Permissive hypercapnia and gas exchange in lungs with high $\dot{Q}_s/\dot{Q}_t$: a mathematical model

C. J. Joyce and K. G. Hickling

Summary

Low volume ventilation with permissive hypercapnia is becoming widely used in the treatment of acute respiratory distress syndrome. A mathematical model was developed to examine the effects of hypoventilation on pulmonary gas exchange in lungs with a range of shunt fractions. Hypoventilation did not worsen gas exchange, provided the inspired oxygen concentration was high enough to maintain $P_{A\text{O}_2}$ at an adequate level. In lungs with a high shunt fraction, some improvement in gas exchange may result, but these effects are small. A rightwards shift of the oxygen-haemoglobin dissociation curve induced by hypercapnia, is likely to be beneficial rather than detrimental in patients with acute respiratory distress syndrome. This analysis was limited to the direct effects of hypoventilation in lungs with constant shunt fractions, and did not encompass a number of possible secondary effects such as changes in cardiac output with $P_{A\text{O}_2}$, changes in shunt fraction associated with a reduction in mean airway pressure and possible direct effects of hypercapnia on the pulmonary vasculature or airways. (Br. J. Anaesth. 1996; 77: 678–683)

Key words


Methods

GENERAL DESCRIPTION

The aim of the model was to describe the effect of hypoventilation on steady state pulmonary gas exchange in lungs with varying degrees of intrapulmonary shunt. The lung was modelled as consisting of two compartments (see fig. 1). One compartment was perfused by mixed venous blood and not ventilated; the other compartment was both perfused and ventilated. It was assumed that the partial pressures of oxygen and carbon dioxide in blood leaving the ventilated lung unit had equilibrated with the lung unit, and that metabolic oxygen consumption and carbon dioxide production by the lung tissue were negligible. The peripheral tissues were modelled as a single compartment, with oxygen consumption and carbon dioxide production determined by the model. Tissue metabolism was modelled in two different ways. In the “constant metabolism” version of the model, $P_{O_2}$ was set at 250 ml (STPD)/min and $P_{CO_2}$ was set at 200 ml (STPD)/min. These values were maintained constant. In the “constant $P_{O_2}$” version, $P_{O_2}$ was maintained constant as might occur when tissue utilization of oxygen is limited by oxygen delivery, and the respiratory quotient was maintained constant at 0.8.

Pulmonary gas exchange was examined by calculating alveolar, arterial and mixed venous partial pressures and contents of oxygen and carbon dioxide for a range of input variables. The input variables $P_{O_2}$, $P_{CO_2}$, $P_{O_2}$, $Q$ and $\dot{Q}_d/\dot{Q}_t$ (and $P_{CO_2}$ in the constant $P_{O_2}$ model) were specified and held constant during each set of calculations. In the model, $P_{O_2}$ is defined as the partial pressure of oxygen necessary to saturate haemoglobin at pH 7.4, $P_{CO_2}$ 5.33 kPa and 37 °C.

Animal models have suggested that orthodox mechanical ventilation during acute respiratory distress syndrome (ARDS), with high peak inspiratory pressures, may result in additional lung injury and possibly remote organ dysfunction. Low volume ventilation with permissive hypercapnia may avoid this ventilator-induced lung injury. However, it has been suggested that the rightward shift of the oxygen-haemoglobin dissociation curve caused by hypercapnia may be detrimental in ARDS, as arterial oxygen content may be reduced more than venous oxygen unloading is facilitated. A theoretical mathematical model was developed to investigate the effects of hypercapnia on pulmonary gas exchange in lungs with high levels of intrapulmonary shunt.

C. J. Joyce*, MB, CHB, PhD, FANZCA, FPICANZCA, K. G. Hickling†, MB, CHB, FANZCA. Department of Intensive Care, Christchurch Public Hospital, Christchurch, New Zealand. Accepted for publication: July 14, 1996.

Present addresses:

*Department of Intensive Care, Princess Alexandra Hospital, Ipswich Rd, Woolloongabba, Brisbane, QLD 4102, Australia.
†Intensive Care Unit, Queen Elizabeth Hospital, 30 Gascoigne Rd, Kowloon, Hong Kong.
MATHEMATICAL ANALYSIS

When the input variables were specified, there was a unique set of alveolar, arterial and mixed venous partial pressures and contents of oxygen and carbon dioxide that satisfied the constraints of a particular version of the model. Thus

\[ \text{alveolar pO}_2 \text{,

arterial pO}_2 \text{, mixed venous pO}_2 \text{, and pCO}_2 \text{ are uniquely determined.}\]

To simplify calculations in the program, this was re-expressed as

\[ \text{alveolar pO}_2 \text{,}

arterial pO}_2 \text{, mixed venous pO}_2 \text{, and pCO}_2 \text{ are uniquely determined.}\]

As the other variables in this function are specified and held constant, this function can be solved for \( \text{alveolar pO}_2 \text{ using the false position method.}\) This method uses a trial value of \( \text{alveolar pO}_2 \text{ and calculates the corresponding value of arterial pO}_2 \text{. Then,}

this information is used to generate a better estimate of \( \text{alveolar pO}_2 \text{ with iteration until the desired precision is obtained.\ Template:ref\)\)

Details of the model equations are in appendix 1.

Both the constant metabolism model and the constant \( \text{PvO}_2 \text{ model were used to study scenarios with \( P_{\text{O}_2} \text{ = 3.57 kPa,\}}

over a range of \( Q \text{ values from 2.5 to 10 litre min}^{-1}.\}

In the constant \( \text{PvO}_2 \text{ model, a range of \( P_{\text{O}_2} \text{ values from 1.33 to 8.00 kPa were studied. In the constant metabolism model, a range of \( P_{\text{O}_2} \text{ from 2.45 to 3.57 kPa, and the effect of varying \( Q \text{ as a function of } \text{PacO}_2 \text{ were studied (see appendix 2). The programs performing these analyses were written using Think Pascal (Symantec) and run on a Macintosh Centris.\)\)\)

Results

CONSTANT METABOLISM MODEL

The effect on oxygen carriage, of increasing \( P_{\text{acO}_2} \text{, when other input variables are held constant, is shown in figure 2. As } P_{\text{acO}_2} \text{ increases, there is a linear decrease in } P_{\text{acO}_2} \text{ caused by increasing } P_{\text{acO}_2}.\)

This has minimal effect on \( \text{Co}_2 \text{, and hence } C_{\text{aCO}_2} \text{, and } C_{\text{VCO}_2}, P_{\text{CO}_2} \text{, and } P_{\text{PVCO}_2} \text{ are readily calculated. Details of the model equations are in appendix 1.}\)

Both the constant metabolism model and the constant \( P_{\text{vO}_2} \text{ model were used to study scenarios with } P_{\text{O}_2} = 3.57 \text{kPa, over a range of } Q \text{ values from 2.5 to 10 litre min}^{-1}, \text{PacO}_2 \text{ from 1.33 to 94.64 kPa, } P_{\text{vO}_2} \text{ from 0.21 to 1.0 and Qs/Qt from 0.05 to 0.8. In the constant } P_{\text{vO}_2} \text{ model, a range of } P_{\text{vO}_2} \text{ values from 1.33 to 8.00 kPa were studied. In the constant metabolism model, a range of } P_{\text{vO}_2} \text{ from 2.45 to 3.57 kPa, and the effect of varying } Q \text{ as a function of } P_{\text{acO}_2} \text{ were studied (see appendix 2). The programs performing these analyses were written using Think Pascal (Symantec) and run on a Macintosh Centris.\)\)

\[ Figure 1 \text{ A model of the effect of hypercapnia on gas exchange.} \]

\[ Figure 2 \text{ Constant metabolism model: effects of } P_{\text{acO}_2} \text{ on } P_{\text{acO}_2}. \text{ Changes in } P_{\text{acO}_2} \text{ with } P_{\text{acO}_2} \text{ for the constant metabolism model, for Qs/Qt of 0.5. Each line of the diagram represents one } P_{\text{acO}_2} \text{. Lines from top to bottom are for } P_{\text{acO}_2} \text{ = 1.0, 0.9, 0.8, 0.7, 0.6, 0.5, 0.4, 0.3 and 0.2. Other input settings were } P_{\text{O}_2} = 3.57 \text{kPa and } Q = 5 \text{ litre min}^{-1}.\)

\[ Figure 3 \text{ Constant metabolism model: effect of } P_{\text{acO}_2} \text{ and } P_{\text{vO}_2} \text{ on } P_{\text{acO}_2}. \text{ Changes in } P_{\text{acO}_2} \text{ with } P_{\text{acO}_2} \text{ for the constant metabolism model, for Qs/Qt of 0.5. Each line of the diagram represents one } P_{\text{acO}_2} \text{. Lines from top to bottom are for } P_{\text{acO}_2} \text{ = 1.0, 0.9, 0.8, 0.7, 0.6, 0.5, 0.4, 0.3 and 0.2. Other input settings were } P_{\text{O}_2} = 3.57 \text{kPa and } Q = 5 \text{ litre min}^{-1}.\)\)
decrease. The $P_{\text{a}CO_2}$ at which this threshold is reached varies with $F_{\text{IO}_2}$. The pattern of change in $P_{\text{a}O_2}$ as $P_{\text{a}CO_2}$ increases is different with low $Qs/Qt$ values (0.05 or 0.1) when $P_{\text{a}O_2}$ decreases in a similar manner to $P_{\text{a}O_2}$ (see fig. 4). With low values of $Qs/Qt$ the reduction in dissolved oxygen in blood leaving the ventilated lung compartment more than offsets the effect on $P_{\text{a}O_2}$ of the right shifted oxygen–haemoglobin dissociation curve, because the ventilated compartment represents most of the lung. With $Qs/Qt = 0$, $P_{\text{a}O_2}$ is identical to $P_{\text{a}O_2}$.

Figures 5 and 6 show the changes in $P_{\text{a}O_2}$ over a

range of $P_{\text{a}CO_2}$. For all $Qs/Qt$ $P_{\text{a}O_2}$ increases as $P_{\text{a}CO_2}$ increases, provided that $F_{\text{IO}_2}$ is adequate to maintain $P_{\text{a}O_2}$ above the threshold level for haemoglobin desaturation (fig. 6). If $F_{\text{IO}_2}$ is not adequate, then the threshold level for haemoglobin desaturation is exceeded within the clinical range of $P_{\text{a}CO_2}$ and $P_{\text{a}O_2}$ decreases (fig. 5).

A similar pattern of results was seen with $P_{\text{so}}$ values of 2.45 and 3.05 kPa. A lower $P_{\text{so}}$ resulted in lower $P_{\text{a}O_2}$ at a given $P_{\text{a}CO_2}$, when the other variables were held constant. With an $F_{\text{IO}_2}$ of 0.6, $Qs/Qt$ of 0.5 and $Q$ of 5 litre min$^{-1}$, at any given $P_{\text{a}CO_2}$ in the range 0–20 kPa, the $P_{\text{a}O_2}$ result for $P_{\text{so}}$ of 2.45 kPa was 69–71% of the $P_{\text{a}O_2}$ result for a $P_{\text{so}}$ of 3.57 kPa.
Similar results were seen with $\dot{Q}$ values of 2.5 and 10 litre min$^{-1}$. A lower $\dot{Q}$ resulted in lower $P_{aCO_2}$ and $P_{VO_2}$ at a given $P_{aCO_2}$, when the other variables were held constant. When $\dot{Q}$ was varied as a function of $P_{aCO_2}$, the pattern was different (fig. 7). Relatively small changes in $\dot{Q}$ (20% decrease in $\dot{Q}$ for a doubling in $P_{aCO_2}$) virtually abolished any increase in $P_{VO_2}$ with increasing $P_{aCO_2}$, and marked decreases in $P_{VO_2}$ were seen within the range of $P_{aCO_2}$ used clinically during low volume ventilation with permissive hypercapnia ($P_{aCO_2}$ of 5.33–20 kPa).

Hypocapnia consistently made gas exchange worse. In all the scenarios modelled, $P_{VO_2}$ decreased as $P_{aCO_2}$ decreased to less than 5.3 kPa. When the shunt fraction was high, $P_{aCO_2}$ also decreased (fig. 4).

![Figure 8](image1)

**Figure 8** Constant $P_{VO_2}$ model: effects of $P_{aCO_2}$. Input variables are $P_{aCO_2} = 0.6, \dot{Q}/\dot{Q}t = 0.5, P_a = 3.57, \dot{Q} = 5$ litre min$^{-1}$ (as in fig. 2) and $P_{VO_2} = 2.67$. In this figure (and fig. 2) the range of $P_{aCO_2}$ is 0–50 kPa, while in all other figures only the clinical range of 0–20 kPa is shown.

![Figure 9](image2)

**Figure 9** Constant $P_{VO_2}$ model: effect of $P_{aCO_2}$ and $P_{VO_2}$ on $V_{O_2}$. Changes in $V_{O_2}$ with $P_{aCO_2}$ for the $P_{VO_2}$ model, for $\dot{Q}/\dot{Q}t$ of 0.5. Each line of the diagram represents one $P_{VO_2}$. Lines from top to bottom are for $P_{VO_2}$ 1.0, 0.9, 0.8, 0.7, 0.6, 0.5, 0.4, 0.3 and 0.2. Other input settings were $P_a = 3.57$ kPa, $\dot{Q} = 5$ litre min$^{-1}$ and $P_{VO_2} = 2.67$.

![Figure 10](image3)

**Figure 10** Constant $P_{VO_2}$ model: effect of $P_{aCO_2}$ and $\dot{Q}/\dot{Q}t$ on $V_{O_2}$. Changes in $V_{O_2}$ with $P_{aCO_2}$ for the constant $P_{VO_2}$ model, for $P_{aCO_2}$ of 0.6. Each line on the diagram represents one $\dot{Q}/\dot{Q}t$. Lines from top to bottom are for $\dot{Q}/\dot{Q}t$ 0.05, 0.1, 0.2, 0.3, 0.4, 0.5, 0.6 and 0.7. Other input settings were $P_a = 3.57$ kPa, $\dot{Q} = 5$ litre min$^{-1}$ and $P_{VO_2} = 2.67$.

**CONSTANT $P_{VO_2}$ MODEL.**

The effect on $V_{O_2}$ and oxygen carriage of increasing $P_{aCO_2}$ when other input variables are held constant is shown in figure 8. The increase in $P_{aCO_2}$ produced an increase in $P_{VO_2}$. The model defines $P_{VO_2}$ as constant, so $C_{VO_2}$ decreases as the increasing $P_{VO_2}$ shifts the dissociation curve to the right. As $P_{aCO_2}$ increases, there is a linear decrease in $P_{aO_2}$ caused by increasing $P_{aCO_2}$. This has minimal effect on $C_{aO_2}$, until $P_{aO_2}$ decreases below a threshold level and desaturation of haemoglobin in blood leaving the ventilated lung compartment begins. $C_{aO_2}$ is determined by mixing of constant proportions of blood with $C_{CO_2}$ and $C_{VO_2}$. Up to the threshold point, $C_{CO_2}$ is relatively constant. Thus as $C_{VO_2}$ decreases, $C_{aO_2}$ also decreases but not to the same extent as $C_{VO_2}$. The difference between $C_{aO_2}$ and $C_{VO_2}$ widens and hence $V_{O_2}$ increases. Another effect of the widening difference between $C_{aO_2}$ and $C_{VO_2}$ as $P_{aCO_2}$ increases is that with similar increases in $P_{aCO_2}$ in both arterial and venous blood, and hence similar rightward shift of the two dissociation curves, the difference between $P_{aO_2}$ and $P_{aCO_2}$ also increases, and $P_{aO_2}$ must increase as $P_{aCO_2}$ is held constant. Beyond the threshold point, $V_{O_2}$, $P_{aCO_2}$, $C_{aCO_2}$ and $P_{aO_2}$ decrease. The pattern of change in $P_{aO_2}$ as $P_{aCO_2}$ increases is different with low $\dot{Q}/\dot{Q}t$ when $P_{aO_2}$ decreases in a similar manner to $P_{aCO_2}$.

Figures 9 and 10 show the changes in $V_{O_2}$ over a range of $P_{aCO_2}$. For all $\dot{Q}/\dot{Q}t$, $V_{O_2}$ increases as $P_{aCO_2}$ increases, provided that $P_{aCO_2}$ is adequate to maintain $P_{aO_2}$ above the threshold level for haemoglobin desaturation (fig. 10). If $P_{aO_2}$ is not adequate, then the threshold level for haemoglobin desaturation is exceeded within the clinical range of $P_{aCO_2}$, and $V_{O_2}$ decreases (fig. 9).

A similar pattern of results was seen with $P_{VO_2}$ set
at 1.33, 4.00 or 5.33 kPa, and with \( P_{\text{CO}_2} \) values of 2.45 and 3.05 kPa. A lower \( P_{\text{CO}_2} \) resulted in a higher \( V_b \) when the other input variables were unchanged. The greatest improvement in \( V_b \) occurred when \( P_{\text{CO}_2} \) was high. With \( P_{\text{CO}_2} \) of 1.33 kPa there was a minimal decrease in \( V_b \) when \( P_{\text{CO}_2} \) increased to greater than 17 kPa. A lower \( P_{50} \) resulted in a lower \( V_b \), for any given \( P_{\text{CO}_2} \). As can be predicted from the equations of the model, any increase in \( Q \) simply increased \( V_b \) by the same factor.

As with the constant metabolism model, hypocapnia consistently made gas exchange worse. In all scenarios modelled, \( V_b \) decreased as \( P_{\text{CO}_2} \) decreased to less than 5.3 kPa.

**Discussion**

It has been suggested that a rightward shift of the dissociation curve may be detrimental in ARDS, because reduction of arterial oxygen content may more than offset the amount by which venous oxygen unloading is facilitated.\(^2\) In a pig model of hypoxaemia caused by low inspired oxygen concentration, and hypocapnia produced by high inspired carbon dioxide concentration, arterial oxygen content was increased and mortality reduced when acidosis was partially corrected by buffering. It was postulated that buffering had reduced the right shift of the dissociation curve thus improving pulmonary oxygen uptake.\(^2\) In rats breathing air at reduced atmospheric pressure, survival was improved with a left-shifted oxygen dissociation curve.\(^4\) A theoretical study suggested that a left shift of the oxygen dissociation curve may improve exercise tolerance at high altitude, if diffusion limitation of oxygen uptake is present.\(^3\) However, these studies examined the response to alteration in \( P_{50} \) with hypocapnia caused by low \( P_{\text{CO}_2} \). In this situation it is the low \( P_{\text{CO}_2} \), which limits oxygen uptake by pulmonary blood flow and determines \( P_{\text{O}_2} \). A right-shifted dissociation curve then results in decreased arterial oxygen content at this limited \( P_{\text{O}_2} \) and is thus potentially detrimental. Hypocapnia has an additional detrimental effect in that it further decreases \( P_{\text{O}_2} \).

In contrast, when hypoxaemia results from intrapulmonary shunt, \( P_{\text{O}_2} \) in ventilated lung remains high even with moderately high \( P_{\text{CO}_2} \) provided that the inspired oxygen concentration is sufficiently high. Under these conditions, blood leaving the ventilated lung compartment is fully saturated, and arterial oxygen content is determined by the shunt fraction and venous oxygen content. The effect of a right-shifted dissociation curve is then to increase \( P_{\text{O}_2} \) associated with this predetermined arterial oxygen content. If cardiac output and oxygen consumption do not change, then mixed venous oxygen content is unaltered and \( P_{\text{O}_2} \) also increases. Our mathematical model confirms that in patients with pure intrapulmonary shunt causing hypoxaemia who are receiving a sufficiently high inspired oxygen concentration to ensure full saturation of the pulmonary blood flow in the ventilated lung compartment, and with other variables remaining constant, acute hypocapnia should result in an increase in \( P_{\text{O}_2} \) and \( P_{\text{O}_2} \) with little change in arterial and mixed venous oxygen contents. If the increase in \( P_{\text{O}_2} \) allows greater oxygen uptake into hypoxic tissues, this could theoretically increase tissue oxygen utilization, and the model predicts that potentially important increases could result. Our model suggests that reversing the rightwards shift of the dissociation curve by buffering may be detrimental to gas exchange.

In reality the situation is more complex, and several of the variables which were assumed to remain constant in this model may alter in patients with ARDS during low volume ventilation with permissive hypercapnia. Alterations in cardiac output affect gas exchange. Acute hypercapnia depresses the contractility of isolated myocardium,\(^6\) although this is compensated rapidly during sustained hypercapnia, as a result of correction of intracellular acidosis.\(^7\) In vivo, decreased contractility is offset by increased sympathetic stimulation, and cardiac output increases.\(^8\) Recent studies of patients with ARDS have found that cardiac output increased in all patients during low volume ventilation with permissive hypercapnia.\(^8\)–\(^11\)

The shunt fraction may also be affected by several factors during low volume ventilation with permissive hypercapnia, including changes in mean airway pressure,\(^12\) changes in cardiac output\(^13\)\(^14\) and direct or autonomically mediated effects on the pulmonary vasculature or the airways.

Our model assumes that either oxygen consumption or carbon dioxide production is constant or limited by the lowest \( P_{\text{O}_2} \), at which tissues can extract oxygen, but it is likely that acute hypercapnia has important metabolic effects. The resulting intracellular acidosis alters the activity of several enzymes, for example phosphofructokinase. Conversely, increased sympathetic activity and increased endogenous catecholamine concentrations may increase metabolic rate and \( V_b \).

Buffering may be detrimental to gas exchange by reversing the rightwards shift of the dissociation curve and by inhibiting the potentiation of hypoxic pulmonary vasoconstriction caused by acidosis.\(^15\) The metabolic compensation that occurs during prolonged hypercapnia shifts the curve to the left and worsens gas exchange.

Several studies have demonstrated that in patients with ARDS, hypoxaemia appears to be predominantly a result of intrapulmonary shunt,\(^16\) and therefore the findings of this study should be applicable to such patients. However, there is some variability in the proportion of intrapulmonary shunt and \( V_b/Q \) inequality between patients, and in those with a substantial proportion of low \( V_b/Q \) regions the model is inaccurate. Another limitation of this study is that the Kelman subroutines used to calculate oxygen contents and tensions have been validated only up to a \( P_{\text{CO}_2} \) value of 20 kPa.\(^17\) While the results at higher partial pressures are inaccurate, the results are valid over the range of \( P_{\text{CO}_2} \) values used in clinical practice.

The constant \( P_{\text{CO}_2} \) model examines the situation where oxygen delivery to the tissues is inadequate, so that oxygen extraction from the blood down to a
limiting level of $P_{\text{O}_2}$. Below a $P_{\text{CO}_2}$ value of 2.67 kPa tissue oxygenation may be inadequate for cellular function. Our data show the level of oxygen consumption that can be supported at this $P_{\text{O}_2}$ value. Patients with ARDS and sepsis often have high oxygen consumption, and it has been suggested that even with normal values for oxygen delivery, oxygen uptake may be limited by its delivery to the tissues.\textsuperscript{18}

Thus the physiological consequences and interactions after the reduction of ventilatory support and onset of hypercapnia are extremely complex, and may vary substantially between patients. Further studies of the effects of hypercapnia are needed. However, this study suggests that the effect of the right-shifted dissociation curve per se in patients with ARDS is likely to be beneficial rather than detrimental.

Appendix 1

**MODEL EQUATIONS**

Procedure used for calculating $F_{\text{I}_{\text{CO}_2}}$ for a trial value of $P_{\text{CO}_2}$

1. $C_{\text{O}_2}$ and $C_{\text{O}_3}$ are calculated from $P_{\text{O}_2}$ and the trial value of $P_{\text{CO}_2}$ using West’s modifications of Kelman’s subroutines.\textsuperscript{17,19–21}

2. In the “constant metabolism” version of the model

$$C_{\text{O}_2} \text{ and } C_{\text{O}_3} \text{ are calculated by}
C_{\text{O}_2} = C_{\text{O}_2}^0 + (\bar{V}_{\text{CO}_2} / \bar{Q})
C_{\text{O}_3} = C_{\text{O}_2}^0 - (\bar{Q}_2 / \bar{Q})
$$

In the “constant $P_{\text{CO}_2}$” version of the model

As $C_{\text{O}_2}$, $C_{\text{O}_3}$, and $P_{\text{O}_2}$ are known, there is a unique set of $P_{\text{CO}_2}$, $C_{\text{O}_2}$, and $C_{\text{O}_3}$ that will satisfy the constraint of the model that $RQ = 0.8$

where $RQ = (C_{\text{O}_2} - C_{\text{O}_3}) / (C_{\text{O}_2} - C_{\text{O}_3})$. Thus $RQ = f(P_{\text{CO}_2})$, and $P_{\text{CO}_2}$ is solved by the false position method. $C_{\text{O}_2}$ and $C_{\text{O}_3}$ are calculated from $P_{\text{O}_2}$ and $P_{\text{CO}_2}$ using Kelman’s subroutines.

3. The $O$ contents of carbon dioxide and oxygen in blood equilibrated with the ventilated compartment are calculated by

$$C_{\text{O}_2} = C_{\text{O}_2}^0 - C_{\text{O}_2} \times \bar{Q}_{\text{O}_2} / \bar{Q} = C_{\text{O}_2}^0 - \bar{Q}_{\text{O}_2}$$

4. $P_{\text{CO}_2}$ and $P_{\text{O}_3}$ are calculated from $C_{\text{O}_2}$ and $C_{\text{O}_3}$ using Kelman’s subroutines and the false position method.

5. $F_{\text{I}_{\text{CO}_2}}$ is calculated by

$$F_{\text{I}_{\text{CO}_2}} = (P_{\text{O}_2} + (P_{\text{CO}_2} / RQ)) / (P_{\text{O}_2} - (P_{\text{O}_2} - (P_{\text{O}_2} / RQ) (1 - RQ)))$$

(This equation was derived by algebraic manipulation of the alveolar gas equation).

Constants used in these calculations were haemoglobin = 15 g dl$^{-1}$, packed cell volume = 0.45, base excess = 0 mmol litre$^{-1}$, temperature = 37.0°C, PB = 101.3 kPa, $SVP_{\text{O}_2}$ = 6.26 kPa, $RQ = 0.8$.

Final calculations

When the solution for $P_{\text{CO}_2}$ for the specified value of $F_{\text{I}_{\text{CO}_2}}$ has been found, then $C_{\text{O}_2}$, $C_{\text{O}_3}$, $C_{\text{O}_2}$, $C_{\text{O}_2}$, $C_{\text{O}_3}$, and $P_{\text{O}_2}$ and $P_{\text{CO}_2}$ are calculated as above in steps 1 to 4. $P_{\text{O}_2}$ and $P_{\text{CO}_2}$ are calculated from $C_{\text{O}_2}$ and $C_{\text{O}_3}$ using Kelman’s subroutines and the false position method.

Appendix 2

**METHOD OF VARYING $\bar{Q}$ AS A FUNCTION OF $P_{\text{CO}_2}$**

The effect of varying $\bar{Q}$ as a function of $P_{\text{CO}_2}$ was investigated. Calculations of the constant metabolism model were followed, except that the $\bar{Q}$ to be used with the other input variables was calculated from the $P_{\text{CO}_2}$, by the equation

$$\bar{Q} = \bar{Q}_{5.33} \Theta (\log(P_{\text{CO}_2} / 5.33))$$

where $\bar{Q}_{5.33}$ is cardiac output at $P_{\text{CO}_2} = 5.33$ kPa and is set at 5 litre min$^{-1}$. This equation produces an increase in $\bar{Q}$ by a factor of $\Theta$ for each doubling of $P_{\text{CO}_2}$. Thus $\bar{Q}_{5.33} = 5$ litre min$^{-1}$, $\bar{Q}_{10.66} = 50$ litre min$^{-1}$, and $\bar{Q}_{21.32} = 500$ litre min$^{-1}$ Values of $\Theta$ examined were 0.8, 1.0 and 1.2.

References


