

## PERSONAL PRACTICE

## Continuous distending pressure

Colin Morley

### Introduction

Continuous positive airway pressure (CPAP), positive end expiratory pressure (PEEP), or continuous negative expiratory pressure (CNEP) all provide low pressure distension of the lungs during expiration. It is one of the most effective treatments in neonatal medicine. This personal review sets out why premature babies need help to prevent airway collapse. It describes different techniques for the administration of CPAP and what has been learnt from previous studies and trials. The references quoted in this paper have been obtained by Medline searching on the keywords, continuous distending pressure, CPAP and PEEP, and from papers, chapters, and books on fetal and neonatal physiology and neonatal ventilation, and the Cochrane Collaboration review.

Premature infants find it difficult to maintain functional residual capacity (FRC) and upper airway patency for many reasons:

- 1 As term infants initiate breathing, large negative and positive pressures are generated to open the lung.<sup>1 2</sup> Preterm infants may not generate enough pressure to achieve an effective FRC.
- 2 The larynx modulates tidal breathing with partial expiratory closure to maintain the end expiratory lung volume.<sup>3 4</sup> The newborn infant with a low lung volume grunts to maintain FRC.<sup>5</sup> If the baby cannot maintain laryngeal tone or is intubated lung volume can be lost.
- 3 The lung fluid clearance is slower after premature birth so that the lung contains more water, especially after caesarean section. Although there is no direct evidence, in very premature babies, fluid may continue to be secreted after birth, adding to the problems of maintaining alveolar patency.<sup>6</sup>
- 4 Lung volume can be preserved by shortening the expiratory time and preventing the lung emptying completely.<sup>3 7</sup> If babies with respiratory distress syndrome fail to do this (because of apnoea or fatigue) atelectasis and subsequently respiratory failure develop.
- 5 Premature infants lack the fat laden superficial fascia in the neck that helps stabilise the airway of older infants. Negative pressures during inspiration may collapse the extrathoracic airway.<sup>8-11</sup> Premature babies are not able to mobilise effectively the genioglossus muscle that normally stabilises the pharynx.<sup>12</sup> Infants with periodic

breathing easily develop obstruction of the pharynx that is reversible by CPAP.<sup>13</sup>

- 6 The premature lung has a relatively undeveloped internal architecture for holding the lung open. The immature lung also has thicker and fewer alveolar septa which reduce the potential for gas exchange.<sup>10 14</sup> There are insufficient numbers of alveolar channels for collateral ventilation.
- 7 The chest wall is so soft and flexible that it may be incapable of holding the lung open during inspiratory efforts. It distorts during inspiration, reducing the tidal volume.<sup>15 16</sup>
- 8 The horizontal ribs and flatter diaphragm of the premature infant reduce the potential for lung expansion. During rapid eye movement sleep, intercostal muscle activity may be lost.<sup>17</sup>
- 9 There is a high incidence of patent ductus arteriosus with a left to right shunt which increases the fluid in the lungs, predisposing to pulmonary oedema.
- 10 Mature lung surfactant lowers the surface tension and facilitates lung expansion at birth, and "solidifies," splinting the lungs open during expiration.<sup>18</sup> Premature lungs lack adequate surfactant. This predisposes to low lung volume and airway collapse.
- 11 The epithelium of the collapsing lung becomes damaged and plasma proteins exude on to the surface. These inhibit surfactant function. This contributes to increased adhesion of the epithelial surfaces.
- 12 Reduced arterial oxygen impairs the function of the respiratory muscles, lung enzymes, and channels clearing lung fluid.
- 13 With decreased lung volume ventilation perfusion mismatch occurs accompanied by an increased alveolar-arterial oxygen gradient with increased arterial carbon dioxide concentrations.

Table 1 gives details of the clinical trials and physiological studies on continuous distending pressure.

### How can CPAP or PEEP help the baby with a respiratory problem?

- 1 It reduces upper airway occlusion by decreasing upper airway resistance and increasing the pharyngeal cross sectional area.<sup>13</sup>
- 2 It reduces right to left shunting.<sup>43</sup>
- 3 It reduces obstructive apnoeas.<sup>44</sup>
- 4 It increases the FRC.<sup>45 46</sup>

Department of  
Neonatal Medicine  
Royal Women's  
Hospital  
132 Grattan Street  
Carlton  
Melbourne  
Victoria 3035  
Australia  
C Morley

Correspondence to:  
Professor Colin Morley.  
Email: morleyc@cryptic.rch.  
unimelb.edu.au

Table 1 Clinical trials and physiological studies of continuous distending pressures

Year	Trials	Results
1971	Gregory <i>et al</i> <sup>19</sup>	First use of CPAP in neonates showed oxygenation increased by 38% within 12 hours and survival improved.
1973	Rhodes and Hall <sup>20</sup>	Randomised infants to face mask CPAP or control. Mortality was 53% in controls and 27% with CPAP.
1973	Kattwinkel <i>et al</i> <sup>21, 22</sup>	Showed that CPAP significantly reduces the duration of exposure to high levels of oxygen.
1973	Herman and Reynolds <sup>23</sup>	Showed that oxygenation increased as PEEP increased from 0 to 5 cm H <sub>2</sub> O with no extra improvement at 10 cm H <sub>2</sub> O. Arterial PaCO <sub>2</sub> increased as the PEEP increased but at 10 cm H <sub>2</sub> O the PaCO <sub>2</sub> was "unacceptably high".
1976	Berman <i>et al</i> <sup>24</sup>	Intubated infants recovering from RDS had the lowest oxygenation and lung volume with zero PEEP. They improved when the infants received a PEEP of 2 cm H <sub>2</sub> O or were extubated.
1976	Speidal <i>et al</i> <sup>25</sup>	Nasal CPAP regularised the respiratory pattern and abolished or reduced apnoeic attacks.
1979	Alexander <i>et al</i> <sup>26</sup>	Nasal CPAP and continuous negative pressure both improved oxygenation. Nasal CPAP was easier. Both techniques produce some air leaks.
1981	Stewart <i>et al</i> <sup>27</sup>	Increases in PEEP improved oxygenation per cm H <sub>2</sub> O mean airway pressure than increasing peak inspiratory pressure or changing the I:E ratio. Increasing PEEP increased the PaCO <sub>2</sub> .
1982	Engelke <i>et al</i> <sup>28</sup>	Nasal CPAP post extubation compared with head box oxygen showed that nasal CPAP improved oxygenation, carbon dioxide levels, pH, chest x-rays and lowered the respiratory rate.
1986	Kim <i>et al</i> <sup>29</sup>	Endotracheal tube CPAP for six hours reduced extubation success compared with extubation to a head box.
1987	Hausdorf <i>et al</i> <sup>30</sup>	Increasing PEEP proportionally reduced the left and right ventricular stroke volume and cardiac output and slightly impaired the systemic and pulmonary blood flows.
1988	Trang <i>et al</i> <sup>31</sup>	Cardiac index fell at PEEP of 3, 6, 9 cm H <sub>2</sub> O by 6%, 11% and 19%. The stiffer the lungs the smaller the effect. Despite this, heart rate and mean blood pressure did not change.
1991	Higgins <i>et al</i> <sup>32</sup>	In a randomised trial of extubation strategies for babies <1 kg: 75% were successfully extubated when treated with nasal CPAP and only 30% if treated in a head box.
1992	Greenough <i>et al</i> <sup>33</sup>	Acutely ventilated infants increased oxygenation and carbon dioxide as PEEP levels increased. Chronically ventilated infants showed the same trends for oxygen but with little effect on PaCO <sub>2</sub> .
1993	Chan <i>et al</i> <sup>34</sup>	Compared extubation to head-box oxygen or nasal CPAP at 3 cm H <sub>2</sub> O and showed no difference in failure rate between the two.
1994	Da Silva <i>et al</i> <sup>35</sup>	Increasing PEEP from 2 to 5 cm H <sub>2</sub> O increased the FRC from 18.4 ml/kg to 22.6 ml/kg (about 20 to 30 ml/kg in healthy neonates). Increasing PEEP by 1 cm H <sub>2</sub> O increased the FRC on average by 1.3 ml/kg.
1994	Bartholomew <i>et al</i> <sup>36</sup>	A 1 cm H <sub>2</sub> O change in PEEP had twice the effect on tidal volume as a 2 cm H <sub>2</sub> O change in peak pressure in paralysed infants. Reductions in PEEP are as effective at reducing PaCO <sub>2</sub> as increasing the peak inspiratory pressure.
1995	Tapia <i>et al</i> <sup>37</sup>	Showed no clear effect of extubating babies to nasal CPAP compared with head-box oxygen at 3 to 4 cm H <sub>2</sub> O.
1995	So <i>et al</i> <sup>38</sup>	Reintubation occurred in 16% of infants treated with CPAP compared with 52% treated in a head box.
1998	Davis <i>et al</i> <sup>39</sup>	Different levels of CPAP applied to infants with tracheomalacia increased the lung volume but did not alter the forced expiratory flow.
1998	Ahluwalia <i>et al</i> <sup>40</sup>	In a cross over study showed there was no difference in oxygenation, other physiological parameters or comfort score between single prong nasal CPAP and the Infant Flow Driver.
1998	Davis <i>et al</i> <sup>41</sup>	This study randomised extubated babies to nasal CPAP or head box and showed that 66% were successfully extubated to CPAP and 40% to head box. Nasal CPAP after extubation reduces the adverse events without increasing side effects.
1998	Robertson <i>et al</i> <sup>42</sup>	Ventilated premature babies were randomised at extubation to nasal CPAP or head box oxygen although the head box group also received CPAP if criteria were met. There was no difference in successful extubation between the groups. Therefore CPAP may be used for prophylaxis or rescue treatment at extubation.

- 5 It reduces inspiratory resistance<sup>45, 47</sup> by dilating the airways. This permits a larger tidal volume for a given pressure, so reducing the work of breathing.<sup>48</sup>
- 6 It reduces the compliance of very compliant lungs<sup>49</sup> and, in these lungs, reduces the tidal volume and minute volume.
- 7 It increases the compliance and tidal volume of stiff lungs with a low FRC by stabilising the chest wall and counteracting the paradoxical movements.<sup>48</sup>
- 8 It regularises and slows the respiratory rate.<sup>25, 28</sup>
- 9 It reduces the incidence of apnoea.<sup>50, 51</sup>
- 10 It increases the mean airway pressure and improves ventilation perfusion mismatch.<sup>43</sup>
- 11 It conserves surfactant on the alveolar surface.<sup>52, 53</sup>
- 12 It diminishes alveolar oedema.
- 13 The increased pressure helps overcome the inspiratory resistance of an endotracheal tube.<sup>54</sup>
- 14 Nasal CPAP after extubation reduces the proportion of babies requiring reventilation.<sup>28, 41, 55</sup>
- 15 Oxygenation is related to the surface area and carbon dioxide elimination is related to the minute volume. Normalising lung volume improves oxygenation and carbon dioxide elimination.<sup>28, 56</sup>

#### Indications for CPAP or increasing PEEP during ventilation

- 1 At birth, in a spontaneously breathing baby who has respiratory difficulty.

- 2 When there is increased work of breathing indicated by: recession, grunting, nasal flaring, increased oxygen requirements or increased respiratory rate.
- 3 Poorly expanded or infiltrated lung fields on chest x-ray picture.
- 4 Atelectasis.
- 5 Pulmonary oedema.
- 6 Pulmonary haemorrhage.
- 7 Apnoea of prematurity.
- 8 Recent extubation.
- 9 Tracheomalacia or other abnormalities of the airways, predisposing to airway collapse.
- 10 Phrenic nerve palsy.<sup>57</sup>

#### How should CPAP be given?

The American Association for Respiratory Care has published some useful advice.<sup>58</sup> The following devices have been used with greater or lesser success:

##### FACE MASK<sup>20</sup>

This provides a positive pressure but it is difficult to get a good seal on the baby's face. Pressure is lost when the mask is removed. It is difficult to use a nasogastric or orogastric tube.

##### HEAD BOX WITH A SEAL<sup>19</sup>

This is a head box which seals round the baby's neck and has a valve to control the pressure. It is difficult to get a good seal, and there is poor access to the baby's face. Attention to the face causes loss of pressure, and the high gas flow cools the baby; it is also noisy.

**NEGATIVE PRESSURE BOX<sup>59</sup>**

This is a negative pressure cuirass around the baby's chest and abdomen. It is difficult to get a good seal, and there is poor access to the baby. Handling the baby causes loss of pressure, and the high gas flow cools the baby.

**NOSE PIECE**

This is difficult to attach to the baby and get a good seal without undue pressure.

**ENDOTRACHEAL TUBE<sup>60</sup>**

An endotracheal tube bypasses the larynx so PEEP should be applied to reduce loss of lung volume. An endotracheal tube should not be used solely for CPAP because the resistance makes it hard for the baby to inspire. Endotracheal CPAP may be used just before extubation, to ensure the baby does not become apnoeic without intermittent inflation.

**NASAL PRONG(S)<sup>22 61</sup>**

This is the most effective and least unsatisfactory method of delivering CPAP. As neonates are nose breathers, nasal CPAP is easily facilitated. One or two prongs are inserted into the nostrils and attached to a ventilator or a device for delivering CPAP. Double prongs have not been shown to be better than a single prong appropriately used. A new device<sup>62</sup> is said to reduce the work of breathing<sup>63</sup> but there are few clinical data to substantiate any superiority over other devices.<sup>40</sup> The prong can be short, inserted about 1.5 cm into the nostril, or deep into the pharynx. Long nasal prongs have not been shown to be any better than short prongs and they have the added difficulty of higher resistance and risk of blockage.

I favour a short soft single nasal prong (the end of an endotracheal tube for convenience and economy). It should be as wide as possible to reduce the resistance. The flow must be high enough to maintain a positive pressure and flow during inspiration. The humidity must be high to reduce damage to the mucosa and prevent secretions drying in the tube. A dummy in the baby's mouth helps maintain the pressure.<sup>64</sup>

The problems with nasal CPAP are that: the tubes become displaced and pressure is lost; the tubes become blocked and pressure is not delivered; the baby cries and pressure is lost; and they make the nose sore.

**What level of CPAP/PEEP should be used?**

Studies have investigated methods to optimise the pressure. These have analysed changes in oesophageal pressure,<sup>65 66</sup> or the slope of the inspiratory limb of the pressure volume curve in paralysed babies.<sup>67 68</sup> No simple and reliable method of finding the optimal level has been found.

The level of CPAP or PEEP needs to be altered to suit the baby's differing problems.

- 1 If the infant has stiff lungs or low lung volumes, increasing the distending pressure improves oxygenation up to about 8 cm H<sub>2</sub>O. Some babies may need a higher pressure. We commonly use 10 cm H<sub>2</sub>O.

- 2 If the pressure is too high overdistension may occur and the oxygenation and carbon dioxide removal may be compromised.
- 3 Increasing pressure increases carbon dioxide retention, although often by not very much,<sup>69</sup> so there is a trade off between improving the oxygenation and a rise in the carbon dioxide concentration.
- 4 Conversely, if a baby is being treated with CPAP or PEEP and the carbon dioxide concentrations are high, then reducing the pressure may improve the carbon dioxide.

Studies by Ahluwalia (personal communication) showed that oxygenation improved with increasing PEEP up to about 8 cm H<sub>2</sub>O. Arterial carbon dioxide also increased linearly. This effect was similar for babies of different gestational ages, postnatal ages, and severity of the lung disease. There was no significant effect on blood pressure with different levels of PEEP. Chan's study<sup>34</sup> showed little effect of nasal CPAP. This may be because the level was too low at 3 cm H<sub>2</sub>O. The Cochrane review of nasal CPAP at extubation<sup>71</sup> suggested a level of 5 cm H<sub>2</sub>O or more was more effective than lower levels.

To determine the CPAP or PEEP pressure:

- 1 Look at the chest x-ray picture. Do the lungs look collapsed or oedematous, or well expanded? High or low pressures may be required depending on the problem.
- 2 If oxygenation is the main problem increase the distending pressure.
- 3 If carbon dioxide retention is the main problem reduce the distending pressure.
- 4 Start at 4–5 cm H<sub>2</sub>O and gradually increase up to 10 cm H<sub>2</sub>O to stabilise the oxygenation while maintaining a pH > 7.25 and PaCO<sub>2</sub> < 8.0 kPa.

**Should CPAP be used early or later?**

Studies<sup>66 68</sup> have shown that early treatment with CPAP reduces the quantity and length of oxygen treatment.

**Should CPAP be used after a baby has been extubated?**

Babies breathe, oxygenate better, and are less likely to need re-intubation, particularly if they were ventilated for respiratory distress syndrome, if they are treated with nasal CPAP immediately after extubation.<sup>70</sup> This may be because the larynx does not function properly during the hours after extubation. The Cochrane Collaboration review<sup>71</sup> concluded: "Nasal CPAP is effective in preventing failure of extubation and reducing oxygen use at 28 days of life in preterm infants following a period of endotracheal intubation and IPPV."

**Contraindications to CPAP**

- 1 The need for ventilation because of ventilatory failure—inability to maintain oxygenation and the arterial PaCO<sub>2</sub> < 8 kPa and pH > 7.25.
- 2 Upper airway abnormalities (cleft palate, choanal atresia, tracheo-oesophageal fistula, diaphragmatic hernia).
- 3 Severe cardiovascular instability.

- 4 Very unstable respiratory drive with frequent apnoeas or bradycardias not improved by CPAP.

#### Hazards/complications of CPAP/PEEP

- 1 Prong obstruction so the baby mouth breathes and receives less oxygen and pressure than expected.
- 2 Overdistension of the lung and reduction in tidal volume if the lung is compliant and the pressure is relatively high predisposing to: air leaks, carbon dioxide retention, increased work of breathing.
- 3 Impedance of pulmonary blood flow with increased pulmonary vascular resistance and decreased cardiac output, resulting in venous pooling.
- 4 Gastric distension.
- 5 Nasal irritation, damage to the septal mucosa,<sup>72</sup> or skin damage and necrosis from the fixing devices.
- 6 Failure of the disconnect alarms because of the increased resistance in the prong or obstruction in the prongs continuing to produce a high pressure.
- 7 The prongs come out of the nose.

#### Inadvertent PEEP

Inadvertent PEEP may be a problem in ventilated babies.<sup>73</sup> Fast rate ventilation may have an expiratory time that is so short that there is inadequate time for full expiration. Old ventilators have a slow responding expiratory valve that impedes the expiratory flow.

Care has to be taken when babies have "normal" expansion of the lungs on the chest x-ray picture—that is, undergoing surgery, or ventilated with low FIO<sub>2</sub> or low peak pressures. It can be recognised clinically when oxygenation deteriorates because the pressure is increased. Except in babies with chronic lung disease, an expiratory time of 0.5 seconds will be sufficient. Remember that babies frequently shorten the expiratory time by increasing the respiratory rate, to create their own intrinsic PEEP.

#### Weaning babies from CPAP

Nasal CPAP is important after babies with respiratory distress syndrome are extubated from IPPV. The pressure required and when it is used have to be determined by clinical experience. A baby who is not having apnoeic or bradycardic episodes and requires a low inspired oxygen concentration does not have to have CPAP. It is a matter of trial and error to see how they manage. Conversely, a baby who requires a high level of inspired oxygen and is clinically unstable will probably benefit from CPAP.

#### Unresolved issues

Some of the areas that need to be addressed are: the role of CPAP at birth, methods for determining the optimal level of CPAP, and the optimal method of delivering it.

To conclude, a continuous distending pressure to the lungs of premature babies aids airway stability, lung expansion and improves oxygena-

tion. Applied early and with pressures of at least 5 cm H<sub>2</sub>O it reduces the need for subsequent support. Ignore it at your babies' peril.

I thank Dr Jag Ahluwalia in Cambridge and Dr Peter Davis in Melbourne for helpful discussions.

- 1 Karlberg MH, Cherry RB. Respiratory studies in newborn infants. II. Development of mechanics of breathing during the first week of life. *Acta Paediatr* 1962;131(suppl):121.
- 2 Milner AD, Vyas H. Lung expansion at birth. *J Pediatr* 1982;101:879–86.
- 3 Kosch PC, Stark AR. Dynamic maintenance of end-expiratory lung volume in full term infants. *J Appl Physiol Respir Environ Exercise Physiol* 1984;57:1126–33.
- 4 Chernick V. Continuous distending pressure in hyaline membrane disease. *Pediatrics* 1973;52:114–5.
- 5 Harrison VC, Heese HB, Klein M. The significance of grunting in hyaline membrane disease. *Pediatrics* 1968;41:549.
- 6 Bland RD. Dynamics of pulmonary water before and after birth. *Acta Paediatrica Scandinavica* 1983;305:12–20.
- 7 Martin RJ, Okken A, Katona PG, Klaus MH. Effect of lung volume on expiratory time in the newborn infant. *J Appl Physiol Respir Environ Exercise Physiol* 1978;45:18–23.
- 8 Wilson SL, Thach BT, Brouillette RT, Abu-Osbar YK. Upper airway patency in the human infant: influence of airway pressure and posture. *J Appl Physiol Respir Environ Exercise Physiol* 1980;48:500–4.
- 9 Thach BT, Tilden JT, et al, eds. The role of pharyngeal airway obstruction in prolonged apneic spells. In: *Sudden Infant Death Syndrome*. New York: Academic Press, 1983: 279–92.
- 10 Mathew OP, Roberts JL, Thach BT. Airway obstruction during mixed and obstructive apnea. *J Pediatr* 1982;100:964–8.
- 11 Cohen G, Henderson-Smart D. Upper airway stability and apnea during nasal occlusion in newborn infants. *J Appl Physiol* 1986;60:1511–7.
- 12 Gauda EB, Miller MJ, Carlo W, DiFiore JM, Johnsen DC, Martin RJ. Genioglossus response to airway occlusion in apneic versus non-apneic infants. *Pediatric Res* 1987;22:683–7.
- 13 Alex CG, Aronson RM, Onal E, Lopata M. Effects of continuous positive airway pressure on upper airway and respiratory muscle activity. *J Appl Physiol* 1987;62:2026–30.
- 14 Hodson A. Normal and abnormal structural development of the lung. In: Polin RA, Fox WW, Eds. *Fetal and Neonatal Physiology*. 2nd edn. Philadelphia: WB Saunders, 1998: 1033–46.
- 15 Gerhardt T, Bancalari E. Chest wall compliance in full term and preterm infants. *Acta Paediatr Scand* 1980;69:359–64.
- 16 Heldt G, McIlroy MB. Dynamics of chest wall in preterm infants. *J Appl Physiol* 1987;62:170–4.
- 17 Guslits BG, Gaston SE, Bryan MH, England SJ, Bryan AC. Diaphragmatic work of breathing in premature human infants. *J Appl Physiol* 1987;62:1410–5.
- 18 Bangham AD. "Surface tensions" in the lung. *Biophys J* 1995;68:1630–3.
- 19 Gregory GA, Kitterman JA, Phibbs RH, Tooley WH, Hamilton WK. Treatment of the idiopathic respiratory distress syndrome with continuous positive airway pressure. *N Engl J Med* 1971;284:1333–40.
- 20 Rhodes PG, Hall RT. Continuous positive airway pressure delivered by face mask in infants with the idiopathic respiratory distress syndrome: a controlled study. *Pediatrics* 1973;52:1–5.
- 21 Bancalari E, Gerhardt T, Monkus EF. Simple device for producing continuous negative pressure in infants with IRDS. *Pediatric Res* 1973;7:396.
- 22 Kattwinkel J, Fleming D, Cha CC, Fanaroff AA, Klaus MH. A device for administration of continuous positive airway pressure by the nasal route. *Pediatrics* 1973;52:131–4.
- 23 Herman S, Reynolds EOR. Methods for improving oxygenation in infants mechanically ventilated for severe hyaline membrane disease. *Arch Dis Child* 1973;48:612–7.
- 24 Berman LS, Fox WW, Raphaely RC, Downes JJ. Optimum levels of CPAP for tracheal extubation of newborn infants. *J Pediatr* 1976;89:109–12.
- 25 Speidel BD, Dunn PM. Effect of continuous positive airway pressure on breathing patterns of infants with respiratory distress syndrome. *Lancet* 1975;i:302–4.
- 26 Alexander G, Gerhardt T, Bancalari E. Hyaline membrane disease. Comparison of continuous negative pressure and nasal positive airway pressure in its treatment. *Am J Dis Child* 1979;133:1156–9.
- 27 Stewart AR, Finer NN, Perters KL. Effects of alterations of inspiratory and expiratory pressures and inspiratory and expiratory ratios on mean airway pressure, blood gases and intracranial pressure. *Pediatrics* 1981;67:474–81.
- 28 Engelke SC, Roloff DW, Kuhns LR. Postextubation nasal continuous positive airway pressure. *Am J Dis Child* 1982;136:359–61.
- 29 Kim EH, Boutwell WC, Ramachandran P. Successful extubation of very low birth weight infants (VLBW) from low intermittent mandatory ventilation rate. *Pediatric Res* 1986;20:1633A.
- 30 Hausdorf G, Hellwege H-H. Influence of positive end-expiratory pressure on cardiac performance in premature infants: a doppler-echocardiographic study. *Crit Care Med* 1987;15:661–4.

- 31 Trang TTH, Tibballs J, Mercier JC, Beaufile F. Optimization of oxygen transport in mechanically ventilated newborns using oximetry and pulsed Doppler-derived cardiac output. *Crit Care Med* 1988;16:1094-7.
- 32 Higgins RD, Richter SE, Davis JM. Nasal continuous positive airway pressure facilitates extubation of very low birth weight neonates. *Pediatrics* 1991;88:999-1003.
- 33 Greenough A, Chan V, Hird MF. Positive end expiratory pressure in acute and chronic respiratory distress. *Arch Dis Child* 1992;67:320-3.
- 34 Chan V, Greenough A. Randomised trial of methods of extubation in acute and chronic respiratory distress. *Arch Dis Child* 1993;68:570-2.
- 35 Da Silva WJ, Abbasi S, Pereira G, Bhutani VK. Role of positive end-expiratory pressure changes on functional residual capacity in surfactant treated preterm infants. *Pediatr Pulmonol* 1994;18:89-92.
- 36 Bartholomew KM, Brownlee KG, Snowden S, Dear PRF. To PEEP or not too PEEP. *Arch Dis Child Fetal Neonatal ed* 1994;70:F209-F12.
- 37 Tapia JL, Bancalari A, Gonzalez A, Mercado ME. Does continuous positive airway pressure (CPAP) during weaning from intermittent mandatory ventilation in very low birth weight infants have risks or benefits? A controlled trial. *Pediatr Pulmonol* 1995;19:269-74.
- 38 So B-H, Tamura M, Mishina J, Watanabe T, Kamoshita S. Application of nasal continuous positive airway pressure to early extubation in very low birthweight infants. *Arch Dis Child Fetal Neonatal Ed* 1995;72:F191-F3.
- 39 Davis S, Jones M, Kislign J, Angelicchio C, Tepper RS. Effect of continuous positive airway pressure on forced expiratory flows in infants with tracheomalacia. *Am J Respir Crit Care Med* 1998;158:148-52.
- 40 Ahluwalia JS, White DK, Morley CJ. Infant Flow Driver or single nasal prong continuous positive airway pressure: short-term physiological effects. *Acta Paediatr* 1998;87:325-7.
- 41 Davis P, Jankov R, Doyle L, Henschke P. Randomised controlled trial of nasal continuous positive airway pressure in the extubation of infants weighing 600 to 1250 g. *Arch Dis Child Fetal Neonatal Ed* 1998;78:F1-F4.
- 42 Robertson NJ, Hamilton PA. Randomised trial of elective continuous positive airway pressure (CPAP) compared with rescue CPAP after extubation. *Arch Dis Child Fetal Neonatal Ed* 1998;79:F58-F60.
- 43 Cotton RB, Lindstrom DP, Kanarek KS, Sundell H, Stahlman MT. Effect of positive-end-expiratory-pressure on right ventricular output in lambs with hyaline membrane disease. *Acta Paediatr Scand* 1980;69:603-6.
- 44 Miller MJ, Carlo WA, Martin RJ. Continuous positive airway pressure selectively reduces obstructive apnea in preterm infants. *J Pediatr* 1985;106:91-4.
- 45 Saunders RA, Milner AD, Hopkin IE. The effects of CPAP on lung mechanics and lung volumes in the neonate. *Biol Neonate* 1976;29:178-81.
- 46 Bose C, Lawson EE, Greene A, Mentz W, Friedman M. Measurement of cardiopulmonary function in ventilated neonates with respiratory distress syndrome using re-breathing methodology. *Pediatric Res* 1986;20:316-20.
- 47 Cogswell JJ, Hatch DJ, Kerr AA, Taylor B. Effects of continuous positive airway pressure on lung mechanics of babies after operation for congenital heart disease. *Arch Dis Child* 1975;50:799-804.
- 48 Harris TR, Wood BR. Physiologic Principles. In: Goldsmith JB, Karotkin EH, eds. *Assisted Ventilation*. 3rd edn. Philadelphia: WB Saunders, 1996: 21-68.
- 49 Field D, Milner AD, Hopkin EK. Effects of positive end expiratory pressure during ventilation of the preterm infant. *Arch Dis Child* 1985;60:843-7.
- 50 Kattwinkel J, Nearnam HS, Fanaroff AA, et al. Apnoea of prematurity: comparative therapeutic effects of cutaneous stimulation and nasal CPAP. *J Pediatr* 1975;86:588
- 51 Martin RJ, Nearnam HS, Katona PG, et al. Effect of low CPAP on the reflex control of respiration in the preterm infant. *J Pediatr* 1977;90:976-9.
- 52 Fariday EE. Effect of distension on release of surfactant in excised dog's lungs. *Respir Physiol* 1976;27:99-114.
- 53 Verder H, Robertson B, Griesen G, et al. The Danish-Swedish multicentre study group. Surfactant therapy and nasal continuous positive airway pressure for newborns with respiratory distress syndrome. *N Engl J Med* 1994;331:1051-5.
- 54 Fiastro JF, Habib MP, Quan SF. Pressure support compensation for inspiratory work due to endotracheal tubes and demand continuous positive airway pressure. *Chest* 1988;93:499-505.
- 55 Higgins RD, Richter SE, Shapiro DL, Davis JM. Nasal continuous positive airway pressure (NCPAP) facilitates successful extubation in very low birth weight (VLBW) infants. *Pediatric Res* 1990;27:209A
- 56 Cotton RB. Pathophysiology of hyaline membrane disease (excluding surfactant). In: Polin RA, Fox WW, eds. *Fetal and Neonatal Physiology*. 2nd edn. Philadelphia: WB Saunders, 1998: 1165-74.
- 57 Bucci G, Marzetti G, Picece-Bucci S, Nodari S, Agostino R, Moretti C. Phrenic nerve palsy treated by continuous positive pressure breathing by nasal cannulae. *Arch Dis Child* 1974;49:230-1.
- 58 AARC Clinical Practice Guideline. Application of continuous positive airway pressure to neonates via nasal prongs or nasopharyngeal tube. *Respiratory Care* 1994;39:817-23.
- 59 Bancalari E, Garcia OL, Jesse MJ. Effects of continuous negative pressure on lung mechanics in idiopathic respiratory distress syndrome. *Pediatrics* 1973;51:485-93.
- 60 Kornhauser MS, Needelman HW, Lealey M. Efficacy of short vs long term CPAP prior to extubation. *Pediatric Res* 1986;20:433A.
- 61 Caliumi-Pellegrini G, Agostino R, Orzalesi M, et al. Twin nasal cannulae for administration of continuous positive airway pressure to newborn infants. *Arch Dis Child* 1974;49:228-9.
- 62 Moa G, Nilsson K, Zetterstrom H, Jonsson LO. A new device for administration of nasal continuous positive airways pressure in the newborn: an experimental study. *Crit Care Med* 1988;16:1238-42.
- 63 Klausner JF, Lee AY, Hutchinson AA. Decreased imposed work with a new nasal continuous positive airway pressure device. *Pediatr Pulmonol* 1996;22:188-94.
- 64 Pedersen JE, Nielsen K. Oropharyngeal and esophageal pressures during mono- and binasal CPAP in neonates. *Acta Paediatr* 1994;83:143-9.
- 65 Bonta BW, Uauy R, Warshaw JB, Motoyama ET. Determination of optimal continuous positive airway pressure for the treatment of IRDS by measurement of esophageal pressure. *J Pediatr* 1977;91:449-54.
- 66 Tanswell AK, Clubb RA, Smith BT, Boston RW. Individualised continuous distending pressure applied within 6 hours of delivery in infants with respiratory distress syndrome. *Arch Dis Child* 1980;55:33-9.
- 67 Patrinos ME, Balaraman V, Ku T, et al. Promoting meconium clearance from the lungs of neonatal piglet with asymmetric high frequency oscillation. *Pediatric Res* 1997;42:342-7.
- 68 Mathe JC, Clement A, Chevalier JY, Gaultier C, Costil J. Use of total inspiratory pressure-volume curves for determination of appropriate positive end-expiratory pressure in newborns with hyaline membrane disease. *Intensive Care Med* 1987;13:332-6.
- 69 Hansen TN, Corbet AJS, Kenny JD, Courtney JD, Rudolph AM. Effects of oxygen and constant positive pressure breathing on aADCO<sub>2</sub> in hyaline membrane disease. *Pediatric Res* 1979;13:1167-71.
- 70 Kim EH, Boutwell WC. Successful direct extubation of very low birthweight infants from low intermittent mandatory ventilation. *Pediatrics* 1987;80:409-14.
- 71 Davis P G, Henderson-Smart D J. Prophylactic post-extubation nasal CPAP in preterm infants. *Neonatal module of the Cochrane database of systematic reviews 1997*. The Cochrane Collaboration. Issue 1. Oxford: Update Software, 1998.
- 72 Robertson NJ, McCarthy LS, Hamilton PA, Moss ALH. Nasal deformities resulting from flow driver continuous positive airway pressure. *Arch Dis Child Fetal Neonatal Ed* 1996;75:F209-F12.
- 73 Simbruner G. Inadvertent positive end-expiratory pressure in mechanically ventilated newborn infants: detection and effect on lung mechanics and gas exchange. *J Pediatr* 1986;108:589-95.