads to tissue hypoxia and chronically to compensation - eg polycythemia in chronic anoxia, increased CO in anaemic patients. Since more than 97% of oxygen is bound to Hb the O2 dissolved in blood is sometimes ignored, although becomes significant in hyperbaric situations. Normal values in a resting patient are CO = 5 litres, Saturation 97%, Hb 140 and the volume of O2 bound by a gram of Hb is 1.39 (1.34 if you correct for dysfunctional Hb - metHb and COHb).

Delivery (O2 FLUX) = CO (Content)
= 5(Sats x Hb x 1.39 + dissolved)
= 960 ml/min (rounded to 1000ml)

Normal consumption is 250ml (25%) resulting in venous sats of 75% or 40mmHg when assessed using the O2-Haemaglobin dissociation curve.



6. Tissue O2. As oxygen is constantly required for aerobic metabolism, the partial pressure of Oxygen in tissues is generally always lower than the capillary bed, therefore there is a diffusion gradient is in place. The interstitial PO2 ranges normally from 40-5mmHg with an average of 23. As mitocondria require an external gradient of only 2-3mmHg there is a good range of safety in place. As the PO2 decreases oxygen is liberated from Hb according to the Hb-O2 Dissociation curve. More O2 may be liberated without a change in PO2 by shifting the dissociation curve to the right. This occurs due to increased H+ ions (pH drop), increased levels of DPG, increased CO2 and increased temperature. This makes sense because these factors are usually increased due to increased O2 consumption. Because the curve is flat at the top of the dissociation curve the decreased lung uptake of O2 with right shift has minimal effect on the saturations.

The **diffusion of oxygen and carbon dioxide** across the blood gas barrier of the alveolar wall, interstitial fluid and pulmonary capillary endothelium is governed by Fick's law of diffusion. This relates the flow of gas across a membrane to the characteristics of the membrane (area and thickness), the pressure gradient (difference in partial pressures) and the characteristics of the gas (solubility and molecular weight).

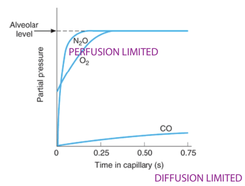
$$\text{Flow of Gas} \propto \frac{\text{Area}}{\text{Thickness}} \cdot \text{Diffusion constant } (P_1 - P_2)$$

Diffusion constant is equal to the gas solubility/ square root of the molecular weight

The pressure gradient for oxygen is the alveolar PO2 to the mixed venous PO2 (105-40 = 65). This is much less than CO2 which has a gradient of (46-40=6). The surface area of the lungs is estimated at around 70m2. The average thickness is about 0.6 micrometers. The square root of O2 and CO2 molecular weights are 4 and 5.29 respectively. Each minute however 250ml of O2 and 200ml of CO2 disffuses. As can be seen from Fick's Law the reason CO2 is so effective must be due to its much higher solubilty, resulting in an increased diffusion constant some 20 times greater than O2.

The diffusion process is rapid, equilibrium is established in 0.25 seconds. As the average capillary transit time is 0.75 seconds this usually ample time for diffusion to take place. In extreme exercise the cardiac output is dramatically increased and the transit time may approach 0.25 seconds which, if there is some impairment of diffusion due to disease may result in a measurable fall in end capillary PO2.

Perfusion and diffusion limited transfer of gases. Whether or not substances passing from the alveoli to the capillary blood reach equilibrium in the 0.75 s that blood takes to traverse the pulmonary capillaries at rest depends on their reaction with substances in the blood. Thus, for example, the anesthetic gas nitrous oxide (N2O) does not react and reaches equilibrium in about 0.1 s. In this situation, the amount of N2O taken up is not limited by diffusion but by the amount of blood flowing through the pulmonary capillaries; that is, it is perfusion-limited. On the other hand, carbon monoxide (CO) is taken up by hemoglobin in the red blood cells at such a high rate that the partial pressure of CO in the capillaries stays very low and equilibrium is not reached in the 0.75 s the blood is in the pulmonary capillaries. Therefore, the transfer of CO is not limited by perfusion at rest and instead is diffusion-limited. O2 is intermediate between N2O and CO; it is taken up by hemoglobin, but much less avidly than CO, and it reaches equilibrium with capillary blood in about 0.3 s. Thus, its uptake is perfusion-limited.



Diffusing capacity 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, 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 above (area, thickness, solubility, molecular weight) that affect diffusion through the respiratory membrane can affect this diffusing capacity.

Diffusing Capacity for Oxygen. In the average young man, the diffusing capacity for oxygen under resting conditions averages 21 ml/min/mm Hg. In functional terms, what does this mean? The mean oxygen pressure difference across the respiratory membrane during normal, quiet breathing is about 11 mm Hg. Multiplication of this pressure by the diffusing capacity (11 x 21) gives a total of about 230 milliliters of oxygen diffusing through the respiratory membrane each minute; this is equal to the rate at which the resting body uses oxygen. The oxygen diffusing capacity can be calculated from measurements of (1) alveolar Po2, (2) Po2 in the pulmonary capillary blood, and (3) the rate of oxygen uptake by the blood. However, measuring the Po2 in the pulmonary capillary blood is so difficult and so imprecise that it is not practical to measure oxygen diffusing capacity directly.

Diffusing Capacity of Carbon Monoxide as a surrogate marker. To obviate the difficulties encountered in measuring oxygen diffusing capacity directly, carbon monoxide diffusing capacity is measured instead and then oxygen diffusing capacity is calculated using the known diffusion coefficients. The principle of the carbon monoxide method is the following: A small amount of carbon monoxide is breathed into the alveoli, and the partial pressure of the carbon monoxide in the alveoli is measured from appropriate alveolar air samples. The carbon monoxide pressure in the blood is essentially zero, because hemoglobin combines with this gas so rapidly that its pressure never has time to build up (it is diffusion limited). Therefore, the pressure difference of carbon monoxide across the respiratory membrane is equal to its partial pressure in the alveolar air sample. Then, by measuring the volume of carbon monoxide absorbed in a short period and dividing this by the alveolar carbon monoxide partial pressure, one can determine accurately the carbon monoxide diffusing capacity. To convert carbon monoxide diffusing capacity to oxygen diffusing capacity, the value is multiplied by a factor of 1.23 because the diffusion coefficient for oxygen is 1.23 times that for carbon monoxide. Thus, the average diffusing capacity for carbon monoxide in young men at rest is 17 ml/min/mm Hg, and the diffusing capacity for oxygen is 1.23 times this, or 21 ml/min/mm Hg.

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