RESPIRATION AND THE AIRWAY

The development of hypoxaemia during apnoea in children: a computational modelling investigation

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Background. Hypoxaemia during apnoea develops earlier and progresses faster in children than in adults. Ethical and practical considerations prevent detailed investigation of the issue.

Methods. We used the Nottingham Physiology Simulator, an integrated, computational model of the respiratory and cardiovascular systems, to model four healthy virtual children (ages: 1 month, 1, 8 and 18 yr) and exposed them to apnoea after a variety of preoxygenation periods (0, 1 and 3 min) and with open and obstructed airways during apnoea.

Results. The rate of oxygen desaturation of haemoglobin from 90 to 40% was similar across the ages studied, being \( \frac{1}{30} \) % min⁻¹. The greatest difference between ages was found in the speed of early desaturation (i.e. between the onset of apnoea and the acceleration of haemoglobin desaturation); in the absence of preoxygenation and with an open airway, this time was 6.6 s in the 1-month-old and 33.6 s in the 8-yr-old.

Conclusions. Preoxygenation had a substantial effect on the speed of early desaturation, but less effect on the time for \( S_aO_2 \) to decrease from 90 to 40%. Preoxygenation substantially delayed dangerous desaturation in all age groups, although the rapidity of denitrogenation in the very young (caused by the large ratio of minute ventilation to functional residual capacity) resulted in lengthy preoxygenation having little benefit over brief preoxygenation. Airway obstruction during apnoea accelerated every child’s hypoxaemia through prevention of mass flow addition to oxygen stores and through intrathoracic depressurization. On average, haemoglobin desaturation from \( S_aO_2 \) 90 to 40% was 33% min⁻¹ with an obstructed airway and 26% min⁻¹ with an open airway; all ages were similarly susceptible to this effect.

Keywords: complications, hypoxaemia; model, computer simulation; model, lung; oxygen, saturation; oxygen, uptake; ventilation, apnoea; ventilation, obstruction

Accepted for publication: May 2, 2006

It is well recognized that young children develop hypoxaemia more quickly than adults during apnoea. However, effective preoxygenation is more difficult to achieve in this age group compared with adults and the subsequent management of the airway can be challenging. A precise understanding of the time course of hypoxaemia development, and how it is affected by the age of the child, would be invaluable to the paediatric anaesthetist. There are clear ethical reasons why such data are difficult to obtain in vivo but there is a core of research into the respiratory physiology of the child that allows use of the Nottingham Physiology Simulator (NPS) to predict the course of hypoxaemia in a variety of situations involving apnoea. The NPS is a validated predictor of the course of hypoxaemia in adults during apnoea and has been used successfully to predict the effects of preoxygenation, functional residual capacity, oxygen consumption (\( V_O_2 \)), airway patency, pulmonary deadspace and shunt during apnoea.¹⁻²

We aimed to determine the influence of age, preoxygenation and airway management on the rate of progression of hypoxaemia during apnoea in children.

Methods

The NPS is a free-standing computational simulator that has been described in previous papers.¹⁻³ Version 251105
was used in this investigation; it is available for download through the corresponding author. The NPS is a multicompartamental computational model that uses an iterative technique to simulate integrated respiratory and cardiovascular pathophysiological scenarios.

Four virtual patients of ages 1 month, 1, 8 and 18 yr were created. Physiological variables pertaining to oxygen uptake, storage and distribution to the tissues were calculated for each virtual patient using data from previously published papers and were used to configure the NPS to create a simulation of each patient; the physiological values used are provided in Table 1.

Each virtual patient underwent apnoea with an obstructed airway after preoxygenation periods of 0, 1 and 3 min until arterial oxygen saturation reached 40%. These apnoeic episodes were repeated in each virtual patient (after 0, 1 and 3 min preoxygenation) with the airway open to 21% oxygen and 33% min⁻¹. The ratio of reduction in PaO₂ over time is less meaningful than that of PaO₂, so it is less meaningful to present an average decline in. However, it was noted that once 90% SaO₂ was passed the rate of decline in SaO₂ was similar between ages (Table 2); the majority of the difference in the speed of haemoglobin desaturation between ages was between the onset of apnoea and 90% SaO₂, with younger children reaching 90% SaO₂ typically three times faster than older children (Table 2).

The SaO₂ inflection point is that point during apnoea when haemoglobin desaturation accelerates significantly. We defined this as the time at which SaO₂ decline reached 50% of the relatively constant terminal rate (Figs 2A–C and 3A–C). The inflection point was between SaO₂ values of 95 and 98% in almost all scenarios (Table 3). The 1-month-old child reached this inflection point very rapidly; in the absence of preoxygenation, desaturation accelerated after only 6.6 s of apnoea. It was in the time from the onset of apnoea to the inflection point that we observed the largest difference between ages (Table 3); typically, the 1-month-old reached the inflection point four times faster than the 18-yr-old. Beyond the inflection point, the rate of decline in SaO₂ was relatively constant, being ~33% min⁻¹ with a closed airway and 26% min⁻¹ with an airway open to air.

The rate of decline of SaO₂ increases from zero to ~30% min⁻¹ in a short period during apnoea. In clinical practice, oximeter alarms typically are set to trigger at SpO₂ values of 90–94%. We suggest that by this time SaO₂ is decreasing at its maximal rate, the inflection point having been passed at

### Table 1: Baseline physiological values for the ages examined. Values for ages 0–1 yr are similar for girls and boys; values for 18-yr-olds are obtained from boys.

<table>
<thead>
<tr>
<th>Age</th>
<th>1 month</th>
<th>1 yr</th>
<th>8 yr</th>
<th>18 yr</th>
</tr>
</thead>
<tbody>
<tr>
<td>Height (cm)</td>
<td>53</td>
<td>76</td>
<td>125</td>
<td>170</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>4.2</td>
<td>10.4</td>
<td>22</td>
<td>54</td>
</tr>
<tr>
<td>Blood volume (litre)</td>
<td>0.34</td>
<td>0.78</td>
<td>1.54</td>
<td>3.78</td>
</tr>
<tr>
<td>Haemoglobin (g litre⁻¹)</td>
<td>120</td>
<td>110</td>
<td>130</td>
<td>140</td>
</tr>
<tr>
<td>BSA (m²)</td>
<td>0.25</td>
<td>0.47</td>
<td>0.87</td>
<td>1.6</td>
</tr>
<tr>
<td>Compliance</td>
<td>13</td>
<td>26</td>
<td>76</td>
<td>144</td>
</tr>
<tr>
<td>(ml cm H₂O⁻¹)</td>
<td>800</td>
<td>1500</td>
<td>2780</td>
<td>5100</td>
</tr>
<tr>
<td>Cardiac output (ml min⁻¹)</td>
<td>30</td>
<td>75</td>
<td>154</td>
<td>380</td>
</tr>
<tr>
<td>Tidal volume (ml)</td>
<td>32</td>
<td>24</td>
<td>18</td>
<td>14</td>
</tr>
<tr>
<td>Ventilatory frequency (bpm)</td>
<td>40</td>
<td>70</td>
<td>130</td>
<td>250</td>
</tr>
<tr>
<td>Oxygen consumption (ml min⁻¹)</td>
<td>58</td>
<td>194</td>
<td>545</td>
<td>1769</td>
</tr>
</tbody>
</table>

### Discussion

This study concentrates on one specific and common situation—that of a child rendered apnoeic. This frequently follows induction of anaesthesia, and may be accompanied by airway obstruction. It is well recognized that hypoxaemia occurs more rapidly in children, especially in the very young, and in patients with an obstructed airway. Additional issues make desaturation even more likely in children than in adults. First, airway management, by facemask, laryngeal mask or tracheal intubation, is frequently more difficult in children and, second, it is often more difficult to achieve effective preoxygenation in the young child.

The clinical implication that the development of hypoxaemia is substantially faster in young children is supported by the results of this investigation. In clinical practice, desaturation accelerated after only 6.6 s of apnoea. It was in the time from the onset of apnoea to the inflection point that we observed the largest difference between ages (Table 3); typically, the 1-month-old reached the inflection point four times faster than the 18-yr-old. Beyond the inflection point, the rate of decline in SaO₂ was relatively constant, being ~33% min⁻¹ with a closed airway and 26% min⁻¹ with an airway open to air.

The rate of decline of SaO₂ increases from zero to ~30% min⁻¹ in a short period during apnoea. In clinical practice, oximeter alarms typically are set to trigger at SpO₂ values of 90–94%. We suggest that by this time SaO₂ is decreasing at its maximal rate, the inflection point having been passed at
94–98% \( S_aO_2 \). Even when sudden and severe haemoglobin desaturation is close, the \( S_aO_2 \) can still be above 95%.

Figures 1–4 show the benefit of preoxygenation in children (compare Panel A with Panel C in each figure). After preoxygenation for 1 or 3 min, the \( P_aO_2 \) reaches 62–80 kPa in all age groups. A 1 min preoxygenation in the neonate is almost as effective in increasing \( P_aO_2 \) as 3 min (\( P_aO_2 74 \text{ kPa after 1 min} \) vs \( 77 \text{ kPa after 3 min} \)), because of the neonate’s larger minute ventilation to functional residual capacity (FRC) ratio and lower maximal \( S_aO_2 \). The difference observed in the 18-yr-old is a more clinically useful 19 kPa (62 vs 81 kPa). However, the 1 min preoxygenation in the neonate substantially extends the safe duration of apnoea, despite the relatively small FRC in this age group (Table 3); a 1 min preoxygenation in the 1-month-old extended the time from the start of apnoea to \( S_aO_2 40\% \) by 94 s (closed airway) and 124 s (open airway); an extra 2 min of preoxygenation in the 1-month-old added only 22 s (closed airway) or 44 s (open airway) to the time to \( S_aO_2 40\% \).

Comparison between Figures 1 and 2 and between Figures 3 and 4 demonstrates the benefit of maintaining an airway after the onset of apnoea; the open airway allows the net loss of intra-alveolar volume to draw ambient gas into the lungs.22 82 9 In this investigation, the airway was open to 21% oxygen. It would be expected that if the airway was open to 100% oxygen the effects would be more marked, as in adults.23 29 Of interest is the finding that the early decline in \( S_aO_2 \) is faster when the airway is open, while the later decline is faster when the airway is closed. This is caused by early mass flow of nitrogen into the alveoli via an open airway, diluting the oxygen stores in the
preoxygenated alveoli. When the airway is closed, reduction in intra-alveolar pressure compounds the effect on the \( P_{aO_2} \) of the late reduction in alveolar oxygen fraction because the alveolar oxygen tension is the product of the intra-alveolar pressure and the alveolar oxygen fraction. Such depressurization (Table 4) may be an important factor in closed airway desaturation during apnoea. Opening such an airway would result in a single, passive inhalation, which could provide useful reoxygenation, especially if supplemental oxygen was supplied; this will be the subject of further investigation.

This investigation is limited in a number of ways. First, our use of a theoretical model means that our findings have to be extrapolated to the clinical environment. However, we have exposed the model to validation previously\textsuperscript{1,2} and we have performed specific validation of the NPS for this investigation; this further validation of the model with respect to apnoea in children is presented as supplementary data online in Appendix 1 (see British Journal of Anaesthesia online). Second, we have examined only healthy virtual children. We recognize that various pathologies, such as an increase in oxygen consumption (e.g. pyrexia) or a reduction in haemoglobin concentration or functional residual capacity may cause substantial variations in the expected rate of desaturation during apnoea; indeed the prevalence of childhood obesity is increasing and we may anticipate that this increasingly relevant pathology will hasten hypoxaemia during apnoea. The effects of such pathophysiological variation on apnoeic desaturation have been considered previously,\textsuperscript{3} and we may extrapolate these previous findings.

**Fig 2** The time course of \( P_{aO_2} \) during preoxygenation and apnoea in children with an obstructed airway. The vertical dashed line shows the start of apnoea. Durations of preoxygenation are shown in Panels A, B and C: A, 0 min; B, 1 min; C, 3 min.
to the virtual children studied in this investigation. Third, clinical scenarios are seldom as simple as those studied in this investigation. We appreciate that the airway will rarely remain open or obstructed throughout apnoea, and that there will be periods of exposure of the airway to oxygen and air. However, we have illustrated idealized/simplified scenarios; more complex combinations of factors may be extrapolated from these data. Finally, we have examined the effect of apnoea to the eventual scenario of reaching 40%. This does not represent death or even serious morbidity; in some children, harm could result from this level of hypoxaemia, but in the majority, no harm would result. Our modelling does not allow us to identify the timing of organ injury, and so we cannot specify how long after the point of $\text{SaO}_2$ 40% the child would be injured. However, we have illustrated that the decline in $\text{SaO}_2$ is effectively linear at this late stage (being $\sim 30\% \text{ min}^{-1}$), so harm would result soon after this time in all the scenarios investigated if the apnoea is not terminated.

In summary, our modelling investigation confirms the clinical impression that young children become hypoxaemic more quickly during apnoea than adults. Preoxygenation delays this hypoxaemia, although prolonged preoxygenation in the very young seems to offer little benefit. Airway obstruction hastens hypoxaemia at all ages through denial of passive gas inflow and thoracic depressurization. The majority of the variability in the rate of desaturation between older and younger children appears to occur in the early

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**Fig 3** The time course of $\text{SaO}_2$ during preoxygenation and apnoea in children with an open airway. The vertical dashed line shows the start of apnoea. Durations of preoxygenation are shown in Panels A, B and C: A, 0 min; B, 1 min; C, 3 min.
Fig 4 The time course of $S_aO_2$ during preoxygenation and apnoea in children with an obstructed airway. The vertical dashed line shows the start of apnoea. Durations of preoxygenation are shown in Panels A, B and C: A. 0 min; B. 1 min; C. 3 min.

Table 2 Minutes from start of apnoea to $S_aO_2$ 90% (early), from $S_aO_2$ 90 to 40% (late) and from start of apnoea to $S_aO_2$ 40% (total)

<table>
<thead>
<tr>
<th>Age</th>
<th>No preO$_2$</th>
<th>1 min preO$_2$</th>
<th>3 min preO$_2$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Early</td>
<td>Late</td>
<td>Total</td>
</tr>
<tr>
<td>Closed airway</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 month</td>
<td>0.25</td>
<td>1.40</td>
<td>1.65</td>
</tr>
<tr>
<td>1 yr</td>
<td>0.36</td>
<td>1.48</td>
<td>1.84</td>
</tr>
<tr>
<td>8 yr</td>
<td>0.47</td>
<td>1.47</td>
<td>1.94</td>
</tr>
<tr>
<td>18 yr</td>
<td>0.74</td>
<td>1.72</td>
<td>2.46</td>
</tr>
<tr>
<td>Open airway</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 month</td>
<td>0.30</td>
<td>1.68</td>
<td>1.98</td>
</tr>
<tr>
<td>1 yr</td>
<td>0.40</td>
<td>1.69</td>
<td>2.09</td>
</tr>
<tr>
<td>8 yr</td>
<td>0.51</td>
<td>1.65</td>
<td>2.16</td>
</tr>
<tr>
<td>18 yr</td>
<td>0.82</td>
<td>1.91</td>
<td>2.73</td>
</tr>
</tbody>
</table>
stages of hypoxaemia (while $aO_2$ remains in the 94–98% range), and the rate of desaturation after 90% $aO_2$ seems relatively constant, being ~30% min$^{-1}$.

### Supplementary data

Appendix 1 and its accompanying figure can be found in *British Journal of Anaesthesia* online.

### References