

An Introduction to Gas Exchange

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Required Reading: Respiratory Physiology: A Clinical Approach, Shwartzstein & Parker, Chapter 5 (pp 95-100; 111-112).

Objectives

1. Distinguish between the following terms: minute, alveolar and dead space ventilation; and anatomic, alveolar and physiologic dead space.
2. Specify the partial pressures of CO₂ and O₂ in the alveoli, mixed venous and arterial blood in normal individuals.
3. Using the alveolar ventilation equation, discuss the factors that determine the partial pressure of carbon dioxide in the alveoli and define the terms hyperventilation and hypoventilation.
4. Be able to calculate the P_AO₂ using the simplified alveolar-air equation.
5. Using Fick's law of diffusion, specify the key factors that affect the exchange of oxygen across the alveolar capillary membrane.

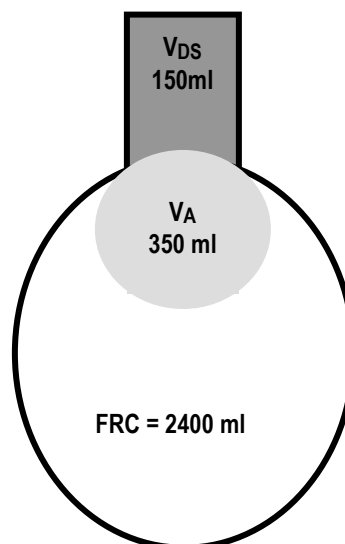
1. Ventilation: Minute, Alveolar and Dead Space

$$V_E = V_T \times RR$$

Ventilation is a general term for the movement of air into and out of the lung. The symbol for ventilation is V. V stands for volume and the dot for "per unit time". **Minute ventilation** is a more specific term referring to the total amount of air moved in or out of the lungs per minute. By convention, minute ventilation is typically measured as the quantity of air expired per minute and symbolized V_E. It is helpful to remember that V_E is the product of the tidal volume expired, written as V_T or V_E and the respiratory rate, RR.

For each tidal volume (V_T) of 500 ml air inspired, 150 ml stays in the conducting airways. This volume is called the **anatomic dead space (V_{DS})** as it does not participate in gas exchange. It merely enters and subsequently leaves the conducting airways. The remaining 350 ml of the tidal breath enters the alveoli (V_A) and participates in gas exchange. Note that this 350 ml inspired air mixes with functional residual capacity (FRC), about 2400ml liters of air already in the lungs.

Typical values for dead space and alveolar ventilation are derived on the right.



$$V_E = V_T \times RR = 500 \times 12 = 6.0 \text{ L/min}$$

$$V_A = V_A \times RR = 350 \times 12 = 4.2 \text{ L/min}$$

$$V_{DS} = V_{DS} \times RR = 150 \times 12 = 1.8 \text{ L/min}$$

In this figure, the entire conducting zone is represented as a single tube and the respiratory zone as a single reservoir.

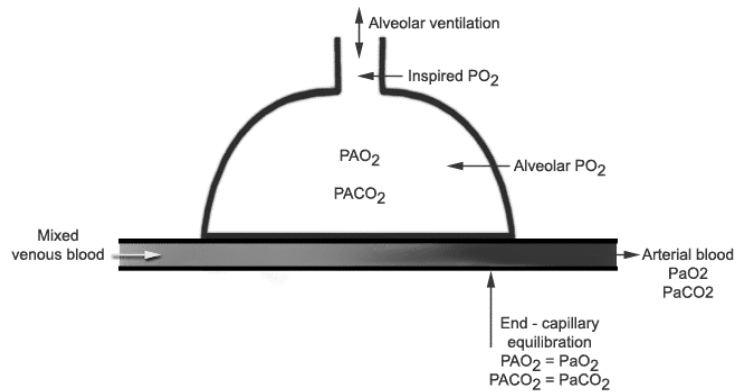
Alveolar ventilation (V_A) is the volume of air breathed per minute that: 1) reaches the alveoli and 2) participates in gas

exchange.

Dead space ventilation (V_{DS}) refers to the portion of minute ventilation that does not participate in gas exchange. Dead space ventilation includes ventilation of **1) the anatomic dead space**: the portion of each breath that enters the conducting airways **and 2) the alveolar dead space**: air that reaches the alveoli but does not participate in exchange (e.g. air that reaches an alveolus that is not perfused). In healthy individuals, alveolar dead space is about 25 ml and considered relatively insignificant. **The sum of the anatomic and alveolar dead space is referred to as the “physiologic dead space”**.

2. The Significance of Partial Pressure values of Alveolar Carbon Dioxide and Oxygen

In the lungs, by the time blood reaches the end of a pulmonary capillary, gas exchange is complete and the partial pressure of oxygen and carbon dioxide in the blood is in equilibrium with the partial pressure of these gases in the alveolus. Therefore, it is important to be aware of the factors that determine the partial pressure of oxygen and carbon dioxide in the alveoli, as they in turn, affect the partial pressure of these gases in the arterial blood supplying the tissues.



	dry air	inspired air	alveolar gas	mixed venous blood	arterial blood
PO ₂ (mmHg)	160	150	100	40	95
PCO ₂ (mmHg)	0	0	40	46	40

You need to memorize the normal PCO₂ and PO₂ values under standard barometric pressure conditions listed in the table above.

2. Alveolar Ventilation and Carbon Dioxide Elimination

Carbon dioxide is a by-product of food metabolism and in high amounts has toxic effects including: dyspnea, acidosis and altered consciousness. The primary means for eliminating carbon dioxide from the body is through the lungs and via the alveoli. Normally, alveolar ventilation is regulated so as to keep the partial pressure of carbon dioxide within a very narrow normal range: 40 ± 5 mmHg. One of the most important equations in clinical medicine, the **Alveolar Ventilation Equation**, describes the excretory function of the lungs with respect to carbon dioxide production (V_{CO_2}).

$$V_A \propto \frac{V_{CO_2}}{P_{ACO_2}}$$

This equation implies that alveolar ventilation is directly proportional to carbon dioxide production: the greater the amount of carbon dioxide production by the body, the greater the alveolar ventilation must be to maintain a constant partial pressure of carbon dioxide in the blood and alveoli. Viewed differently from a clinical perspective then, if the partial pressure of CO₂ is high, it is a tell tale sign that alveolar ventilation is not adequate for the level of carbon dioxide production and serves as a cue that there is a problem with the ventilation: either its regulation at the CNS level, along the relay of information to the ventilatory pump, or a problem with the ventilatory pump itself.

The terms **hyperventilation** and **hypoventilation** refer to elevated or reduced **alveolar ventilation**. These terms are defined by the partial pressure of carbon dioxide in the arterial blood (P_aCO_2). Low P_aCO_2 is called hypocapnia and defines a state of hyperventilation. High P_aCO_2 , hypercapnia or hypercarbia, defines a state of hypoventilation. Hence, hyperventilation and hypoventilation refer to the state of alveolar ventilation in relation to carbon dioxide production - a relationship that can only be known by measuring P_aCO_2 . The terms **hyperpnea** and **hypopnea** on the other hand are often used when referring to increase or decreased minute ventilation.

4. The Alveolar-Air Equation (simple form)

The partial pressure of oxygen in the alveoli (P_{AO_2}) depends on partial pressure of oxygen inspired into the alveoli (P_{in}) minus the partial pressure of oxygen removed from the alveoli (P_{out}) by blood. The partial pressure of oxygen entering the alveolus is the partial pressure of inspired oxygen in the conducting airways.

In turn, the partial pressure of inspired oxygen in the conducting airways (P_{iO_2}), depends on the barometric pressure (P_B), the partial pressure of water vapour (P_{H_2O}) in the lungs and the fraction of inspired oxygen (F_{iO_2}).

$$P_{AO_2} = P_{in} - P_{out}$$

$$P_{in} = P_{iO_2}$$

$$P_{iO_2} = (P_B - P_{H_2O}) \times F_{iO_2}$$

$$P_{out} = P_aCO_2 / R$$

The alveolar air equation (simple form) :

$$P_{AO_2} = [(P_B - P_{H_2O}) \times F_{iO_2}] - P_aCO_2 / R$$

The partial pressure of oxygen leaving the alveoli (P_{out}) must equal the partial pressure of carbon dioxide divided by 0.8, R, or the respiratory exchange ratio. The respiratory exchange ratio reflects to the ratio of carbon dioxide molecules to oxygen molecules exchanged within the alveoli. At rest, under steady state conditions this ratio is typically 0.8 that is for every 10 molecules of oxygen leaving the alveoli, 8 molecules of carbon dioxide enter the alveoli from blood. Normally, the partial pressure of carbon dioxide in the alveolus is the same as that in the arterial blood and either term can be used in the equation. Arterial blood gas values can be measured, and for this reason, the equation is written in terms of the arterial partial pressure of carbon dioxide.

The alveolar air equation is the second most important equation in clinical medicine. It allows the clinician to calculate an approximate value for P_{AO_2} and predict what the resulting P_aO_2 should be, if the lungs were functioning normally. When the difference between the calculated P_{AO_2} and P_aO_2 measured from a sample of blood is increased, the lungs are not transferring oxygen properly. This occurs with ventilation perfusion mismatch or less commonly with diffusion abnormalities. The difference between alveolar and arterial blood partial pressure of oxygen is referred to as the A-a gradient or the A-a difference in oxygen.

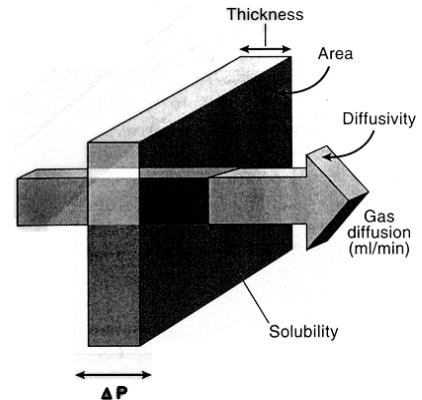
There are several assumptions made in the clinical application of alveolar air equation. These are listed below:

- **The F_{iO_2} is known**- This is not always the case. Face masks, nasal prongs and other methods of oxygen delivery do not deliver a precise F_{iO_2} .
- **The barometric pressure is known**. Often the barometric pressure is approximated to sea level (760 mmHg) and not measured. Weather conditions and altitude affect barometric pressure. Barometric pressure decreases with increasing altitude.
- **Water vapour pressure is 47 mmHg**. This value is temperature-dependent and assumes that the subject is at normal body temperature of 37°C which may not be the case.
- **R-value is 0.8**. This value can vary widely depending on the fuel substrate utilized and whether the patient is at steady state. Examples: patients on i.v. carbohydrate diet ($R=1$); over fed patients whose carbon dioxide production exceeds oxygen consumption ($R>1$) due to carbon dioxide production from non-energy producing pathways (lipogenesis).
- **P_aCO_2 is assumed equal to P_aCO_2** . This assumption holds true in health but not in disease states such as cases of severe ventilation-perfusion mismatching.

5. Fick's Law of Diffusion

Diffusion of gases across the alveolar-capillary membrane is governed by Fick's law of diffusion: the amount of gas transferred across the membrane (V_{gas}) is proportional to the surface area (A) of the membrane, the diffusion constant (D) for the gas, the difference in partial pressure (ΔP) of the gas across the membrane and it is inversely proportional to the thickness (T) of the membrane. The diffusion constant (D) is proportional to the solubility of the gas across the membrane and inversely proportional to the square root of the molecular weight (MW) of the gas.

$$V_{\text{gas}} \propto \frac{A (\Delta P) D}{T}$$



By the time blood has reached the end of a pulmonary capillary, the partial pressures of oxygen and carbon dioxide in the blood are at equilibrium with the partial pressure of these gases in the alveoli. Given that carbon dioxide is 20 fold more soluble than oxygen, what other factor do you think is at play here allowing for oxygen transfer in a similar amount of time?

A common clinical tool in determining whether gases, in particular oxygen are transferred across the lungs is to examine the **“diffusing capacity of the lungs”** also known as the **“transfer factor”**.

If we rearrange the Fick's equation for diffusion as:

$$\frac{Ad}{T} \equiv \frac{V_{\text{gas}} (\text{ml/min})}{[\Delta P]}$$

then the variable, diffusing capacity of the lungs [D_L] will replace Ad/T and reflect the quantity of gas transferred in unit time per unit pressure difference (units ml/min/mmHg):

$$D_{L\text{gas}} = \frac{V_{\text{gas}}}{P_{A\text{gas}} - P_{c\text{gas}}} \quad \text{where } D = \text{diffusing capacity; } L = \text{lung; } A = \text{alveolar; } c = \text{mean capillary value}$$

For gases that combine chemically with hemoglobin in blood, there are two components:

1. The resistance offered by alveolar capillary membrane, $1/D_M$.
2. The resistance offered by the kinetics of the chemical reaction of the gas with the Hb molecule, $1/\Theta V_c$. Where Θ = gas rate constant in ml gas bound to Hb per ml blood/min/mmHg partial pressure gradient of the gas between plasma & the red blood cells; V_c = pulmonary capillary blood volume)

Since these resistances are in series the total diffusion resistance is $1/D_L = 1/D_M + 1/\Theta V_c$ and in practice the two components are approximately equal. Therefore, a reduction in capillary blood volume by disease would reduce the diffusing capacity of the lungs. For technical reasons, the diffusing capacity of the lungs is measured using the rate or transfer of carbon monoxide [D_{LCO}].

Interpretation of D_{LCO} : Measurements of D_{LCO} depend not only on the area and thickness of the blood gas barrier but also on the volume of blood in the pulmonary capillaries. In disease states, the measurement can be affected by the distribution of diffusion properties, alveolar and capillary blood volume. For this reason, the term **transfer factor** is used in the U.K. to emphasize that the measurement is not simply a reflection of diffusion properties of the lungs and can be affected by ventilation perfusion changes as well.