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FCA 1 REFRESHER COURSE

Respiratory equations – behind the numbers

T Leonard

Department of Anaesthesia, School of Clinical Medicine, Faculty of Health Sciences, Chris Hani Baragwanath Academic Hospital, University of the Witwatersrand, South Africa
Corresponding author, email: *tristan.leonard@wits.ac.za*

Summary

Candidates for the FCA 1 exam will come across dozens of equations that eventually all merge into something complicated and daunting. The purpose of this review is to highlight some of the respiratory equations that are important and that candidates find confusing and explain the mathematical and physiological principles behind them.

Keywords: equations, respiratory physiology, ventilation, perfusion, dead space

Introduction

There are many equations that candidates will come across in their study of respiratory physiology. These equations describe principles of ventilation, perfusion and diffusion within the respiratory system. This review attempts to explain the origins and make sense of the numbers in some of these equations.

Equations to be covered:

- Dead space equations
- The alveolar gas equation
- Diffusion equations
- Ventilation-perfusion equations

Dead space equations

Physiological dead space represents the portion of ventilation that does not eliminate carbon dioxide (CO_2).[1] This consists of the anatomical dead space (the fraction of ventilation delivered to the conducting airways – roughly 150 ml)[1,2] and the alveolar dead space (the fraction of ventilation delivered to alveoli with no pulmonary artery perfusion).[2] In 1891, Christian Bohr introduced his equation to represent the volume of gas that constitutes the dead space.

The original version of this equation is:[2]

$$\mathbf{V_D / V_T = (F_ACO_2 - F_ECO_2) / F_ACO_2}$$

V_D	respiratory dead space volume
V_T	tidal volume
F_ACO_2	mean estimate of alveolar CO_2 concentration
F_ECO_2	CO_2 concentration in the total mixed exhaled breath

This equation has undergone some changes due to difficulties in measuring F_ACO_2 and F_ECO_2. Using Dalton's law (the concentration of a gas is proportional to its partial pressure)[3] we can substitute F_A and F_E for partial pressures.[4]

$$\mathbf{V_D / V_T = (P_ACO_2 - P_ECO_2) / P_ACO_2}$$

P_ACO_2	partial pressure of CO_2 in alveolar gas
P_ECO_2	partial pressure of CO_2 in the total mixed exhaled breath

A further modification was made by Henrik Enghoff due to difficulties measuring the P_ACO_2.[2] This gives the physiological dead space equation:[1]

$$\mathbf{V_D / V_T = (P_aCO_2 - P_eCO_2) / P_aCO_2}$$

V_D	physiological dead space volume
V_T	tidal volume
P_aCO_2	partial pressure of carbon dioxide in arterial blood
P_eCO_2	partial pressure of carbon dioxide in expired gas

Important in this equation is understanding the derivation.

The derivation is based on the principal that only the gases involved in alveolar ventilation (V_A) are involved in gas exchange and produce CO_2. The total tidal volume (V_T) is made up of $V_A + V_D$; we can substitute V_A for $V_T - V_D$.[1,2,4]

Now we must look at the fraction of expired (F_E) and inspired (F_i) CO_2. This can be done for nitrogen and oxygen, but CO_2 is most commonly used.

In one exhalation the expired $CO_2 = F_E.V_T$ and this must be made of alveolar gas and dead space gas. Therefore $V_T.F_E = V_A.F_A + V_D.F_i$ and it is assumed that the F_iCO_2 is 0.

Therefore:[1,2,4]

$$V_T.F_E = V_A.F_A$$

Substitute V_A for $V_T - V_D$

$$V_T.F_E = (V_T - V_D).F_A$$

Multiply out the brackets

$V_T.F_E = (V_T.F_A) – (V_D.F_A)$

Rearrange to get V_D on the left of the equation

$V_D.F_A = V_T(F_A – F_E)$

Divide V_T and F_A

$V_D / V_T = (F_A – F_E) / F_A$

Substitute with partial pressure

$V_D / V_T = (P_ACO_2 – P_ECO_2) / P_ACO_2$

Now use the Enghoff modification

$V_D / V_T = (P_aCO_2 – P_eCO_2) / P_aCO_2$

The alveolar gas equation (AGE)

The AGE describes the alveolar concentration (or partial pressure) of oxygen (O_2) in terms of the inspired oxygen concentration, the alveolar concentration of CO_2 and the respiratory quotient (R).[5]

$\mathbf{F_AO_2 = F_IO_2 – (F_ACO_2 / R)}$

Rewriting the equation applying Dalton's law again gives this equation:

$\mathbf{P_AO_2 = P_IO_2 – (P_ACO_2 / R)}$

P_AO_2	alveolar partial pressure of O_2
P_IO_2	inspired partial pressure of O_2
P_ACO_2	alveolar partial pressure of CO_2
R	respiratory quotient

Derivation of the AGE:

To derive and understand the AGE (as well as its limitations) we need to look at each component of the equation.

Carbon dioxide:

At steady state all CO_2 produced by the body (VCO_2) must be removed by the alveolar ventilation each minute and because CO_2 is highly diffusible we can assume that P_ACO_2 very closely approximates P_aCO_2.[5]

$\mathbf{VCO_2 = F_ACO_2 \ x \ V_A}$

Dalton's law of partial pressures needs to be applied again and states that in a mixture of gases the individual gas CO_2 will be present in a concentration that is the same proportion as P_ACO_2 is of the total pressure P_I.[5]

$\mathbf{VCO_2 = (P_ACO_2 / P_I) \ x \ V_A}$

The equation can be rearranged

$\mathbf{P_ACO_2 = (VCO_2 \ x \ P_I) / V_A = P_aCO_2}$

Oxygen:

All oxygen entering the alveoli must equal the oxygen leaving the alveoli. Input into the alveoli is from the inspired air whereas the output of oxygen is a combination of oxygen consumption (VO_2) and expired oxygen.[5]

Input = output

Input = $V_A \ x \ F_IO_2$

Output = $VO_2 + (V_A \ x \ F_AO_2)$

$V_A \ x \ F_IO_2 = VO_2 + (V_A \ x \ F_AO_2)$

Solve for VO_2

$VO_2 = V_A \ x \ (F_IO_2 – F_AO_2)$

Respiratory quotient:

This is defined as "the volume of carbon dioxide released over the volume of oxygen absorbed during respiration. It is a dimensionless number used in the calculation for basal metabolic rate."[6]

$\mathbf{R = VCO_2 / VO_2}$

The final derivation:

$\mathbf{R = VCO_2 / VO_2 = (F_ACO_2 \ x \ V_A) / [V_A \ x \ (F_IO_2 – F_AO_2)]}$

Cancel out V_A in the numerator and denominator

$R = F_ACO_2 / (F_IO_2 – F_AO_2)$

Solve for F_AO_2

$(F_IO_2 – F_AO_2) = F_ACO_2 / R$

$F_AO_2 = F_IO_2 – F_ACO_2 / R$

Convert to partial pressures and assume $P_ACO_2 = P_aCO_2$

$P_AO_2 = P_IO_2 – (P_aCO_2 / R)$

This is AGE that is most often used. However, there is a problem with this equation in that it may be too simplistic when the value of R does not equal 1.[1,5] In the derivation of the AGE we substituted R for VCO_2 / VO_2 and indeed when R = 0.8 as it most often does this would mean a VCO_2 of 0.20 l/min and VO_2 of 0.25 l/min which is a discrepancy of 50 ml per minute.

Thus, the modified AGE is:[1,5,7]

$\mathbf{P_AO_2 = P_IO_2 – (P_aCO_2 / R) + [F_IO_2 \ x \ P_aCO_2 \ x \ ((1 – R) / R)]}$

The additional part of the equation has relatively minor effect in usual clinical practice.

Diffusion equations

In 1855 Adolf Fick described how a gas moves across a membrane. It is not an equation that can be solved with measurable numbers but rather shows the factors that affect the movement of a gas (oxygen) across the alveolar membrane.[8]

Flow of gas $\propto [A \ x \ D \ (P1 – P2)] / T$

A	area of the membrane
D	diffusion constant of the gas
(P1 – P2)	partial pressure (or concentration) gradient across the membrane
T	thickness of the membrane

$D \propto$ solubility of gas / √molecular weight of gas

This states that the rate of transfer of a gas is directly proportional to the area of a membrane, the diffusion constant for that gas and the concentration gradient across the membrane and it is inversely proportional to the thickness of the membrane.[1,8]

Ventilation and perfusion relationship equations

The concept of dead space has been discussed previously but there are two other equations that can be used to describe ventilation and perfusion relationships in the lung.

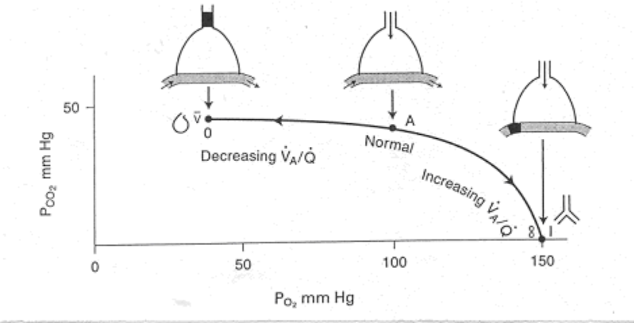

Figure 1: O_2-CO_2 diagram showing a ventilation-perfusion (V/Q) ratio line[1]

The figure illustrates the relationship between alveolar O_2 and CO_2 partial pressure at varying V/Q ratios. Numerically this can be described using the Bohr equation, V/Q ratio equation and the shunt equation.

Ventilation-perfusion ratio equations:

The basic V/Q ratio describes the ratio of ventilation to perfusion in the lung as a whole at a specific point in time. The equation below describes the overall V/Q relationship in the lung.[9]

$$\mathbf{V_A / Q = [8.63 \times R \times (C_aO_2 - C_VO_2)] / P_ACO_2}$$

V_A / Q	ventilation-perfusion ratio
8.63	conversion constant
R	respiratory exchange ratio
$(C_aO_2 - C_VO_2)]$	difference in O_2 content in arterial and mixed venous blood
P_ACO_2	alveolar partial pressure of CO_2

To understand this equation we have to understand that pulmonary gas exchange is based on three principles: ventilation, diffusion and perfusion.[10] The fundamental principle behind these three processes is the conservation of mass. Every molecule of O_2 that enters the lungs has to go into the blood or be exhaled and every molecule of CO_2 that leaves the lungs has to come from the blood or the atmosphere.[10]

$$VO_2 = V_E \times (F_IO_2 - F_EO_2) = V_A \times (F_IO_2 - F_AO_2)$$

And

$$VO_2 = Q \times (C_aO_2 - C_vO_2)$$

Combining these two equations

$$\mathbf{V_A \times (F_IO_2 - F_AO_2) = Q \times (C_aO_2 - C_vO_2)}$$

Solve for V/Q and apply Dalton's law

$$\mathbf{V_A / Q = 8.63 \times (C_aO_2 - C_vO_2)/(P_IO_2 - P_AO_2)}$$

The constant allows for standardisation when the units used for V_A and Q are l/min, C_aO_2 and C_vO_2 are ml/dl and for P_IO_2 and P_AO_2 are mmHg.[10]

The same principle can be applied for CO_2 except that the CO_2 content of mixed venous and arterial blood are reversed because CO_2 is being eliminated.[10]

$$\mathbf{V_A / Q = 8.63 \times (C_VCO_2 - C_aCO_2) / (P_ACO_2 - P_ICO_2)}$$

These two equations explain why in an area of lung with reduced V_A / Q ratio the P_AO_2 and C_aO_2 will fall greater than the P_ACO_2 will rise while in areas with high V_A / Q ratio the P_AO_2 rises while P_ACO_2 falls. Therefore, low V_A / Q areas affect O_2 more and high V_A / Q areas affect CO_2 more.[10]

The shunt equation:

This equation gives a ratio of the shunt blood flow to total blood flow. Shunt blood flow is blood that is not exposed to any gas exchange. This may be areas of the lung with V/Q ratio of 0 or venous blood that enters the arterial system directly.[11]

Important in understanding and deriving this equation is to be able to draw a theoretical alveolus with blood being oxygenated and blood being shunted passed the alveolus.

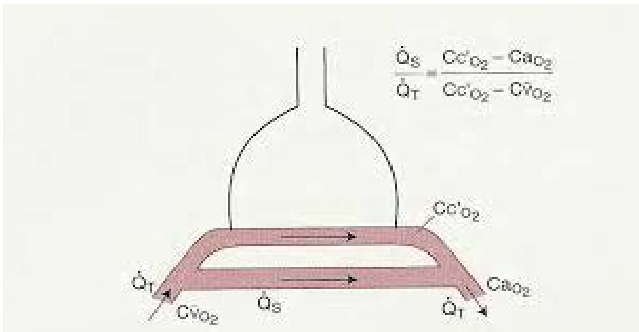

Figure 2: A visualisation of the shunt equation[11]

Q_s	shunted blood flow
Q_T	total blood flow
CcO_2	end-capillary oxygen content
CaO_2	arterial oxygen content
CvO_2	mixed venous oxygen content

Flow entering the system $Q_T.CvO_2$ must equal flow leaving the system $Q_T.CaO_2$ but this flow is made up of two components – shunted blood ($Q_s.CvO_2$) and oxygenated capillary blood [$(Q_T - Q_s).CcO_2$]

Therefore

$$Q_T.CaO_2 = (Q_s.CvO_2) + [(Q_T - Q_s).CcO_2]$$

Rearrange the brackets

$$Q_T.CaO_2 = (Q_s.CvO_2) + (Q_T.CcO_2) - (Q_s.CcO_2)$$

Move Q_s to the left

$$(Q_s.CcO_2) - (Q_s.CvO_2) = (Q_T.CcO_2) - (Q_T - CaO_2)$$

Simplify the brackets

$$Q_s\,(CcO_2 - CvO_2) = Q_T\,(CcO_2 - CaO_2)$$

Divide by Q_s and $(CcO_2 - CvO_2)$

$$Q_s / Q_T = (CcO_2 - CaO_2) / (CcO_2 - CvO_2)$$

CcO_2 is the end capillary oxygen content – blood that has been exposed to the alveolus and will always have the highest oxygen content.

Calculating CvO_2 and C_aO_2 is done by blood sampling from the central line and arterial line and is done using the following equations:

$$CvO_2 = (1.34)(Hb)(Sats) + (0.003.PvO_2)$$

$$CaO_2 = (1.34)(Hb)(Sats) + (0.003.PaO_2)$$

Measuring P_cO_2 requires a catheter in the pulmonary vein and is technically difficult. As such it is assumed to be in equilibrium with the P_AO_2 and therefore:

$$CcO_2 = (1.34)(Hb)(Sats) + (0.003.P_AO_2)$$

A reminder of the final equation:

$$Q_s / Q_T = (CcO_2 - CaO_2) / (CcO_2 - CvO_2)$$

Thus, by calculating CcO_2, CvO_2 and CaO_2 from blood sampling it is possible to quantify the shunt fraction – which is the percentage of blood not exposed to ventilation. Normal shunt fraction is around 5% and once it increases above 30% increasing the FiO_2 will not be able to increase PaO_2.[12]

Conflict of interest

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ORCID

T Leonard https://orcid.org/0000-0003-4426-3972

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