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 (CO₂). This consists of the anatomical dead space (the fraction of ventilation delivered to the conducting airways – roughly 150 ml) and the alveolar dead space (the fraction of ventilation delivered to alveoli with no pulmonary artery perfusion). 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:

\[ \frac{V_D}{V_T} = \frac{(F_AC_{O_2} - F_EC_{O_2})}{F_EC_{O_2}} \]

\( V_D \) = respiratory dead space volume
\( V_T \) = tidal volume
\( F_AC_{O_2} \) = mean estimate of alveolar CO₂ concentration
\( F_EC_{O_2} \) = CO₂ concentration in the total mixed exhaled breath

This equation has undergone some changes due to difficulties in measuring \( F_AC_{O_2} \) and \( F_EC_{O_2} \). Using Dalton’s law (the concentration of a gas is proportional to its partial pressure) we can substitute \( F_A \) and \( F_E \) for partial pressures.

\[ \frac{V_D}{V_T} = \frac{(P_A C_{O_2} - P_E C_{O_2})}{P_E C_{O_2}} \]

\( P_A C_{O_2} \) = partial pressure of CO₂ in alveolar gas
\( P_E C_{O_2} \) = partial pressure of CO₂ in the total mixed exhaled breath

A further modification was made by Henrik Enghoff due to difficulties measuring the \( P_A C_{O_2} \). This gives the physiological dead space equation:

\[ \frac{V_D}{V_T} = \frac{(P_a C_{O_2} - P_E C_{O_2})}{P_a C_{O_2}} \]

\( P_a C_{O_2} \) = partial pressure of carbon dioxide in arterial blood
\( P_E C_{O_2} \) = 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 CO₂. The total tidal volume (\( V_T \)) is made up of \( V_A + V_D \); we can substitute \( V_A \) for \( V_T - V_D \).

In one exhalation the expired CO₂ = \( F_E \cdot V_T \) and this must be made of alveolar gas and dead space gas. Therefore \( V_T \cdot F_E = V_A \cdot F_A + V_D \cdot F_A \) and it is assumed that the \( F_A C_{O_2} \) is 0.

Now we must look at the fraction of expired (\( F_E \)) and inspired (\( F_I \)) CO₂. This can be done for nitrogen and oxygen, but CO₂ is most commonly used.

In one exhalation the expired CO₂ = \( F_E \cdot V_T \) and this must be made of alveolar gas and dead space gas. Therefore \( V_T \cdot F_E = V_A \cdot F_A + V_D \cdot F_A \) and it is assumed that the \( F_A C_{O_2} \) is 0.

Therefore:

\[ V_T \cdot F_E = V_A \cdot F_A \]

Substitute \( V_A \) for \( V_T - V_D \):

\[ V_T \cdot F_E = (V_T - V_D) \cdot F_A \]

Multiply out the brackets:

\[ V_T \cdot F_E = V_T \cdot F_A - V_D \cdot F_A \]
Respiratory equations – behind the numbers


VT.FE = (VT.FA) – (VD.FA)
Rearrange to get VD on the left of the equation
VD.FA = VT(FA – FE)
Divide VT and FA
VD / VT = (FA – FE) / FA
Substitute with partial pressure
VD / VT = (PACO2 – PECO2) / PACO2
Now use the Enghoff modification
VD / VT = (PaCO2 – PeCO2) / PaCO2

The alveolar gas equation (AGE)

The AGE describes the alveolar concentration (or partial pressure) of oxygen (O2) in terms of the inspired oxygen concentration, the alveolar concentration of CO2 and the respiratory quotient (R).5

FAO2 = FIO2 – (FACO2 / R)
Rewriting the equation applying Dalton’s law again gives this equation:
PAO2 = PIO2 – (PACO2 / R)

PAO2
alveolar partial pressure of O2
PIO2
inspired partial pressure of O2
PACO2
alveolar partial pressure of CO2
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 CO2 produced by the body (VCO2) must be removed by the alveolar ventilation each minute and because CO2 is highly diffusible we can assume that PACO2 very closely approximates PaCO2.5

VCO2 = FACO2 x VA

Dalton’s law of partial pressures needs to be applied again and states that in a mixture of gases the individual gas CO2 will be present in a concentration that is the same proportion as Pco2 is of the total pressure P,5

VCO2 = (Pco2 / P) x VA

The equation can be rearranged
Pco2 = (VCO2 x P) / VA = Pco2

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 (VO2) and expired oxygen.5

Input = VO2 + (FAO2 x VA)
Output = VO2 + (FAO2 x VA)
Solve for VO2
VO2 = (FAO2 x (FIO2 – FEO2))

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

R = VCO2 / VO2

The final derivation:

R = VCO2 / VO2 = (FACO2 x VA) / [VA x (FIO2 – FAO2)]
Cancel out VA in the numerator and denominator
R = FACO2 / (FIO2 – FAO2)
Convert to partial pressures and assume Pco2 = PaCO2
Pco2 = FACO2 / (FIO2 – FAO2)

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 VCO2 / VO2 and indeed when R = 0.8 as it most often does this would mean a VCO2 of 0.20 l/min and VO2 of 0.25 l/min which is a discrepancy of 50 ml per minute.

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

Pco2 = FACO2 / (FIO2 – FAO2) + [FIO2 x Pco2 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 ∝ [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 ∝ 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.

**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

\[
V_a / Q = \frac{8.63 \times R \times (C_aO_2 - C_vO_2)}{P_{ACO_2}}
\]

- \( V_a / Q \): ventilation-perfusion ratio
- 8.63: conversion constant
- \( R \): respiratory exchange ratio
- \( (C_aO_2 - C_vO_2) \): difference in O2 content in arterial and mixed venous blood
- \( P_{ACO_2} \): alveolar partial pressure of CO2

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 O2 that enters the lungs has to go into the blood or be exhaled and every molecule of CO2 that leaves the lungs has to come from the blood or the atmosphere.10

\[
V_O = V_a \times (F_iO_2 - F_aO_2) = V_a \times (F_iO_2 - F_a)
\]

And

\[
V_O = Q \times (C_iO_2 - C_vO_2)
\]

Combining these two equations

\[
V_a \times (F_iO_2 - F_a) = Q \times (C_iO_2 - C_vO_2)
\]

Solve for V/Q and apply Dalton’s law

\[
V_a / Q = 8.63 \times \frac{(C_aO_2 - C_vO_2)}{(P_{O_2} - P_{A_2})}
\]

The constant allows for standardisation when the units used for \( V_a \) and Q are l/min, C_aO2 and C_vO2 are ml/dl and for \( P_{O_2} \) and \( P_{A_2} \) are mmHg.10

The same principle can be applied for CO2 except that the CO2 content of mixed venous and arterial blood are reversed because CO2 is being eliminated.10

\[
V_a / Q = 8.63 \times \frac{(C_vCO_2 - C_aCO_2)}{(P_{CO_2} - P_{ACO_2})}
\]

These two equations explain why in an area of lung with reduced \( V_a / Q \) ratio the \( P_{O_2} \) and \( C_aO_2 \) will fall greater than the \( P_{CO_2} \) will rise while in areas with high \( V_a / Q \) ratio the \( P_{O_2} \) rises while \( P_{CO_2} \) falls. Therefore, low \( V_a / Q \) areas affect O2 more and high \( V_a / Q \) areas affect CO2 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 past the alveolus.

\[
Q_s \quad \text{shunted blood flow}
\]

\[
Q_t \quad \text{total blood flow}
\]

\[
CcO_2 \quad \text{end-capillary oxygen content}
\]

\[
CaO_2 \quad \text{arterial oxygen content}
\]

\[
CvO_2 \quad \text{mixed venous oxygen content}
\]

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, CVO_2)\]

Therefore

\[
Q_t, CaO_2 = (Q_s, Cvo_2) + [(Q_t - Q_s, CVO_2)]
\]

Rearrange the brackets

\[
Q_t, CaO_2 = (Q_s, Cvo_2) + (Q_t, CCO_2) - (Q_t, CVO_2)
\]

Move \( Q_s \) to the left

\[
(Q_s, CVO_2) - (Q_s, Cvo_2) = (Q_t, CCO_2) - (Q_t, CVO_2)
\]
Respiratory equations – behind the numbers

Simplify the brackets

\[ Q_s (C_{O2} - C_{vO2}) = Q_t (C_{O2} - C_{aO2}) \]

Divide by \( Q_s \) and \( (C_{O2} - C_{vO2}) \)

\[ \frac{Q_s}{Q_t} = \frac{(C_{O2} - C_{aO2})}{(C_{O2} - C_{vO2})} \]

\( C_{O2} \) is the end capillary oxygen content – blood that has been exposed to the alveolus and will always have the highest oxygen content.

Calculating \( C_{vO2} \) and \( C_{aO2} \) is done by blood sampling from the central line and arterial line and is done using the following equations:

\[ C_{vO2} = (1.34)(Hb)(Sats) + (0.003.PvO_2) \]

\[ C_{aO2} = (1.34)(Hb)(Sats) + (0.003.PaO_2) \]

Measuring \( P_{CO2} \) requires a catheter in the pulmonary vein and is technically difficult. As such it is assumed to be in equilibrium with the \( P_{A2} \) and therefore:

\[ C_{O2} = (1.34)(Hb)(Sats) + (0.003.P_{A2}) \]

A reminder of the final equation:

\[ Q_s / Q_t = (C_{O2} - C_{aO2}) / (C_{O2} - C_{vO2}) \]

Thus, by calculating \( C_{O2}, C_{vO2} \) and \( C_{aO2} \) 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 FiO2 will not be able to increase PaO2.\(^{12}\)

Conflict of interest

The author declares no conflict of interest.

Funding source

None.

ORCID

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

References