Journal of Paediatrics and Child Health

doi:10.1111/jpc.13078

REVIEW ARTICLE

Respiratory support for children in the emergency department

Andreas Schibler and Donna Franklin

Paediatric Critical Care Research Group, Mater Research University Queensland, Lady Cilento Children's Hospital, Brisbane, Queensland, Australia

Abstract: Respiratory support in paediatric emergency settings ranges from oxygen delivery with subnasal oxygen to invasive mechanical ventilation. Recent data suggest that oxygen can cause reperfusion injuries and should be delivered with caution within well-defined clinical target ranges. Most mild to moderate respiratory distress conditions with an oxygen requirement may benefit from early use of continuous positive airway pressure. High-flow nasal cannula therapy (HFNC) is an emerging alternative way to support the inspiratory effort combined with oxygen delivery and positive expiratory pressures without the need of complicated equipment or good compliance from the child. Besides a positive pressure support effect, HFNC therapy reduces the physiological dead space with improved CO_2 clearance. A decrease in heart and respiratory rate within the first few hours after initiation of HFNC therapy is likely to identify responders of the treatment. The use of non-invasive ventilation such as continuous positive airway pressure or the use of bi-level positive airway pressure ventilation in emergency departments has increased, and it has been recognised that continuous positive airway pressure support for older children with asthma is particularly efficient.

Key words: continuous positive airway pressure; emergency; oxygen toxicity; respiratory distress.

Introduction: The Need of Oxygen Therapy in Acute Respiratory Distress

Oxygen requirement in a child presenting with acute respiratory distress is representing the dysfunctional state of pulmonary gas exchange. The main goal of respiratory support is prevention of severe hypoxaemia and maintenance of oxygen delivery to protect cerebral function and prevent organ failures.[1] It is of utmost importance that respiratory support is not discussed in isolation but related to oxygen delivery, which is defined by the product of cardiac output, haemoglobin and haemoglobin saturation ($DO_2 = CO \times Hb \times SaO_2$). In a profound hypoxaemic child, rapid administration of oxygen is the first line therapy followed by support of the respiratory system. Caution of excessive use of oxygen has been recognised, and its toxicity is related to the concentration and length of exposure.[2–4] For these reasons, other than emergency usage of 100% oxygen, it is recommended that inspired oxygen concentration (FiO_2) should be carefully titrated against SaO_2. In several areas of emergency care and resuscitation, the use of oxygen is now being challenged by new evidence from clinical trials and systematic reviews. In neonates, use of 100% oxygen during resuscitation increases mortality, myocardial injury and renal injury,[5] and even following an asphyxiating perinatal event, it is thought to increase the risk of cerebral damage.[6] The current neonatal resuscitation guidelines advise that the initial gas administered for ventilation should be air (resus.org.au/guidelines-section 13 neonatal guidelines). In patients with an acute myocardial infarct, systematic reviews have found that, compared with room air, there is no evidence that oxygen therapy is of benefit,[7] as is the case in acute stroke.[8] In a long-term follow-up study of mechanically ventilated adult patients with acute lung injury, a lower partial pressure of arterial oxygen (but not oxygen saturation) was associated with cognitive impairment.[9] A systematic review, in children with chronic or recurrent hypoxia, indicated that high-level or prolonged use of oxygen caused adverse effects on development, behaviour and academic achievement; however, most studies did not stratify by SaO_2.[10]

Current WHO guidelines recommend a normal range of acceptable SaO_2 at sea level to be $SaO_2 \geq 94\%$. Thresholds for administering oxygen differ among international guidelines – some target <92%, whilst others target <94%. The 2012 WHO *Recommendations for management of common childhood conditions* identified a number of key research questions as 'research gaps'; these included 'Large-scale effectiveness trials of improved oxygen systems on outcomes from pneumonia' and 'Clinical studies comparing outcomes when oxygen is given at different thresholds'.

Key points

- Oxygen is a drug, and the use of oxygen needs to be titrated carefully against measured haemoglobin oxygen saturation. Most causes for an oxygen requirement can be treated with positive pressure support rather than increased oxygen provision.
- Maintaining spontaneous breathing in respiratory distress through non-invasive techniques of respiratory support is desirable to preserve the patients' own expiratory support/effort.

Correspondence: Dr Andreas Schibler, Paediatric Intensive Care Unit, Lady Cilento Children's Hospital, 501 Stanley Street, South Brisbane, Queensland 4101, Australia. Fax: +61 73068 1499; email: a.schibler@uq.edu.au

Conflict of Interest: None declared.

Accepted for publication 26 November 2015.

Oxygen delivery is only one side of the gas exchange. Failure of the respiratory system is divided into pump failure (carbon dioxide retention) versus gas exchange failure with a decreased alveolar–capillary diffusion capacity resulting in oxygenation failure. Pump and exchange failure are interlinked. Arterial $PaCO_2$ can only be improved by increased alveolar ventilation (greater gas exchange), either with assisted breathing or by reversing a cerebral cause for hypoventilation. Oxygen requirement occurs if (a) the alveolar surface is reduced (atelectasis, consolidation, reduced lung volumes or alveolar surface), (b) ventilation perfusion mismatch is present (increased shunt fraction), (c) ventilation inhomogeneity occurs (increased physiological dead space) and (d) in the presence of an impaired diffusion capacity of the alveolar–capillary membrane. Only the latter responds well to an increased oxygen fraction, whereas the first three causes respond to increased lung inflation pressures delivered, that is, with continuous positive airway pressure (CPAP) breathing or mechanical ventilation with positive end expiratory pressure (PEEP). The respiratory work load is separated into inspiratory or expiratory work load. During regular breathing, the inspiration is active (with the use of diaphragm and intercostal muscles) and passive during expiration (elastic recoil of the chest). In the presence of respiratory distress, the expiratory phase can become active with the use of auxiliary, abdominal and intercostal muscles. To overcome and compensate for increased expiratory resistance, patients tend to increase their functional residual capacity. This allows an increased airway diameter and the use of a higher recoil pressure to work against airway resistance during the following expiration. In a paralysed patient, positive pressure ventilation supports only the inspiratory phase, whereas the expiratory phase is entirely dependent on the recoil pressure of the chest and lung. PEEP may assist to stent airways and maintain functional residual capacity. Any spontaneous breathing in a ventilated patient may assist significantly during the expiratory phase with an active expiratory effort. In summary, having a spontaneous breathing patient with some form of CPAP and minimal oxygen exposure is an ideal approach to respiratory support in emergency settings.

High-flow Nasal Cannula Therapy

The use of high-flow nasal cannula (HFNC) therapy as an alternative form to standard oxygen delivery is rapidly growing despite limited evidence of its efficacy in paediatrics. There are a growing number of studies demonstrating the physiological effect of high flow, which can be summarised as follows: The inspired gas is heated and humidified and reduces the metabolic demand associated with gas conditioning. The provision of warmed and humidified gas to the conducting airways improves conductance and pulmonary compliance compared with dry, cooler gas. The anatomical nasopharyngeal dead space of the patient is rapidly washed out during the expiratory phase such that during the next inspiration, CO_2 rebreathing is minimised.[11] High flow rates during the inspiratory phase deliver some degree of respiratory support. Ideally, the delivered flow rate should match the maximal inspiratory flow rate generated by the patient in order to avoid the need to entrain gas during inspiration around the nasal prongs. During the expiratory phase, the unidirectional flow is directed against the expiratory gas flow of the patient creating positive expiratory pressures.

Several studies have shown that HFNC therapy creates a distending pressure of the lung with a PEEP effect of approximately 4–6 cmH_2O using flow rates of 1.5–2 L/kg/min in infants <12 months of age,[12] demonstrating HFNC therapy decreases the work of breathing. Additionally, physiological data suggest that flow rates of 1.6–1.8 L/kg/min are matching the majority of inspiratory flows in infants with bronchiolitis.[12] Intrathoracic (oesophagus) pressure swings are reduced, and the electrical activity of the diaphragm decreased on HFNC therapy.[13–15]

The clinical benefit of high flow in bronchiolitis is subject to many current and ongoing trials. Because of its simple application, and the fact that little cooperation of the patient is needed, HFNC therapy in emergency departments has become popular. Particularly, in infants with a moderate oxygen requirement and increased work of breathing, many practitioners have observed an impressive clinical benefit.[16] Observational studies in emergency and intensive care have shown that infants with bronchiolitis responding to HFNC therapy reduce their heart and respiratory rate within the first few hours of admission[17,18] and that these criteria discriminate well between responders (Table 1) and non-responders of HFNC therapy. It has been recognised that it is important to encourage the early use of non-invasive (non-invasive ventilation (NIV)) respiratory support or HFNC therapy in less-intensive scenarios, to facilitate early respiratory support and decrease the prevalence of respiratory deterioration.[19] A recent randomised controlled trial using HFNC therapy in adult patients with acute hypoxic respiratory failure showed that HFNC therapy as compared with standard oxygen therapy or NIV resulted in reduced mortality at 90 days.[20]

HFNC – how to do it?

Given that the evidence for the use of high flow is rapidly growing in the paediatric field, these following suggestions represent a growing consensus of current practice. Ideally, the flow rate used should match the patients' maximal inspiratory flow. The individual inspiratory flow rate is not known in any clinical settings; hence, as previously suggested, using a flow rate of 2 L/kg/min in infants with bronchiolitis will match the expected maximal inspiratory flow rates in this population. In older children, we aim to use flow rates of 2 L/kg/min with an upper limit currently of 40–60 L/min. This upper limit is based on the reported discomfort of patients (noise and nasal distension experienced). The oxygen fraction is titrated against SpO_2 to maintain values between 92% and 98%. HFNC therapy is weaned by reducing FiO_2 down to room air preferentially whilst maintaining the

Table 1 Responders to HFNC, CPAP or BiPAP support[28]

Decrease in respiratory rate
Decrease in retractions and accessory muscle use
Reduced FiO2
Improved radiological findings (reversed atelectasis)

BiPAP, bi-level positive airway pressure; CPAP, continuous positive airway pressure; HFNC, high-flow nasal cannula therapy.

flow rates. Once in room air, the high flow is ceased after 4 h. If an oxygen requirement reoccurs after ceasing HFNC therapy (rebound after PEEP effect is taken off), HFNC therapy is recommenced in room air initially and if needed, FiO_2 increased. A large multicentre randomised controlled trial comparing standard oxygen delivery versus HFNC therapy in moderately sick infants with bronchiolitis is currently being undertaken in Australia and New Zealand, involving regional and tertiary hospitals.

Non-invasive Continuous Positive Airway Pressure and Bi-level Positive Airway Pressure

Non-invasive ventilation decreases the work of breathing, reverses hypoventilation, increases functional residual capacity, maintains upper airway patency and improves cardiac output with a decrease in oxygen consumption, which is a highly important factor for a child fatigued by respiratory distress.[21] CPAP delivery maintains a continuous set airway pressure during the inspiratory and expiratory phase, whereas with bi-level positive airway pressure during the inspiratory phase, a greater airway pressure is delivered to support the inspiratory effort. NIV in paediatric emergency settings is difficult to apply because of the limited compliance and cooperation of infants or children to tolerate a face mask for CPAP delivery. CPAP is usually only tolerated with some form of sedation, which can compromise respiratory drive. Considerably higher levels of nursing skill are required for NIV. Hence, careful consideration regarding the type and dose of sedation needs to be taken. Since the introduction of dexmedetomidine, the authors' own clinical practice has changed significantly. Dexmedetomidine is an agonist of α_2-adrenergic receptors in certain parts of the brain without any respiratory depression. The use of dexmedetomidine is currently limited to the paediatric intensive care unit.

Similar to many other emergency treatments, NIV should preferentially be started in emergency departments and then continued in intensive care.[22] Paediatric clinical trials have shown that the early use of CPAP in asthmatic paediatric patients is beneficial[23,24]; however, the studies and reports are predominantly performed and described from within an intensive care setting.[25] Most of these paediatric trials in asthmatics demonstrated an improved oxygenation and reduced need for paediatric intensive care admission or intubation. Similarly, the use of CPAP in bronchiolitis has been well documented and described in the literature, but again most likely limited to paediatric intensive care settings.[26] The use of NIV in adults in emergency department settings has become common practice, and it will be only a matter of time until paediatric emergency services will use NIV more frequently. Success of NIV can be measured by a reduction in heart and respiratory rate within the first few hours of treatment.[27–30]

NIV – how to do it?

Good patient selection is the key to successful NIV. Good patient cooperation and synchrony needs to be established. Children with reduced conscious level, cardiovascular instability and reduced upper airway reflexes or control should not be considered for NIV.[27] Children after upper airway surgery or upper gastrointestinal tract surgery, and upper gastrointestinal tract bleeding should not be offered NIV. NIV can be provided using a full face mask or a nasal mask only. The latter is more reserved for long-term NIV patients, as factors of mouth opening and leak impact on the quality of respiratory support. With a full face mask, CPAP can be delivered with or without positive inspiratory pressure support (PS). The key for success of PS is accurate triggering, which requires a system with minimal leakage (tight fit of the mask to face). Commonly, CPAP is commenced at 5 cmH_2O in any child or infant, and the level of CPAP is then adapted as clinically needed. It is not uncommon that CPAP levels of 10–12 cmH_2O are required for improved gas exchange. The PS usually initiates at 5 cmH_2O above PEEP and will then increase if significant work of breathing persists. Most infants and children need some form of sedation to tolerate a full face mask, which can be offered with midazolam, chloral hydrate or as aforementioned, dexmedetomidine. Responders to NIV are clinically reducing their work of breathing with a reduction in use of intercostal and auxiliary muscles, resulting in a reduction of heart and respiratory rate. Instead of serial blood gases, the measurement of SpO_2 in relation to the delivered FiO_2 is important. If a patient fails to maintain $SpO_2 > 92\%$ with a $FiO_2 < 60\%$, invasive mechanical ventilation should be considered.

The Transitional Phase During Intubation and Mechanical Ventilation

Maintaining haemoglobin saturation during airway management is critical for patient safety and poses a challenge for the clinician to secure the airway with tracheal intubation as quickly as possible. For a septic patient with severe pneumonia who is already hypoxaemic despite oxygen therapy, there is an immediate risk of critical tissue hypoxia during intubation. Preoxygenation is the key to avoid or limit induction-related tissue hypoxaemia particularly during a rapid sequence induction. Prior to rapid sequence induction, an adult patient breathing room air will desaturate within 45–60 s; however, in a child or infant, this occurs in less than 20 s. To prevent hypoxaemia, the alveolar space is filled prior to intubation with a high O_2 fraction. If saturations remain <94% despite 100% rebreathing bag/mask ventilation, major shunt pathology either within the lung or on a cardiac level needs to be considered. Pulmonary shunt physiology refers to alveoli that are perfused but not ventilated because of conditions such as pulmonary oedema, pneumonia or atelectasis. In the presence of severe respiratory disease, the alveolar space is significantly reduced because of atelectasis or pus and secretion, and the diffusion of gas is impaired because of interstitial thickening with oedema and inflammation. The application of CPAP prior to induction may recruit alveolar volume. With the introduction of HFNC therapy, this provides an attractive method for pre-oxygenation with the application of CPAP, and without the disadvantage and discomfort of a face mask. An interesting study by Mundel *et al.* showed that the application of HFNC therapy reduced the respiratory rate zsignificantly so that other mechanisms of gas exchange such as tracheal gas insufflation were considered.[31] In some adult emergency departments, clinicians have started to use HFNC

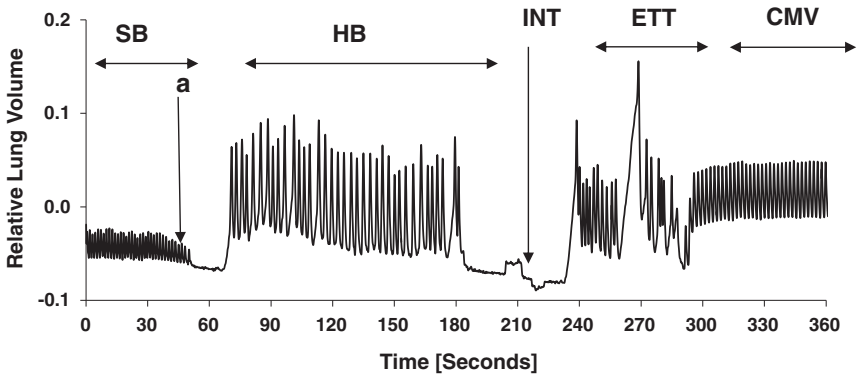

Fig. 1 Change of relative lung volume during induction of anaesthesia. SB: spontaneous breathing followed by i.v. injection of muscle paralysis, then mask hand bagging (HB). During insertion of the endotracheal tube (INT), the lung volume is as its lowest level. ETT: manual ventilation followed by continuous mechanical ventilation (CMV) applying positive end expiratory pressure.

therapy for pre-oxygenation. The transition from spontaneous to assisted breathing is also associated with significant shifts in ventilation distribution and loss of lung volume.[32] Humphrey *et al.* (Fig. 1) showed in infants and children during regular induction of anaesthesia that there is a significant loss in lung volume and lung mechanics and these changes can be reversed by applying PEEP.[33] Infants and children have in comparison with adults a much smaller functional residual capacity of the lung, which normally acts as the oxygen reservoir during induction of anaesthesia. Hence, any sedation in small infants, even if spontaneous breathing is being maintained, will rapidly develop into an oxygen requirement.

The use of ketamine, however, may be one of the exceptional sedatives that may preserve lung volume in healthy pre-school children undergoing a ketamine anaesthesia for small procedures.[34]

Conclusion

There is a strong physiological rational to shift the paradigm for first line treatment of mild to moderate hypoxaemia. Initial focus of respiratory treatment should be on delivering positive pressure, followed by, if necessary, increased oxygen fraction. With the introduction of HFNC therapy, this shift is facilitated as CPAP, and oxygen delivery is made clinically much easier with one therapy.

References

1 Askie LM, Henderson-Smart DJ, Irwig L, Simpson JM. Oxygen-saturation targets and outcomes in extremely preterm infants. *N. Engl. J. Med.* 2003; **349**: 959–67.
2 Jackson RM. Pulmonary oxygen toxicity. *Chest* 1985; **88**: 900–5.
3 Davis WB, Rennard SI, Bitterman PB, Crystal RG. Pulmonary oxygen toxicity. Early reversible changes in human alveolar structures induced by hyperoxia. *N. Engl. J. Med.* 1983; **309**: 878–83.
4 Davis WB, Rennard SI, Bitterman PB *et al.* Pulmonary oxygen toxicity. Bronchoalveolar lavage demonstration of early parameters of alveolitis. *Chest* 1983; **83**: 35S.
5 Davis PG, Tan A, O'Donnell CP, Schulze A. Resuscitation of newborn infants with 100% oxygen or air: a systematic review and meta-analysis. *Lancet* 2004; **364**: 1329–33.
6 Munkeby BH, Borke WB, Bjornland K *et al.* Resuscitation with 100% O2 increases cerebral injury in hypoxemic piglets. *Pediatr. Res.* 2004; **56**: 783–90.
7 Cabello JB, Burls A, Emparanza JI, Bayliss S, Quinn T. Oxygen therapy for acute myocardial infarction. *Cochrane Db. of Sys. Rev*. 2013; **8**: CD007160.
8 Ronning OM, Guldvog B. Should stroke victims routinely receive supplemental oxygen? A quasi-randomized controlled trial. *Stroke; J. Cerebral Circulation* 1999; **30**: 2033–7.
9 Mikkelsen ME, Christie JD, Lanken PN *et al.* The adult respiratory distress syndrome cognitive outcomes study: long-term neuropsychological function in survivors of acute lung injury. *Am. J. Respir. Crit. Care Med.* 2012; **185**: 1307–15.
10 Bass JL, Corwin M, Gozal D *et al.* The effect of chronic or intermittent hypoxia on cognition in childhood: a review of the evidence. *Pediatr* 2004; **114**: 805–16.
11 Dysart K, Miller TL, Wolfson MR, Shaffer TH. Research in high flow therapy: mechanisms of action. *Respir. Med.* 2009; **103**: 1400–5.
12 Milesi C, Baleine J, Matecki S *et al.* Is treatment with a high flow nasal cannula effective in acute viral bronchiolitis? A physiologic study. *Intensive Care Med.* 2013; **39** (6): 1088–94.
13 Hough JL, Pham TM, Schibler A. Physiologic effect of high-flow nasal cannula in infants with bronchiolitis. *Pediatric Crit. Care Med.* 2014; **15**: e214–9.
14 Pham TM, O'Malley L, Mayfield S, Martin S, Schibler A. The effect of high flow nasal cannula therapy on the work of breathing in infants with bronchiolitis. *Pediatr. Pulmonol.* 2015 Jul; **50**: 713–20.
15 Rubin S, Ghuman A, Deakers T, Khemani R, Ross P, Newth CJ. Effort of breathing in children receiving high-flow nasal cannula. *Pediatric Crit. Care Med.* 2014; **15**: 1–6.
16 Bressan S, Balzani M, Krauss B, Pettenazzo A, Zanconato S, Baraldi E. High-flow nasal cannula oxygen for bronchiolitis in a pediatric ward: a pilot study. *Eur. J. Pediatr.* 2013; **172**: 1649–56.
17 Mayfield S, Jauncey-Cooke J, Hough JL, Schibler A, Gibbons K, Bogossian F. High-flow nasal cannula therapy for respiratory support in children. *Cochrane Db. Syst. Rev.* 2014; **3**: CD009850.
18 Schibler A, Pham TM, Dunster KR *et al.* Reduced intubation rates for infants after introduction of high-flow nasal prong oxygen delivery. *Intensive Care Med.* 2011; **37**: 847–52.
19 Kelly GS, Simon HK, Sturm JJ. High-flow nasal cannula use in children with respiratory distress in the emergency department: predicting the need for subsequent intubation. *Pediatr. Emerg. Care* 2013; **29**: 888–92.

20 Frat JP, Thille AW, Mercat A *et al.* High-flow oxygen through nasal cannula in acute hypoxemic respiratory failure. *N. Engl. J. Med.* 2015 Jun 4; **372**: 2185–96.
21 Carrey Z, Gottfried SB, Levy RD. Ventilatory muscle support in respiratory failure with nasal positive pressure ventilation. *Chest* 1990; **97**: 150–8.
22 Teague WG. Noninvasive ventilation in the pediatric intensive care unit for children with acute respiratory failure. *Pediatr. Pulmonol.* 2003; **35**: 418–26.
23 Beers SL, Abramo TJ, Bracken A, Wiebe RA. Bilevel positive airway pressure in the treatment of status asthmaticus in pediatrics. *Am. J. Emerg. Med.* 2007; **25**: 6–9.
24 Thill PJ, McGuire JK, Baden HP, Green TP, Checchia PA. Noninvasive positive-pressure ventilation in children with lower airway obstruction. *Pediatric Critical Care Med.* 2004; **5**: 337–42.
25 Basnet S, Mander G, Andoh J, Klaska H, Verhulst S, Koirala J. Safety, efficacy, and tolerability of early initiation of noninvasive positive pressure ventilation in pediatric patients admitted with status asthmaticus: a pilot study. *Pediatr. Crit. Care Med.* 2012; **13**: 393–8.
26 ten Brink F, Duke T, Evans J. High-flow nasal prong oxygen therapy or nasopharyngeal continuous positive airway pressure for children with moderate-to-severe respiratory distress?*. *Pediatr. Crit. Care Med.* 2013; **14**: e326–31.
27 Essouri S, Chevret L, Durand P, Haas V, Fauroux B, Devictor D. Noninvasive positive pressure ventilation: five years of experience in a pediatric intensive care unit. *Pediatric Crit. Care Med.* 2006; **7**: 329–34.
28 Munoz-Bonet JI, Flor-Macian EM, Brines J *et al.* Predictive factors for the outcome of noninvasive ventilation in pediatric acute respiratory failure. *Pediatric Crit. Care Med.* 2010; **11**: 675–80.
29 Mayordomo-Colunga J, Pons M, Lopez Y *et al.* Predicting non-invasive ventilation failure in children from the SpO(2)/FiO(2) (SF) ratio. *Intensive Care Med.* 2013; **39**: 1095–103.
30 Balfour-Lynn RE, Marsh G, Gorayi D, Elahi E, LaRovere J. Non-invasive ventilation for children with acute respiratory failure in the developing world: literature review and an implementation example. *Paediatr. Respir. Rev.* 2014; **15**: 181–7.
31 Mundel T, Feng S, Tatkov S, Schneider H. Mechanisms of nasal high flow on ventilation during wakefulness and sleep. *J. Appl. Physiol. (1985)* 2013; **114**: 1058–65.
32 von Ungern-Sternberg BS, Regli A, Schibler A, Hammer J, Frei FJ, Erb TO. The impact of positive end-expiratory pressure on functional residual capacity and ventilation homogeneity impairment in anesthetized children exposed to high levels of inspired oxygen. *Anesth. Analg.* 2007; **104**: 1364–8 table of contents.
33 Humphreys S, Pham TM, Stocker C, Schibler A. The effect of induction of anesthesia and intubation on end-expiratory lung level and regional ventilation distribution in cardiac children. *Paediatr. Anaesth.* 2011; **21**: 887–93.
34 von Ungern-Sternberg BS, Regli A, Frei FJ *et al.* A deeper level of ketamine anesthesia does not affect functional residual capacity and ventilation distribution in healthy preschool children. *Paediatr. Anaesth.* 2007; **17**: 1150–5.

Crocodile's craving by Ethan Harithupan (13).