

# The alveolar gas equation

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## Key points

The alveolar gas equation (AGE) relates  $P_{A\text{O}_2}$  to  $P_{I\text{O}_2}$ ,  $P_{A\text{CO}_2}$  and the respiratory quotient ( $R$ ).

Depending which quantities we fix and which we allow to vary, the AGE describes a linear or non-linear relationship.

The AGE predicts an absurdity (i.e. negative  $P_{A\text{O}_2}$  at low  $P_{I\text{O}_2}$ ).

Derivation of the equation shows how this arises and restricts the validity of the equation to reasonable (non-hypoxic) levels of  $F_{I\text{O}_2}$ .

The full version of the AGE has an extra term which is trivial for most clinical purposes. This relates to passive inflow of gas for  $R$  less than unity.

The alveolar gas equation (AGE) is well known and relates the alveolar concentration of oxygen  $F_{A\text{O}_2}$  (or equivalently partial pressure  $P_{A\text{O}_2}$ ) to three variables:  $F_{I\text{O}_2}$ ,  $F_{A\text{CO}_2}$  and the respiratory quotient ( $R$ ). However, the AGE predicts an absurdity: if we input a  $F_{I\text{O}_2}$  sufficiently low, say 0.05 (i.e. a  $P_{I\text{O}_2}$  of about 5 kPa), into the equation

$$F_{A\text{O}_2} = F_{I\text{O}_2} - \frac{F_{A\text{CO}_2}}{R}$$

then for typical values of  $F_{A\text{CO}_2} = 0.05$  and  $R = 0.8$ , a negative value for  $F_{A\text{O}_2}$  is predicted. Therefore, it is plain that the AGE is not true for all conditions. Where does the AGE come from, and will the derivation explain the problem and define the conditions under which it is true?

## Derivation of the AGE

### Carbon dioxide

The metabolic minute production of carbon dioxide ( $\dot{V}_{\text{CO}_2}$ ) is approximately 200 ml (0.20 litre  $\text{min}^{-1}$ ) in a resting adult. We will assume this value is constant. Under steady-state conditions where the  $P_{a\text{CO}_2}$  is unchanging with time, this amount must be removed by alveolar ventilation each minute. The alveolar membrane is thin and carbon dioxide is highly diffusible and we may therefore assume that  $P_{A\text{CO}_2} = P_{a\text{CO}_2}$  to a close approximation (i.e. that there is a negligible  $P_{\text{CO}_2}$  gradient between blood and alveolar space).

### Partial pressures

The concentration of a component gas in a mixture of gases is related to the partial pressure by Dalton's law of partial pressures. This states that an individual gas such as carbon dioxide in the mixture of gases in the alveolar space will be present in a concentration (or fraction) that is the same proportion as  $P_{A\text{CO}_2}$  is of the total pressure (i.e. approximately  $P_1$  at the end of inspiration). For typical values of  $P_1 = 100$  kPa and  $P_{a\text{CO}_2} = P_{A\text{CO}_2} = 5$  kPa, we have  $F_{A\text{CO}_2} = 0.05$  or 5%. The quantity of carbon dioxide removed from the alveolar

space in 1 min is simply the alveolar ventilation ( $\dot{V}_A$ ) multiplied by  $F_{A\text{CO}_2}$ . Since, for steady-state conditions, this must be the same as  $\dot{V}_{\text{CO}_2}$ , we have

$$\dot{V}_{\text{CO}_2} = F_{A\text{CO}_2} \times \dot{V}_A$$

$$\dot{V}_{\text{CO}_2} = \frac{P_{A\text{CO}_2}}{P_1} \times \dot{V}_A$$

Rearranging and using our assumption that  $P_{A\text{CO}_2} = P_{a\text{CO}_2}$ , we obtain the following (Fig. 1):

$$P_{A\text{CO}_2} = \frac{\dot{V}_{\text{CO}_2} \times P_1}{\dot{V}_A} = P_{a\text{CO}_2}$$

### Oxygen

The input of oxygen into the alveolar space, and the output from it, must, in steady-state conditions, be equal.

Input is by alveolar ventilation and using the same arguments as for carbon dioxide:

$$\text{Input} = \dot{V}_A \times F_{I\text{O}_2}$$

Output, on the other hand, is in two directions:

- (i) across the alveolar membrane into the blood – in steady-state conditions, the oxygen consumption  $\dot{V}_{\text{O}_2}$ ; and
- (ii) in the expired gas ( $\dot{V}_A \times F_{A\text{O}_2}$ ):

$$\text{Output} = \dot{V}_{\text{O}_2} + \dot{V}_A \times F_{A\text{O}_2}$$

So, for steady-state conditions, we can write

$$\text{Input} = \text{Output}$$

$$\dot{V}_A \times F_{I\text{O}_2} = \dot{V}_{\text{O}_2} + \dot{V}_A \times F_{A\text{O}_2}$$

which rearranges as

$$\dot{V}_{\text{O}_2} = \dot{V}_A \times [F_{I\text{O}_2} - F_{A\text{O}_2}]$$

We are now ready to complete the derivation by noting that

$$R = \frac{\dot{V}_{\text{CO}_2}}{\dot{V}_{\text{O}_2}}$$

so that

$$R = \frac{\dot{V}_{\text{CO}_2}}{\dot{V}_{\text{O}_2}} = \frac{F_{A\text{CO}_2} \times \dot{V}_A}{\dot{V}_A \times [F_{I\text{O}_2} - F_{A\text{O}_2}]}$$

which, in turn, with cancellation and rearrangement, becomes

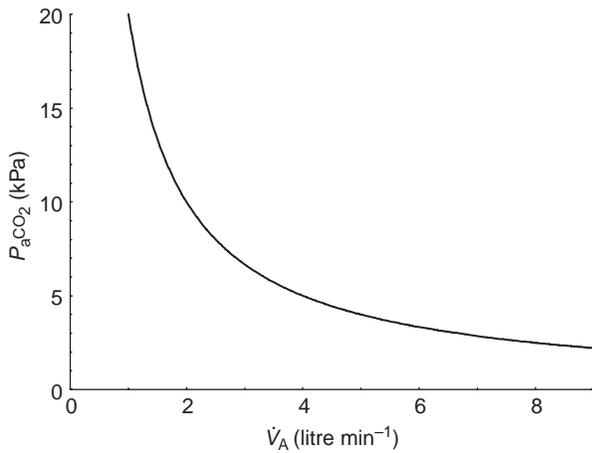
$$R = \frac{F_{A\text{CO}_2}}{[F_{I\text{O}_2} - F_{A\text{O}_2}]}$$

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**Fig. 1** The relationship of alveolar ventilation ( $\dot{V}_A$ ) to the resulting  $P_{aCO_2}$  for constant  $\dot{V}_{CO_2}$  is a non-linear one. It is a rectangular hyperbola.

$$[F_{I_{O_2}} - F_{A_{O_2}}] = \frac{F_{A_{CO_2}}}{R}$$

$$F_{A_{O_2}} = F_{I_{O_2}} - \frac{F_{A_{CO_2}}}{R}$$

which is almost the familiar version of the AGE. Converting to partial pressures (Dalton) and using our assumption that  $P_{A_{CO_2}} = P_{a_{CO_2}}$ , this finally becomes the familiar ‘short’ AGE:

$$P_{A_{O_2}} = P_{I_{O_2}} - \frac{P_{a_{CO_2}}}{R}$$

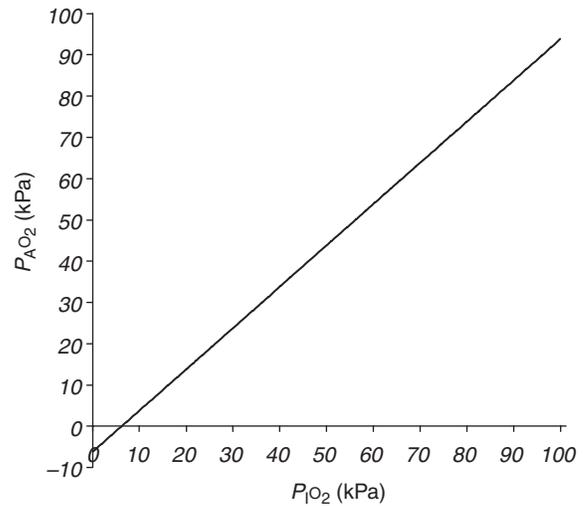
### What does the AGE say?

We have derived the usual ‘short’ AGE using the assumption of steady-state conditions. The AGE will only be valid so long as the assumptions upon which we constructed it remain true. It is evident that, at low  $F_{I_{O_2}}$ , the steady-state assumption will be violated – the required  $\dot{V}_{O_2}$  cannot be supplied at the lowered  $F_{A_{O_2}}$  – and therefore we cannot expect the AGE to describe the resulting  $F_{A_{O_2}}$  accurately. In fact,  $F_{A_{O_2}}$  then becomes a time-dependent variable rather than a constant equilibrium quantity, since more is being taken up than supplied and the AGE relationship breaks down at some ill-defined (*i.e.* not defined by our simple model)  $F_{I_{O_2}}$ ; the patient becomes progressively hypoxic.

$F_{A_{O_2}}$  is dependent upon three variable quantities:  $P_{I_{O_2}}$ ,  $P_{A_{CO_2}}$  and  $R$ . Although all are variables, they are not equally easily engineered.  $P_{I_{O_2}}$  is very easily manipulated, of course.  $P_{A_{CO_2}}$ , on the other hand, is quite easy to manipulate in the intubated, ventilated patient but much less so in the spontaneously breathing subject.  $R$  is alterable by manipulation of the diet but not in any rapid, simple and predictable manner.

$$P_{A_{O_2}} = P_{I_{O_2}} - \frac{P_{a_{CO_2}}}{R}$$

- With  $P_{I_{O_2}}$  as the input variable and  $P_{A_{CO_2}}$  and  $R$  fixed, we have a linear relationship of the type  $y = mx + c$ , where  $y = P_{A_{O_2}}$ ,



**Fig. 2** The alveolar gas equation predicts a relationship of inspired oxygen partial pressure ( $P_{I_{O_2}}$ ) to the resulting alveolar partial pressure ( $P_{A_{O_2}}$ ) that is linear. It also predicts a nonsensical negative  $P_{A_{O_2}}$  at low  $P_{I_{O_2}}$ . The equation is valid only at values of  $P_{I_{O_2}}$  sufficient to allow normal oxygen uptake  $\dot{V}_{O_2}$ .

$m = 1$ ,  $x = P_{I_{O_2}}$  and  $c = [-P_{A_{CO_2}}/R]$ . The graph of  $P_{A_{O_2}}$  vs  $P_{I_{O_2}}$  is linear with unity gradient (Fig. 2). The intercept on the vertical axis is negative, as we have noted. This is a graph of the equation, not of the physiology. In the physiological range (above, say, 8–9 kPa), it will describe the physiology reasonably well.

- With  $P_{I_{O_2}}$  fixed and  $P_{A_{CO_2}}$  as the input variable, we also have a linear relationship. However, if we ask how  $P_{A_{O_2}}$  is related to  $\dot{V}_A$  – which, with  $\dot{V}_{CO_2}$ , determines  $P_{A_{CO_2}}$  – then the relationship is non-linear. We have from before

$$P_{A_{CO_2}} = \frac{\dot{V}_{CO_2} \times P_1}{\dot{V}_A} = P_{a_{CO_2}}$$

Substituting for  $P_{a_{CO_2}}$  in the AGE:

$$P_{A_{O_2}} = P_{I_{O_2}} - \frac{\dot{V}_{CO_2} \times P_1}{\dot{V}_A \times R}$$

$$P_{A_{O_2}} = P_{I_{O_2}} - \frac{1}{\dot{V}_A} \times \left[ \frac{\dot{V}_{CO_2} \times P_1}{R} \right]$$

This is an equation of the form

$$y = m \times \frac{1}{x} + c$$

with  $y = P_{A_{O_2}}$  as before,

$$m = - \left[ \frac{\dot{V}_{CO_2} \times P_1}{R} \right]$$

$x = \dot{V}_A$  and  $c = P_{I_{O_2}}$ . This is an equation of inversely related quantities whose graph is a rectangular hyperbola, but the negative sign before the coefficient modifying the  $x$ -term turns the hyperbola of Figure 1 upside down so that we subtract it from the (assumed

constant)  $P_{I\text{O}_2}$ . The hyperbola is also amplified by division by  $R$  if it is less than unity. The effect of the scaling for various values of  $R$  is shown. A  $P_{I\text{O}_2}$  of 20 kPa is taken to represent breathing air with allowance for water vapour (Fig. 3). It is apparent from the graph that a reduction in  $\dot{V}_A$  to levels which allow very high levels of  $P_{a\text{CO}_2}$  similarly predict a negative value for  $P_{A\text{O}_2}$  as before. Once again, we have to be careful to use the equation only in circumstances where it is valid; if the steady-state condition is violated, the equation does not apply.

It is evident from these graphs that  $P_{A\text{O}_2}$  is much more effectively raised by increasing the inspired concentration than it is by hyperventilation. However, in the spontaneously breathing patient in air, hyperventilation is the only option.

### Refining the AGE

In the appendix to West's *Respiratory Physiology*, and in other texts, a more elaborate version of the AGE is given:

$$P_{A\text{O}_2} = P_{I\text{O}_2} - \frac{P_{a\text{CO}_2}}{R} + \left[ F_{I\text{O}_2} \times P_{a\text{CO}_2} \times \left( \frac{1 - R}{R} \right) \right]$$

Where does the fearsome-looking extra term in the expression come from, and is it important?

In our derivation of the AGE, we obtained expressions for  $\dot{V}_{\text{O}_2}$  and  $\dot{V}_{\text{CO}_2}$  and substituted these into the definition of  $R$ . This is actually not a valid procedure, since we need to look at input and

output volumes in the functional residual capacity (FRC). The FRC volume is constant in our model, and yet when the  $R$ -value is not unity, more gas is extracted from the FRC by oxygen uptake  $\dot{V}_{\text{O}_2}$  (say 0.25 litre  $\text{min}^{-1}$ ) than is added to it by  $\dot{V}_{\text{CO}_2}$  (0.20 litre  $\text{min}^{-1}$ , when  $R = 0.8$ ). This is plainly incompatible with a constant FRC volume; the 50 ml discrepancy must be made up by an additional passive inflow of gas. Even at end-inspiration or expiration, there must be a small difference in pressure between atmosphere and alveolus such that this volume

$$\dot{V}_p = [\dot{V}_{\text{O}_2} - \dot{V}_{\text{CO}_2}]$$

is delivered to the alveolar space each minute. This delivers a small extra amount of oxygen, which acts to boost the  $F_{A\text{O}_2}$  a little. This is a bulk flow of gas caused by pressure difference which is not a result of diffusion; it follows from the general gas law  $PV = nRT$ , since  $n$  (the number of moles of, in this case, oxygen) is being continuously removed by uptake into the blood.  $RT$  and  $V$  are constant. This same process is at work in more dramatic fashion during apnoeic mass-transfer oxygenation, such as during brain death testing procedures or bronchoscopy. Details, for those with a head for algebra, are shown in the box.

Figure 4 shows the effect of taking the extra term into consideration on the linear relationship between  $P_{I\text{O}_2}$  and  $P_{A\text{O}_2}$ . We can see that it is a pretty small modification. It is directly proportional to  $F_{I\text{O}_2}$  and indeed is barely apparent at  $F_{I\text{O}_2} < 0.5$ . Note that we cannot have both  $P_{I\text{O}_2}$  and  $P_{a\text{CO}_2}$  multiplied together in the

Let us modify the AGE derivation according to the refined model:

$$\text{O}_2\text{-Input} = F_{I\text{O}_2} \times \dot{V}_A + F_{I\text{O}_2} \times \dot{V}_p = F_{I\text{O}_2} \times [\dot{V}_A + \dot{V}_p]$$

$$\text{O}_2\text{-Output} = \dot{V}_{\text{O}_2} + F_{A\text{O}_2} \times \dot{V}_A$$

Since  $\text{O}_2\text{-Input} = \text{O}_2\text{-Output}$ ,

$$F_{I\text{O}_2} \times \dot{V}_A + F_{I\text{O}_2} \times \dot{V}_p = \dot{V}_{\text{O}_2} + F_{A\text{O}_2} \times \dot{V}_A$$

Rearranging,

$$\dot{V}_{\text{O}_2} = \dot{V}_A [F_{I\text{O}_2} - F_{A\text{O}_2}] + F_{I\text{O}_2} \times \dot{V}_p$$

Now, using the expression for

$$\dot{V}_{\text{CO}_2} = F_{A\text{CO}_2} \times \dot{V}_A$$

$$R = \frac{\dot{V}_{\text{CO}_2}}{\dot{V}_{\text{O}_2}} = \frac{F_{A\text{CO}_2} \times \dot{V}_A}{\dot{V}_A [F_{I\text{O}_2} - F_{A\text{O}_2}] + F_{I\text{O}_2} \times \dot{V}_p}$$

$$\dot{V}_A [F_{I\text{O}_2} - F_{A\text{O}_2}] + F_{I\text{O}_2} \times \dot{V}_p = \frac{F_{A\text{CO}_2} \times \dot{V}_A}{R}$$

$$[F_{I\text{O}_2} - F_{A\text{O}_2}] + \frac{F_{I\text{O}_2} \times \dot{V}_p}{\dot{V}_A} = \frac{F_{A\text{CO}_2}}{R}$$

$$F_{A\text{O}_2} = F_{I\text{O}_2} - \frac{F_{A\text{CO}_2}}{R} + \left[ \frac{F_{I\text{O}_2} \times \dot{V}_p}{\dot{V}_A} \right]$$

So we have a rather more complicated expression for the AGE. We can tidy this up a little further by manipulating the extra term in brackets:

$$\left[ \frac{F_{I\text{O}_2} \times \dot{V}_p}{\dot{V}_A} \right] = \frac{F_{I\text{O}_2} (\dot{V}_{\text{O}_2} - \dot{V}_{\text{CO}_2})}{\dot{V}_A}$$

But

$$\dot{V}_{\text{O}_2} = \frac{\dot{V}_{\text{CO}_2}}{R}$$

from the definition of  $R$ ,

$$\frac{F_{I\text{O}_2} \times \dot{V}_{\text{CO}_2} \left[ \frac{1}{R} - 1 \right]}{\dot{V}_A} = \frac{F_{I\text{O}_2} \times \dot{V}_{\text{CO}_2} \left[ \frac{1-R}{R} \right]}{\dot{V}_A}$$

Finally, from before we have

$$F_{A\text{CO}_2} = \frac{\dot{V}_{\text{CO}_2}}{\dot{V}_A}$$

so the expression in brackets becomes

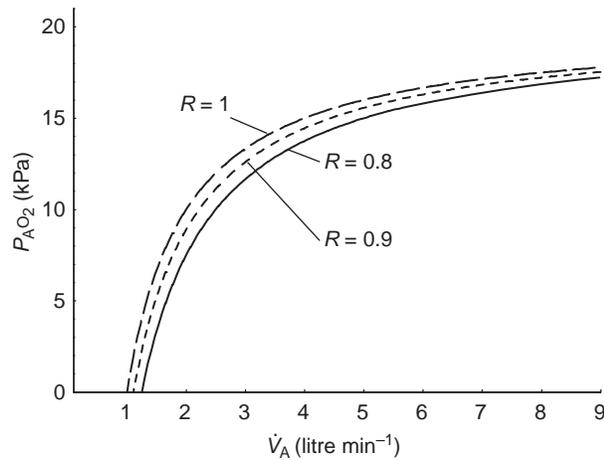
$$\frac{F_{I\text{O}_2} \times \dot{V}_{\text{CO}_2} ((1 - R)/R)}{\dot{V}_A} = F_{I\text{O}_2} \times F_{A\text{CO}_2} \times \left( \frac{1 - R}{R} \right)$$

So we obtain the final form of our modified AGE:

$$F_{A\text{O}_2} = F_{I\text{O}_2} - \frac{F_{A\text{CO}_2}}{R} + \left[ F_{I\text{O}_2} \times F_{A\text{CO}_2} \times \left( \frac{1 - R}{R} \right) \right]$$

Put into partial pressure terms, this becomes

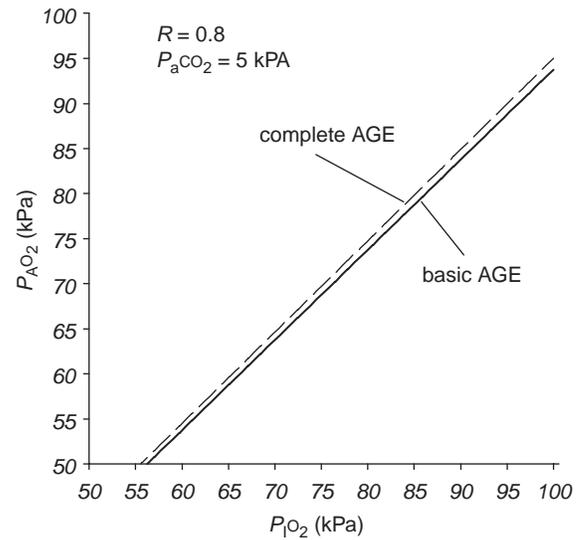
$$P_{A\text{O}_2} = P_{I\text{O}_2} - \frac{P_{a\text{CO}_2}}{R} + \left[ F_{I\text{O}_2} \times P_{a\text{CO}_2} \times \left( \frac{1 - R}{R} \right) \right]$$



**Fig. 3** The relationship of alveolar ventilation ( $\dot{V}_A$ ) to the resulting  $P_{A_{O_2}}$  for constant  $P_{i_{O_2}}$  is non-linear.

extra term in the brackets, since this would give a {pressure squared}; we must use  $F_{I_{O_2}}$  instead.

We can discard the extra term in the full AGE for any usual clinical purpose; it is complicated and simply too small to make a difference. By taking the discrepancy in the volumes entering the FRC into consideration, however, we have understood a minor detail of the physiology in this context which achieves major importance in another. In apnoea,  $P_{a_{CO_2}}$  increases by 0.3–0.7 kPa  $\text{min}^{-1}$ , say 0.5 kPa  $\text{min}^{-1}$ . If  $P_{a_{CO_2}}$  increases at this rate, then, by our assumption that  $P_{a_{CO_2}} = P_{A_{CO_2}}$ , so does  $P_{A_{CO_2}}$ . Since this is in the gas phase, we can apply Dalton's law and know that carbon dioxide is entering the FRC at  $0.05 \times 2$  litre  $\text{min}^{-1}$  (i.e. about 10 ml of the 200 ml  $\text{min}^{-1}$   $\dot{V}_{CO_2}$ ). The remainder of the  $\dot{V}_{CO_2}$  remains in the aqueous phase in the body water. Provided  $P_{A_{O_2}}$  is sufficient to saturate the Hb (preoxygenation), then uptake  $\dot{V}_{O_2}$  (say 0.25 litre  $\text{min}^{-1}$ ) will proceed normally, and if the airway is filled with oxygen (flowing through catheter in trachea) this will be drawn into the FRC at a rate of 0.24 litre  $\text{min}^{-1}$  by bulk flow: this is apnoeic mass-transfer oxygenation.



**Fig. 4** The extra term in the complete form of the alveolar gas equation (AGE), where  $R$  is less than unity, adds a small amount to the predicted  $P_{A_{O_2}}$ . This is interesting but clinically trivial and may be neglected for practical purposes.

Under ideal circumstances (preoxygenation and normal gas exchange), this technique is limited by carbon dioxide toxicity and not hypoxia.

## Key references

- Cruickshank S. *Mathematics and Statistics in Anaesthesia*. Oxford: Oxford University Press, 1998
- West JB. *Respiratory Physiology: The Essentials*, 6th edn. Baltimore: Lippincott Williams and Wilkins, 2000

See multiple choice questions 23–26.