A tidal ventilation model for oxygenation in respiratory failure

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Abstract

We develop tidal-ventilation pulmonary gas-exchange equations that allow pulmonary shunt to have different values during expiration and inspiration, in accordance with lung collapse and recruitment during lung dysfunction [Am. J. Respir. Crit. Care Med. 158 (1998) 1636]. Their solutions are tested against published animal data from intravascular oxygen tension and saturation sensors. These equations provide one explanation for (i) observed physiological phenomena, such as within-breath fluctuations in arterial oxygen saturation and blood-gas tension; and (ii) conventional (time averaged) blood-gas sample oxygen tensions. We suggest that tidal-ventilation models are needed to describe within-breath fluctuations in arterial oxygen saturation and blood-gas tension in acute respiratory distress syndrome (ARDS) subjects. Both the amplitude of these oxygen saturation and tension fluctuations, and the mean oxygen blood-gas values, are affected by physiological variables such as inspired oxygen concentration, lung volume, and the inspiratory:expiratory (I:E) ratio, as well as by changes in pulmonary shunt during the respiratory cycle.

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1. Introduction

There is a significant amount of published physiological experimental evidence of within-breath variations in arterial oxygen saturation and tension that cannot be explained by conventional mathematical models of the lung where pulmonary shunt is constant.

Bergman (1961) reported within-breath cyclical fluctuations in arterial oxygen saturation, \( \text{SaO}_2 \), in an experimental dog (open chest) model when breathing room air. These cyclical variations could be measured in the femoral artery when the mean \( \text{SaO}_2 \) was on the ‘steep’ part of the oxyhaemoglobin dissociation curve, and were at the same frequency as the applied positive pressure ventilation. Changing the ventilation rate and/or the end-expired lung volume varied their amplitude. However, on application of sufficient positive end expired pressure (PEEP) such that the arterial haemoglobin became more fully saturated, the \( \text{SaO}_2 \) oscillations disappeared. Bergman considered

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that the $\text{SaO}_2$ oscillations might be caused either by changes in pulmonary shunt or alveolar volume during the respiratory cycle. Pulmonary lung dysfunction was not deliberately induced in Bergman's studies. Table 1 shows a selection of five animal results (breathing room air) extracted from his work. We have drawn in Fig. 1 a stylised (square wave) plot of $\text{SaO}_2$ (for subject 14 from Bergman's work) over two ventilator cycles. In this plot, measured $\text{SaO}_2$ varies from 79% during inspiration to 59% during expiration, at the given respiratory rate of 5 min$^{-1}$ (Bergman, 1961). We have assumed a typical inspiratory to expiratory ratio (I:E) of 1:2 although this was not quoted in the original work. Fig. 2 shows the amplitude of these $\text{SaO}_2$ oscillations superimposed on the mean (time-averaged) $\text{SaO}_2$, and mean $\text{PaO}_2$ point, on a standard oxyhaemoglobin dissociation curve. The inspired and expired $\text{PaO}_2$ values correspond to the measured $\text{SaO}_2$ minimum and maximum excursions. Fig. 2 also shows the $\text{SaO}_2$ value (marked as a single point because the amplitude oscillation was minimal in this instance) recorded by Bergman after the imposition of 3–4 cmH$_2$O PEEP.

Within-breath fluctuations, or oscillations, in arterial oxygen tension, $\text{PaO}_2$, were later reported by Purves (1966) and then by Folgering et al. (1978), again in animal models of the healthy lung when breathing room air or high concentrations of oxygen. However, both these sets of workers, unlike Bergman, had access to very fast $\text{P}O_2$ sensors. Folgering et al. (1978) used a miniature intravascular sensor with a time response of less than 1 sec, and recorded $\text{PaO}_2$ oscillations up to an amplitude of 45 mmHg. Purves (1966) used a much larger ex-situ sensor, with a similar response time, inserted into an extra corporeal arterial loop. Both groups reported that large $\text{PaO}_2$ oscillations could be observed at the ventilator frequency, with amplitudes that depended upon the mean $\text{PaO}_2$, the respiration rate, the tidal volume, and the application of PEEP.

Williams et al. (2000) have shown, in an animal model of Acute Respiratory Distress Syndrome (ARDS) and using slower (2–4 sec response time) commercial prototype intravascular $\text{P}O_2$ sensors (IE Sensors Inc, Salt Lake City, UT, USA), that $\text{PaO}_2$ oscillations could be measured in the femoral artery when the lung became atelectatic. They

<table>
<thead>
<tr>
<th>Dog</th>
<th>Inspiration</th>
<th>Expiration</th>
<th>Mean $\text{PaO}_2$ (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$\text{SaO}_2$ (%)</td>
<td>with PEEP (%)</td>
<td>$\text{SaO}_2$ (%)</td>
</tr>
<tr>
<td>9</td>
<td>82</td>
<td>87</td>
<td>73</td>
</tr>
<tr>
<td>12</td>
<td>80</td>
<td>93</td>
<td>71</td>
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<td>14</td>
<td>79</td>
<td>92</td>
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<td>17</td>
<td>88</td>
<td>92</td>
<td>75</td>
</tr>
<tr>
<td>22</td>
<td>81</td>
<td>90</td>
<td>69</td>
</tr>
</tbody>
</table>

$\text{SaO}_2$ and $\text{PaO}_2$ are arterial oxygen saturation and tension, respectively.
reported that the slow response of the sensor would have attenuated the amplitude of the true PaO2 oscillations considerably, perhaps by a factor of three (Williams et al., 2000). However, the time-averaged mean PaO2 value of their recordings agreed with the ‘blood-gas’ value recorded from a conventional blood sample. This work has been confirmed recently in a report by Baumgardner et al. (2002) who used fast fibre optic PaO2 probes in a rabbit model of lung lavage to record PaO2 oscillations with an average maximum amplitude of 390 ± 39 mmHg.

In this study we show that a tidal ventilation model can simulate these experimental observations, and we use this model to predict the effects of various ventilator settings on the PaO2 oscillations. The key to this particular explanation is to use a mathematical model that allows pulmonary shunt to vary between inspiration and expiration, a physiological phenomenon that is apparent from Neumann et al. (1998) computed lung tomography (CT) scans in animal models of ARDS.

2. Methods

In this section, we use a tidal-ventilation lung model of gas exchange for oxygen (described in Appendix A) that can not only simulate respiratory PaO2 oscillations, but can also reveal how the inspiratory:expiratory (I:E) ratio can affect the magnitude of the conventional time averaged blood-gas PaO2 values when FIO2 remains constant. The key to simulating PaO2 oscillations is to have a pulmonary shunt fraction that can vary with time, following the report of Neumann et al. (1998) that atelectasis follows a cyclical pattern during respiration. We assume in this study, for simplicity, that the pulmonary shunt takes a constant value during inspiration and another (different) constant value during expiration. The model could of course be used conventionally with shunt taking the same constant value during the respiratory cycle.

Fig. 2. The peak-to-trough (inspiration to expiration) oxygen saturation amplitude seen in Bergman’s data (subject 14) imposed onto the oxyhaemoglobin dissociation curve. The corresponding within-breath oxygen tension amplitude (ΔPaO2) is also shown. The point where the saturation and tension amplitudes cross the dissociation curve defines the conventional mean oxygen saturation and tension values. The upper solid point corresponds to the experimental arterial oxygen saturation and tension obtained when 3–4 cmH2O PEEP was imposed.

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moglobin oxygen content–partial pressure relationship (Kelman, 1986).

A large number of combinations of physiological parameters could be examined, but only a limited number are considered here. In the simulations, unless otherwise stated, lung volume was 2.4 L (for reasons given below), tidal volume was 0.5 L, cardiac output was 5 L min$^{-1}$, and dead-space volume was 0.15 L. For ‘normal’ ventilation, the inspiratory time was 1.67 sec and expiratory time was 3.33 sec, corresponding to an I:E ratio of 1:2 and a respiration rate of 12 breaths min$^{-1}$. For ‘inverse ventilation’, the I:E ratio was changed to 2:1, at the same respiratory rate. Shunt fraction was either kept constant during the whole respiratory cycle (the conventional approach) or was allowed to vary between two different values during the separate inspiratory and expiratory ventilator phases. Oxygen consumption was fixed at 250 ml min$^{-1}$.

3. Results

3.1. Variations in physiological parameters

3.1.1. End-expired alveolar volume

The effect of changing end-expired alveolar volume, $V_A$, on the time-averaged $P_{A\text{O}_2}$ was examined in the absence of any significant shunt, when all other parameters were kept constant. As expected, there was no noticeable effect on $P_{A\text{O}_2}$ until $V_A$ fell below 0.5 L, when the model predicted that the mean $P_{A\text{O}_2}$ fell very steeply. Alveolar volume does not, therefore, play a major role in determining the magnitude of the mean $P_{A\text{O}_2}$ in our model and was set at 2.4 L in the following sections.

3.1.2. Constant shunt fraction

We begin by considering a lung that has the same shunt fraction, $\dot{Q}_s/\dot{Q}_t$, during both inspiration and expiration. This is the conventional view of shunt. When the constant shunt fraction was 0.02 and the inspired oxygen concentration was 21 and 50%, simulations showed that the variations in $P_{A\text{O}_2}$ and $P_{A\text{O}_2}$ were less than 5 mmHg in both cases.

Fig. 3 shows the plots of $P_{A\text{O}_2}(t)$ and $P_{A\text{O}_2}(t)$ over the course of two whole breaths, together with the time-averaged blood-gas $P_{A\text{O}_2}$, for inspired oxygen concentrations of 21 and 50%. In both examples, shunt fraction was 0.2 throughout.

Fig. 3. (a) Inspired oxygen is 21%; in (b) inspired oxygen is 50%.
the respiratory cycle. Here, the solid line is \( P_{A02}(t) \), the broken line is \( P_{A02}(t) \), and the dotted line is the mean \( P_{A02} \) of a blood sample, drawn over a complete breath, i.e. the conventional blood-gas \( P_{A02} \) analysis, time averaged over a whole breath (5 sec). The alveolar \( P_{O2} \) oscillations, \( \Delta P_{A02} \), are almost identical to those when the shunt fraction was 0.02, and so \( \Delta P_{A02} \) is little affected by the magnitude of a prevailing constant pulmonary shunt fraction. However, the arterial \( P_{O2} \) oscillation amplitude, \( \Delta P_{A02} \), is reduced by the increase in shunt and is less than 1 mmHg. As expected, the difference between the mean \( P_{A02} \) and \( P_{A02} \) values (the conventional \( A \)–\( A \) difference) also greatly increases with increasing shunt.

3.1.3. Variable (within breath) shunt fraction

Fig. 4 considers the effect of allowing shunt fraction during inspiration, \( \dot{Q}_{SI}/\dot{Q}T \), and during expiration, \( \dot{Q}_{SE}/\dot{Q}T \), to take different values. The inspired oxygen concentration is set at 50% to simulate the human Intensive Care Unit (ICU) situation. In Fig. 4(a), \( \dot{Q}_{SI}/\dot{Q}T = 0.02 \) and \( \dot{Q}_{SE}/\dot{Q}T = 0.02 \); in Fig. 4(b), \( \dot{Q}_{SI}/\dot{Q}T = 0.02 \) and \( \dot{Q}_{SE}/\dot{Q}T = 0.2 \); in Fig. 4(c), \( \dot{Q}_{SI}/\dot{Q}T = 0.02 \) and \( \dot{Q}_{SE}/\dot{Q}T = 0.4 \); in Fig. 4(d), \( \dot{Q}_{SI}/\dot{Q}T = 0.1 \) and \( \dot{Q}_{SE}/\dot{Q}T = 0.6 \). As in Figs. 3 and 4, the solid line is \( P_{AO2}(t) \), the broken line is \( P_{AO2}(t) \), and the dotted line is the time averaged arterial \( P_{A02} \). Fig. 4 shows that both the mean alveolar \( P_{O2} \) and its oscillation amplitude are identical in each example shown. It is thus clear that the small alveolar \( P_{O2} \) amplitude cannot contribute to the generation of the magnitude of \( \Delta P_{A02} \). In sharp contrast, it is clear from Fig. 4 that, when \( \dot{Q}_{SI}/\dot{Q}T \) is no longer equal to \( \dot{Q}_{SE}/\dot{Q}T \), large variations in \( P_{AO2} \) can occur during the course of a breath. Fig. 4(c) and (d) shows an extreme case where simulated \( P_{AO2} \) varies by more than 250 mmHg over the course of a single breath. It is also clear from Fig. 4 that the time averaged arterial \( P_{O2} \) (i.e. the conventional blood-gas sample) is heavily weighted towards the expiratory phase \( P_{AO2}(t) \). This is due not only to the weighting effect of the I:E ratio, but also to the influence of the non-linear characteristic of the oxyhaemoglobin dissociation curve.

Taking Bergman’s Dog 14 data, illustrated in Figs. 1 and 2, a calculation reveals that an inspired shunt value of 34% and an expired shunt of 68%, in our model, will generate this data for a 21% inspired oxygen concentration (the normal inspired oxygen concentration used in Bergman’s studies).

Extrapolating this approach to human physiology, Table 2 illustrates the effects of some selected combinations of \( \dot{Q}_{SI}/\dot{Q}T \) and \( \dot{Q}_{SE}/\dot{Q}T \) on the mean arterial oxygen tension, concentration and saturation for a simulated ICU patient inspiring 50% oxygen. The table also shows the resulting conventional shunt for the simulated patient, and the Pa/Fi ratio, both calculated from the mean blood-gas values as if they were from patient blood-gas samples collected in normal clinical practice. The I:E ratio was 1:2 in each case. It is apparent from Table 2 that a Pa/Fi ratio of less than 150 mmHg, the conventional clinical definition for hypoxemia for a patient breathing high values of oxygen (Gilbert and Keighley, 1974; Gould et al., 1997), can be generated not only by a constant (conventional) shunt greater than 25%, but by a wide combination of different inspired and expired shunt fractions.

3.2. Dependence of \( P_{AO2} \) and \( \Delta P_{AO2} \) on the I:E ratio

It must be noted that the I:E ratio plays no part in the conventional continuous ventilation mathematical model (Nunn, 1993) of gas exchange, but its effect on the our tidal ventilation model is investigated below.

Fig. 5 is generated using exactly the same parameters as Fig. 4(c) with the exception that the I:E ratio is now 2:1 rather than 1:2. In Fig. 5, the solid line is \( P_{AO2}(t) \), the broken line is \( P_{AO2}(t) \), and the dotted line is the time averaged arterial \( P_{AO2} \). By comparing with Fig. 4(c), we see that the ‘inverse’ I:E ratio simulation has raised the time averaged arterial \( P_{O2} \) by 58 mmHg. Arterial \( P_{O2} \) has risen because inspiration now takes a greater proportion of the total breath cycle, and there is less shunt operating on arterial blood during inspiration.

In Fig. 6 we take this further. We use the same parameters that were used to generate Fig. 4(c), with the exception of the I:E ratio. In Fig. 6 we
We see that as the I:E ratio is increased, the mean PaO₂ increases considerably. However, simulating ΔPaO₂ against the I:E ratio showed that the magnitude of the PaO₂ oscillations rose only slightly by 3 mmHg.

4. Discussion

4.1. General comments on the model

The possibility that shunt fraction can vary with time over the respiratory cycle means that the
other model variables, and their interactions with each other, could produce an array of interrelated effects on the lung’s PaO₂ output signal. We have been deliberately selective in our choice of the parameters presented here, and have confined our attention to (i) two ventilatory variables over which the experimentalist has control, the I:E ratio and FIO₂; and (ii) selected physiological parameters such as lung volume and shunt fraction. The effects of time delays between the inspiratory wave form and the arterial P O₂ wave form; cardiac output variation; pulsatile blood flow; oxygen consumption; carbon dioxide production; ventilation–perfusion inhomogeneity etc. are not considered here.

We have simulated here the effects of controlled artificial ventilation on one of the lung’s main output signals, namely the time varying arterial PaO₂. In this work, we have imposed a flow generator pattern ventilation on the ‘patient’, and have concentrated on oxygen tension only.

Table 2
Simulated adult intensive care patient results for various combinations of inspired and expired shunt, with resulting mean PaO₂, mean C Ao₂, and mean SaO₂ values, and corresponding calculations of conventional shunt and Pa/Fi ratios

<table>
<thead>
<tr>
<th></th>
<th>Qs/Qt (%)</th>
<th>Qse/Qt (%)</th>
<th>PaO₂ (mmHg)</th>
<th>C Ao₂ (ml dl⁻¹)</th>
<th>SaO₂ (%)</th>
<th>Qs/Qt (%) conventional</th>
<th>Pa/Fi (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>2</td>
<td>2</td>
<td>300</td>
<td>17.9</td>
<td>99.7</td>
<td>1.7</td>
<td>600</td>
</tr>
<tr>
<td>B</td>
<td>2</td>
<td>5</td>
<td>267</td>
<td>17.8</td>
<td>99.7</td>
<td>3.8</td>
<td>534</td>
</tr>
<tr>
<td>C</td>
<td>2</td>
<td>10</td>
<td>211</td>
<td>17.6</td>
<td>99.5</td>
<td>7.4</td>
<td>422</td>
</tr>
<tr>
<td>D</td>
<td>10</td>
<td>20</td>
<td>104</td>
<td>17.0</td>
<td>97.7</td>
<td>16.8</td>
<td>208</td>
</tr>
<tr>
<td>E</td>
<td>15</td>
<td>30</td>
<td>71</td>
<td>16.3</td>
<td>94.2</td>
<td>25.4</td>
<td>142</td>
</tr>
<tr>
<td>F</td>
<td>20</td>
<td>50</td>
<td>51</td>
<td>15.9</td>
<td>85.8</td>
<td>40.2</td>
<td>102</td>
</tr>
<tr>
<td>G</td>
<td>30</td>
<td>60</td>
<td>43</td>
<td>14.9</td>
<td>77.9</td>
<td>50.2</td>
<td>86</td>
</tr>
</tbody>
</table>

Inspired oxygen concentration is 50% in all examples. PaO₂, C Ao₂ and SaO₂ are mean arterial oxygen tension, content and saturation, respectively. Qs/Qt and Qse/Qt are the given inspired and expired shunt fractions, respectively. Qs/Qt is the conventionally calculated shunt fraction. Fi is the inspired oxygen fractional concentration (0.5).
We have not considered the effects of pressure-controlled ventilation.

4.2. General discussion on the simulation results

Neumann et al. (1998) have already demonstrated, using sequential CT scans every 0.8 sec in an oleic acid animal model of ARDS, that cyclic collapse and recruitment of alveoli does occur during lung expiration and inspiration. Time constants for atelectasis formation during expiration averaged $0.86 \pm 0.67$ sec, and $0.69 \pm 0.54$ sec for recruitment during inspiration, with lung area demonstrating almost 40% atelectasis by the end of expiration even with 10 cmH\(2\)O PEEP. Therefore, lung tissue collapse and recruitment, although not ‘instantaneous’, appears to be fast enough for our simple mathematical model to be used to simulate reported physiology. Similarly, Baumgardner et al. (2002) argued that the large PaO\(_2\) oscillations measured in their studies provided compelling evidence for variations in shunt fraction throughout the respiratory cycle in their experiments.

Accordingly, the results presented in Figs. 3–6, and in Table 2, show that a single-alveolar compartment model of the lung (Appendix A), when adapted to take account of tidal volume, respiratory rate, I:E ratio and with shunt fraction varying between the inspiratory and expiratory phases, can simulate the SaO\(_2\) and PaO\(_2\) oscillations reported by the various experimental teams in animals (Bergman, 1961; Purves, 1966; Folgering et al., 1978; Williams et al., 2000; Baumgardner et al., 2002) and in humans (Goeckenjan, 1979; and authors quoted by Lovell et al., 1997) over the past 40 years. Of course, other mathematical models of ARDS may show the same outcome. However, this is, to the best of our knowledge, the first time that a relatively simple mathematical model has been used to simulate these particular experimental results.

Our simulations showed that a ‘normal healthy human’, with a residual shunt of a few percent, does not display any significant APaO\(_2\) oscillations at any FiO\(_2\) above room air. This suggests that the carotid body O\(_2\) sensors should normally see a stable O\(_2\) signal, with an essentially ‘constant’ value. ‘Steady state’ PaO\(_2\) conditions might, therefore, prevail in the healthy lung. The simulation confirmed this even when a 20% shunt, constant throughout the respiratory cycle, is imposed (Fig. 3). Thus, modelling human blood-gas exchange on the ‘fish gill model’ of constant gas and blood flow (Weibel, 1984; Erdmann, 1992) may appear to be valid in the healthy subject or in a patient with a constant pulmonary shunt fraction.

However, the studies of Neumann et al. (1998) suggest that a constant shunt situation does not occur in ARDS until high PEEP values circa 25 cmH\(2\)O are employed. So, the continuous ventilation theory has to be discarded when shunt fraction is allowed to vary between inspiration and expiration, as illustrated in the three examples shown graphically in Fig. 4 and, more fully, in Table 2.

4.3. Comparison with previous published results

Given the constraints described above, Fig. 4 illustrates one way that the results published by Bergman over 40 years ago (Bergman, 1961) could have been generated in his room air (and supplemental oxygen) breathing open chest animal studies. Although he had no access to a fast intravascular PaO\(_2\) sensor, he was able to use breath-by-breath changes in SaO\(_2\) as a surrogate for PaO\(_2\) until saturation began to reach the ‘plateau’ part of the oxyhaemoglobin dissociation curve. Our translation of his SaO\(_2\) results into changes in PaO\(_2\), varying over two respiratory cycles (Fig. 1), agrees well with the type of simulation depicted in Fig. 4.

Bergman (1961) noted that the lungs of his animals tended to collapse on expiration, and to open again during positive pressure ventilation. Furthermore, he reported that the imposition of PEEP prevented the collapse of the lung, with a concomitant rise in SaO\(_2\) during both inspiration and expiration. In the light of knowledge at that time, he did not concentrate on the hypothesis that atelectasis (and thus an inevitable increase in pulmonary shunt) was occurring during expiration (as described much later by Neumann et al., 1998), but focussed his attention on the reduction in lung volume per se during expiration. His preferred
hypothesis was that cyclical changes in alveolar volume were translated into cyclical variations in alveolar PaO₂, which, in turn, generated the arterial So₂ oscillations. He, therefore, did not appear to pursue the possibility that the inspired and expired pulmonary shunts were different in his animals, and were thus the most likely cause of his experimental SaO₂ results.

Fig. 4 shows quite clearly that changes in lung volume, creating alveolar P O₂ oscillations, cannot, in our model, be the cause of the large inspiratory–expiratory arterial P O₂ oscillations generated in our simulations. In each instance, the oscillations in alveolar P O₂ are very small and the conclusion from the simulation presented here is that it would take a catastrophic fall in alveolar volume for PaO₂ oscillations to make an impact on the arterial P O₂ oscillations.

Fig. 4 also illustrates how the animal ARDS model results of Williams et al. (2000) might have been generated. These authors observed a biphasic relationship between ΔPaO₂ and PEEP. The imposition of PEEP initially increased ΔPaO₂, but further increases in PEEP decreased the amplitude of these oscillations, although the mean PaO₂ continued to rise. This may be explained by reference to Fig. 4 and supposing that the animals had initial inspired and expired shunt fractions similar to those in Fig. 4(d). Increasing PEEP takes the simulation subject progressively through the situations shown in Fig. 4(c) and (b), finally reaching (a). During the course of this progression, carried out in this order, the time averaged (mean) PaO₂ always continues to increase whereas ΔPaO₂ increases at first but then decreases.

In physiological terms, as PEEP is increased there is an increase in alveolar recruitment as reported by Neumann et al. (1998). The effect of this will be to reduce the mean shunt, and thereby increase the mean PaO₂, and to reduce the slope of the oxyhaemoglobin dissociation curve at this point—such that when, in inspiration, an extra ‘bolus’ of oxygenated end-capillary blood is added to the mixed arterial blood, the resulting ΔPaO₂ will be increased. Further increases in PEEP initially continue this process, with the net result that both the mean PaO₂ and the PaO₂ oscillation (ΔPaO₂) continue to increase. However, a second effect of PEEP will dominate as baseline alveolar recruitment increases. As fewer alveoli remain to be recruited during tidal inflation, the intra-breath variation in shunt becomes smaller with a concomitant decrease in ΔPaO₂, although the mean PaO₂ will continue to rise. This mechanism matches the experimental observations of Williams et al. (2000), although the slow response time of their PaO₂ sensors must have underestimated the magnitude of the oscillation amplitude, as they reported.

In the published normoxic and hyperoxic studies of Purves (1966) and Folgering et al. (1978), no effort was made to induce acute lung injury and so prevailing pulmonary shunt was presumed to be low. However, in one hypoxaemic animal (with presumed shunt) PEEP was applied and an increase in both ΔPaO₂ and mean PaO₂ were observed (Purves, 1966). Modern knowledge (Neumann et al., 1998) would suggest that this therapeutic manoeuvre reduced atelectasis during expiration.

4.4. The I:E ratio

Fig. 6 illustrates yet another interesting outcome of the patient simulation. Although the model predicts that the ΔPaO₂ magnitude is primarily governed by Qs/Qt and Qse/Qt, Fig. 6 shows that, in our model, the magnitude of the mean (that is the time averaged) PaO₂ is heavily dependent on the ventilator I:E ratio. For normal I:E ratios of less than 1:1, the expiratory time dominates the time averaged arterial blood oxygen content, and thus the blood sample P O₂. Under these circumstances, the mean PaO₂ will be heavily weighted towards the expired PaO₂ value. Of course, the inverse is true when the I:E ratio is reversed. Although we have not presented plots of respiratory rate (RR) against either mean PaO₂ or ΔPaO₂, our calculations show that RR itself has only a small influence on their magnitude.

4.5. Limitations of the model

The rider must be added here that our model could have numerous modifications, such as the timing of the lung inflation and deflation occur-
ring at various stages in the respiratory cycle, although the results of Neumann et al. (1998) suggest that atelectasis occurred rapidly during expiration after an initial delay period of 0.6 sec. No doubt these modifications will produce different mean PaO₂ calculations, since they would change the timing of the ‘square wave’ shunts that we have imposed. We have examined shunt having a low value for part of the respiratory cycle where VA is largest and a high value when VA is smaller, but this makes minor differences to our results.

Furthermore, (i) our model has only a single well-mixed alveolar compartment and oxygen consumption remains at a normal level; and (ii) the mathematical model does not possess any spatial variation in partial pressure, as must occur in the human respiratory tree. A different picture may emerge when the interplay between multiple changes in the various physiological variables is investigated, and spatial variations in partial pressure are modelled. Our purpose here has been to identify the major factors that generate, and affect, the ΔPaO₂ phenomena in a balloon-on-a-straw tidal ventilation model.

4.6. Conclusions

We have shown that a relatively simple mathematical tidal ventilation model of shunt is one way (but not necessarily the only way) to describe physiological observations of intra-breath oscillations in SaO₂ and PaO₂. One conclusion from the simulation is that static conventional blood-gas data, interpreted with the continuous ventilation models of gas exchange (Weibel, 1984; Nunn, 1993; Erdmann, 1992), can only lead to clinical or physiological interpretations for those patients who are both in a ‘steady state’ and have a constant shunt throughout the respiratory cycle. Table 2 demonstrates that conventional blood gas sample results can be interpreted as either (i) being produced by a constant shunt throughout the respiratory cycle; or (ii) by two different pulmonary shunts occurring during the inspiratory and expiratory phases. The full implications of this can only be examined if fast (breath-by-breath) clinical PaO₂ sensors become readily available once more, as in the recent Baumgardner et al. (2002) studies, to verify the predictions of the model and to examine these in human subjects.

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Appendix A: Tidal ventilation model relationships

Fig. a1 shows diagrammatically the tidal-ventilation (‘balloon-on-a-straw’) lung model, with a single alveolar volume, VA(t), that can expand and contract with time during respiration and with a series dead-space volume, VD. The tidal volume is Vt.

Inspiration. The time-varying oxygen mass balance equation for the inspiratory phase of respira-

![Diagram](image-url)
tion is given by

\[
\frac{d}{dt}[F_A(t)V_A(t)] = F_{IA}(t)\frac{dV_A(t)}{dt} + \dot{Q}_p(t)[C\bar{v}(t) - C\bar{a}(t)]
\]  

(1)

where \(F_{IA}(t)\) is the time-varying inspired oxygen concentration entering the alveolar compartment. \(F_A(t)\) is the time-varying alveolar gas concentration. The gas inspired by the alveolar compartment \(F_{IA}(t)\) has two phases. The first phase is the inspiration of the fractional concentration of the oxygen left in the dead space from the previous breath, and the second is the fresh inspired oxygen with concentration \(F_i(t)\). \(V_A(t)\) varies linearly with time during this phase, for constant inspired gas flow. The second term on the right hand side of Eq. (1) is the net flux of oxygen from the blood flowing through the compartment. This mass balance occurs over the inspiration period \(T_I\). It is important to note here that both \(C\bar{a}(t)\) and \(C\bar{v}(t)\) have mean, \(\bar{C}\bar{a}\) and \(\bar{C}\bar{v}\), components (Hahn, 1996), but only arterial blood has (for reasons given below) a time varying oscillation component, \(\Delta C\bar{a}(t)\).

In the model presented in this paper, it must be remembered that the driving function for \(\bar{C}\bar{a}(t)\) is the pulmonary shunt fraction. The driving function is not the inspired oxygen fraction \(F_{IA}(t)\), as in the sine-wave technique (Gavaghan and Hahn, 1996). The pulmonary shunt during the inspiratory period is defined as \(\dot{Q}_{SI}/\dot{Q}_T\), and the mixed arterial oxygen content, \(\bar{C}\bar{a}\), is given by:

\[
\bar{C}\bar{a} = \left[1 - \frac{\dot{Q}_{SI}}{\dot{Q}_T}\right] C_{AI} + \frac{\dot{Q}_{SI}}{\dot{Q}_T} C\bar{v}
\]

(2)

where \(C_{AI}\) is the end-capillary, and \(C\bar{v}\) is the mixed-venous, blood oxygen content, respectively, over the inspiratory period.

Expiration. The mass balance occurring during the expiration period, \(T_E\), is given by

\[
\frac{d}{dt}[F_A(t)V_A(t)] = F_A(t)\frac{dV_A(t)}{dt} + \dot{Q}_p(t)[C\bar{v}(t) - C\bar{a}(t)]
\]

(3)

which reduces to

\[
V_A\frac{dF_A(t)}{dt} = \dot{Q}_p(t)[C\bar{v}(t) - C\bar{a}(t)]
\]

(4)

where \(V_A(t)\) decays exponentially with time to its end-expiratory resting volume (Gavaghan and Hahn, 1996). There is no \(F_{IA}(t)\) term in Eqs. (3) and (4), since oxygen mixing in the alveolar compartment can (in the expiratory phase) only take place through the net flux of oxygen from the arterial and mixed-venous circulation mixing with the end-inspiratory oxygen already contained in that compartment. Gas mixing continues to take place as the gas is expired.

The pulmonary shunt during the expiratory period is defined as \(\dot{Q}_{SE}/\dot{Q}_T\), and the mixed arterial oxygen content, \(\bar{C}\bar{a}\), is given by:

\[
\bar{C}\bar{a} = \left[1 - \frac{\dot{Q}_{SE}}{\dot{Q}_T}\right] C_{AE} + \frac{\dot{Q}_{SE}}{\dot{Q}_T} C\bar{v}
\]

(5)

where \(C_{AE}\) is the end-capillary, and \(C\bar{v}\) is the mixed-venous, blood oxygen content, respectively, over the expiratory period.

The mixed-venous oxygen content signal, \(C\bar{v}(t)\), does not have a term, \(\Delta C\bar{v}(t)\), oscillating at the respiration frequency around the mean mixed-venous content, unlike the arterial oxygen content signal, \(C\bar{a}(t)\). The effect of the relatively fast changing \(\Delta C\bar{a}(t)\) oscillation term on \(C\bar{v}(t)\), via differential equations relating the time varying \(\bar{a} - \bar{v}\) content difference to oxygen consumption, will be minimal because (a) the blood flowing through the individual body organ compartments, with individual oxygen consumptions, will damp the arterial \(\Delta C\bar{a}_O_2\) oscillations (12 min \(^{-1}\)) as they pass through them; and (b) the transit time for blood to flow from the lungs to body organs and back again will be different for different organs and this will add to the venous content damping process. Thus, the mixed-venous oxygen content term returning to the lung will only comprise the (damped) mean
mixed-venous content term, $C\bar{v}$, in Eqs. (1)–(5). The $\Delta C\bar{v}(t)$ term will disappear. The mean mixed-venous blood oxygen content in this study is, therefore, assumed to be a constant such that the body’s total oxygen consumption takes a prescribed value, $250 \text{ ml min}^{-1}$.

References


Purves, M.J., 1966. Fluctuations of arterial oxygen tension which have the same period as respiration. Respir. Physiol. 1, 281–296.
