# Table of Contents

## KEY REFERENCES

### THERAPY OVERVIEW

| S1 | Continuous positive airway pressure: Physiology and comparison of devices (Gupta) | 2 |

### COMPARISON TO MECHANICAL VENTILATION

| S2 | Randomized trial of early bubble continuous positive airway pressure for very low birth weight infants (Tapia) | 5 |
| S3 | Early CPAP versus surfactant in extremely preterm infants (SUPPORT) | 8 |
| S4 | Early bubble CPAP and outcomes in ELBW preterm infants (Narendran) | 11 |
| S5 | Is chronic lung disease in low birth weight infants preventable? A survey of eight centers (Avery) | 13 |
| S6 | Bubble CPAP versus ventilator CPAP in preterm neonates with early onset respiratory distress – a randomized controlled trial (Tagare) | 15 |

### COMPARISON TO OTHER TYPES OF CPAP

| S7 | Bubble and ventilator-derived nasal continuous positive airway pressure in premature infants: work of breathing and gas exchange (Courtney) | 18 |
| S8 | A Randomized Controlled Trial of Post-extubation Bubble Continuous Positive Pressure Versus Infant Flow Driver Continuous Positive Airway Pressure in Preterm Infants with Respiratory Distress Syndrome (Gupta) | 20 |
| S9 | A Comparison of Underwater Bubble Continuous Positive Airway Pressure with Ventilator-Derived Continuous Positive Airway Pressure in Premature Neonates Ready for Extubation (Lee) | 23 |
**Infant Key References**

**THERAPY OVERVIEW**


**COMPARISON TO MECHANICAL VENTILATION**


**COMPARISON TO OTHER TYPES OF CPAP**


Continuous positive airway pressure: physiology and comparison of devices

AIM:
AIM: This review discusses the physiologic effects of continuous positive airway pressure (CPAP) and factors affecting CPAP delivery, and reviews the available data comparing different CPAP devices.

DETAILS:
The non-invasive respiratory support technique CPAP has been studied extensively in pre-term infants, tested both as the primary method of respiratory support and as continuing support following mechanical ventilation. CPAP maintains functional residual capacity, reducing the work of breathing and conserving surfactant on the alveolar surface through a variety of actions including increasing pharyngeal cross-sectional area, improving diaphragmatic activity, enhancing pulmonary compliance, and decreasing airway resistance.

CPAP involves the delivery of continuous distending pressure (CDP) using a mixture of air and oxygen and a CDP-generating device. Nasal CPAP (nCPAP) can be generated using two main device types, variable flow or continuous flow.

RESPIRATORY PHYSIOLOGY AND CPAP:
The mechanism by which CPAP improves respiratory function in newborns has not been fully elucidated. CPAP induces changes in intra-pleural pressure and improves pulmonary mechanics and thoraco-abdominal synchrony through increasing end-expiratory lung volume and stabilizing the chest wall. CPAP may decrease the resistance to gas flow by increasing the cross-sectional area of the upper airway and preventing the lateral pharyngeal walls from collapsing.

Physiologic effects of CPAP include abolition of upper airway occlusion, decreased resistance of the upper airway, increased diaphragmatic tone and contractility, improvement of lung compliance, increased tidal volume in stiff lungs with low functional residual capacity, improved ventilation/perfusion and decreased oxygen requirement, conservation of surfactant on the alveolar surface and reduction of alveolar edema. nCPAP of ≥5 cm H₂O effectively abolishes mixed or obstructive apnea, but has little to no effect on central apnea. The effectiveness of CPAP in improving outcomes is dependent on the type of CPAP used and the severity of the underlying lung disease.

METHODS OF GENERATING CPAP AND EFFECT OF BUBBLING:
Variable-flow CPAP, such as the Infant Flow Driver (IFD) or Benveniste gas jet-valve CPAP, generates pressure at the airway proximal to the nostrils, using the Bernoulli effect to alter gas flow and maintain constant pressure. IFD CPAP uses the Bernoulli effect to direct gas flow towards each nostril, and the Coanda effect to flip the inspiratory flow and have it exit the generator chamber via the expiratory limb. Decreasing expiratory resistance and maintaining a stable airway pressure during respiration in this way may assist spontaneous breathing and reduce the work of breathing. Benveniste gas-jet valve CPAP uses the Venturi principle to generate variable-flow pressure.
Continuous-flow CPAP, such as bubble/water seal CPAP (bCPAP) or ventilator-derived CPAP, directs gas flow against the resistance of the expiratory limb of the breathing circuit. In bCPAP, heated, humidified blended gas is delivered through a low resistance nasal prong cannula, while the distal end of the expiratory tubing is submerged. The CPAP generated is equal to the depth of this expiratory limb submersion. Bubbling may increase gas exchange through the delivery of low-amplitude, high-frequency oscillations to the lungs, and the degree of bubbling is affected by gas flow rate. In ventilator-derived CPAP, generally changing the expiratory orifice size on the ventilator increases or decreased the CPAP generated, with the exhalation valve, flow and pressure working together to maintain the desired CPAP.

Comparison of CPAP devices: Given the availability of multiple CPAP devices, choosing the most appropriate for a given situation can be complicated, and efforts to optimize delivery of CPAP are ongoing. It is well established that nCPAP decreases the work of breathing; however, there are differences between variable and continuous flow devices. Studies investigating respiratory factors such as work of breathing, lung volume changes, thoraco-abdominal synchrony, changes in pleural pressure and resistance to breathing have generally found advantages associated with variable-flow devices over continuous-flow devices, with variable-flow devices having a more favorable or similar effect on breathing to continuous-flow devices.

In terms of clinical outcomes, comparisons between bCPAP and other CPAP devices in cohort and observational studies suggest advantages associated with bCPAP with respect to delivery room intubations, the use of postnatal steroids, and duration of mechanical ventilation. In randomized controlled trials investigating the use of CPAP at birth, results were more varied; in one study comparing IFD CPAP with binasal prongs versus bCPAP given <12 hours after birth to preterm infants <36 weeks of gestation, oxygen requirement and respiratory rate was significantly (p<0.0001) better with IFD CPAP. In preterm neonates 25–32 weeks of gestation who received either bCPAP or ventilator-derived CPAP with Hudson prongs following initial stabilization, there were no differences in respiratory measurements, CPAP failures, days on CPAP, surfactant use, oxygen need, or rates of bronchopulmonary dysplasia between groups at 36 weeks. In contrast, a study of bCPAP versus ventilator-derived CPAP in preterm neonates with respiratory distress receiving support with either bCPAP or ventilator-derived CPAP found that bCPAP significantly reduced the need for mechanical ventilation in these infants (p=0.03). bCPAP was equivalent to IFD CPAP in terms of the number of days CPAP was required in infants <37 weeks gestation another study, and a comparison of bCPAP with the variable-flow Jet-CPAP showed no significant differences between devices in the CPAP failure rates at 72 hours or the time to CPAP failure.

In randomized studies of infants requiring CPAP after extubation comparing IFD CPAP with ventilator-derived CPAP generally found that IFD CPAP was either superior or similar to ventilator-derived CPAP when used following extubation. A randomized trial of 140 preterm (<30 weeks) neonates and then received bCPAP or IFD CPAP, bCPAP significantly reduced the median duration of CPAP support versus IFD CPAP (2 vs 4 days; p=0.031), and also decreased the extubation failure rate in neonates who were ventilated for ≤14 days (14.1% vs 28.6%; p=0.046).
THE NASAL INTERFACE: ROLE IN DEVICE COMPARISONS AND NASAL SEPTAL INJURY:

It should be noted that use of a comparable nasal interface is important if two CPAP devices are to be compared; the results of studies that use different nasal interfaces for their CPAP devices should be interpreted with caution.

An important complication of nCPAP use is nasal septal injury, which in some cases may destroy the nasal septum and require surgery to repair. Nasal trauma can occur in as many as 35% of neonates undergoing CPAP with nasal prongs, and in some studies those infants who developed nasal septum injuries were managed with a nasal mask. The use of a nasal cannula interface appears to reduce nasal injury according to data gathered to date, but further studies are required to confirm this.

Overall, the success of CPAP depends on factors such as the nasal interface, the experience of the staff and the associated nursing practices employed during its use, and the ease of use of the apparatus.

CONCLUSION:

Overall there are only minor differences between CPAP devices, but evidence to date suggests a trend toward bCPAP being the favored device for post-extubation support. The available evidence should be utilized by neonatal units to select the most appropriate CPAP device and minimize complications.

KEY POINTS

- The effectiveness of CPAP in improving outcomes is dependent on the type of CPAP used and the severity of the underlying lung disease.
- Other factors influencing efficacy include the CPAP generation, the nasal interface used, and the level of nursing care.
- When used for respiratory support after birth, the currently available CPAP devices have comparable efficacy.
- The use of bCPAP in neonates ventilated for less than 2 weeks may reduce extubation failures.
- Nasal injury is still an important issue in settings using CPAP; appropriate choice of nasal interface may assist in minimizing the incidence of these events.
Randomized trial of early bubble continuous positive airway pressure for very low birth weight infants

AIM:
To determine whether early use of bubble continuous positive airway pressure (CPAP) followed by treatment with the INSURE (intubation, surfactant, and extubation) protocol (CPAP/INSURE) reduces the requirement for mechanical ventilation (MV) compared with use of supplemental oxygen, surfactant and MV as required (oxygen/MV) in very low birth weight (VLBW) infants.

METHOD:
This was a randomized, controlled trial conducted in 12 tertiary neonatal intensive care units in South America (Argentina, Chile, Paraguay, Peru and Uruguay). Pre-term infants who were spontaneously breathing 5 minutes post-birth, with a birth weight of 800-1500g were randomized to the two treatment groups. The oxygen saturation target (SpO2) for both groups was 88-94%, and the partial pressure of carbon dioxide (pCO2) target was 45-55 mmHg. Infants randomized to oxygen/MV treatment received oxygen via an oxyhood or a low-flow nasal cannula as required. Infants randomized to CPAP/INSURE received CPAP as soon as possible after randomization using a bubble CPAP system (Fisher & Paykel Healthcare), with a distending pressure of 5cm H2O. CPAP was discontinued after 3-6 hours if there were no signs of respiratory distress syndrome (RDS). Those who developed RDS and had a fraction of inspired oxygen (FiO2) >0.35 were intubated and received surfactant as per the INSURE protocol. During administration of surfactant, ventilation was provided via a T-piece resuscitator with a peak inspiratory pressure of 20cm H2O and a positive-end expiratory pressure of 5cm H2O for 5-10 minutes. Nasal CPAP was then resumed. Infants received a maximum of 4 doses of surfactant; if a third dose of surfactant was required, MV was initiated. The criteria for CPAP failure, intubation and MV were: FiO2 ≥0.60 at least 2 hours post-surfactant administration; three doses of surfactant required; >3 episodes of apnea and bradycardia (heart rate <80 bpm) per hour; a pCO2 >60 mmHg with pH <7.20 on consecutive analyses of arterial blood gases within 30 minutes. If an infant with RDS had been stable for 24 hours and had a FiO2 <0.30 with a CPAP pressure of 4-5cm H2O and RDS had resolved, CPAP was discontinued.

The primary outcome was any requirement for MV between enrollment in the study and hospital discharge. Secondary outcomes included surfactant requirement, bronchopulmonary dysplasia (BPD), pneumothorax, days of oxygen therapy, days of MV, length of hospitalization and death.

RESULTS:
Between November 2006 and September 2009, 256 infants were enrolled in the study and randomized to CPAP/INSURE (n=131) or oxygen/MV (n=125). No significant differences were found in baseline demographics between groups.

Significantly fewer patients in the CPAP/INSURE group than the oxygen/MV group required MV, and the surfactant requirement was also significantly less in those infants receiving CPAP/INSURE therapy (see table). There were no significant differences between groups in any other endpoint. Only infants in the CPAP/INSURE group experienced nasal lesions, but these were considered minor. No other adverse events were found.
### Variable CPAP/INSURE Oxygen/MV p-value

<table>
<thead>
<tr>
<th>Variable</th>
<th>CPAP/INSURE (n=131)</th>
<th>Oxygen/MV (n=125)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RDS, % pts</td>
<td>50.0</td>
<td>56.0</td>
<td>NS</td>
</tr>
<tr>
<td>MV, % pts</td>
<td>29.8</td>
<td>50.4</td>
<td>0.001</td>
</tr>
<tr>
<td>Surfactant requirement, % pts</td>
<td>27.5</td>
<td>46.4</td>
<td>0.002</td>
</tr>
<tr>
<td>Pneumothorax, % pts</td>
<td>3.1</td>
<td>5.6</td>
<td>NS</td>
</tr>
<tr>
<td>O₂ at 28 days of life, % pts</td>
<td>16.0</td>
<td>24.8</td>
<td>0.081</td>
</tr>
<tr>
<td>BPD, % pts</td>
<td>6.9</td>
<td>9.6</td>
<td>NS</td>
</tr>
<tr>
<td>Death, % pts</td>
<td>8.4</td>
<td>9.6</td>
<td>NS</td>
</tr>
<tr>
<td>BPD/Death, % pts</td>
<td>13.7</td>
<td>19.2</td>
<td>NS</td>
</tr>
<tr>
<td>Rate of supplemental O₂ use, % pts</td>
<td>73.3</td>
<td>87.2</td>
<td>NR</td>
</tr>
<tr>
<td>Infants receiving 1 surfactant dose, % pts</td>
<td>69.5</td>
<td>58.6</td>
<td>NS</td>
</tr>
<tr>
<td>Duration of O₂ therapy, median days (range)</td>
<td>4.0 (0.1-116)</td>
<td>3.0 (0.1-144)</td>
<td>NS</td>
</tr>
<tr>
<td>Duration of MV, median days (range)</td>
<td>2.5 (0.1-51)</td>
<td>2.0 (0.1-68)</td>
<td>NS</td>
</tr>
<tr>
<td>Duration of hospitalisation, median days (range)</td>
<td>48 (1-118)</td>
<td>50 (0-173)</td>
<td>NS</td>
</tr>
</tbody>
</table>

BPD, bronchopulmonary dysplasia; CPAP, continuous positive airway pressure; INSURE, intubation, surfactant, and extubation; MV, mechanical ventilation; NR, not reported; NS, not significant; O₂, oxygen; Pts, patients.

**DISCUSSION:**
This study showed that the use of a CPAP/INSURE strategy reduced the requirement for MV in VLBW infants weighing between 800g and 1500g at birth, compared with a strategy involving oxygen via an oxyhood or nasal cannula and early surfactant administration followed by MV. These results suggest that the disease course of RDS in infants treated with early CPAP is more benign, leading to less need for surfactant and MV. Although the study was not powered to detect differences in secondary endpoints, there were non-significant trends towards reductions in the incidence of BPD, pneumothorax and death in patients treated with CPAP/INSURE versus oxygen/MV. Both strategies were not associated with any significant adverse events.

**CONCLUSION:**
The study findings show that the use of less invasive ventilator strategies in VLBW infants is a feasible option in the South American health system. These results could be very useful in developing countries where resources such as ventilators and surfactants are in short supply, since it shows that early provision of nasal CPAP administered inexpensively can significantly reduce the requirement for mechanical ventilation and surfactant with no increase in morbidity or death.
KEY POINTS:

• Use of the less invasive CPAP/INSURE strategy to treat VLBW infants with RDS is a feasible strategy.
• Early CPAP treatment leads to less need for mechanical ventilation (MV) and use of surfactant with no increase in morbidity of death.
• In health systems in developing countries, use of the CPAP/INSURE strategy may result in less use of expensive resources.
Early CPAP versus surfactant in extremely preterm infants

AIM:
To compare early treatment with surfactant and early treatment with continuous positive airway pressure (CPAP) in extremely low birth weight infants.

METHOD:
In this multicenter trial, 1316 infants born at 24 weeks to 27 weeks 6 days of gestation were randomized to early intratracheal administration of surfactant within 1 hour of birth followed by a conventional ventilation strategy (n=653), or to early treatment with CPAP with subsequent intubation and ventilation if prespecified criteria were met (n=663). Infants in the CPAP group who were intubated within 48 hours after birth were also given surfactant. In the delivery room, CPAP was delivered using a T-piece resuscitator, a neonatal ventilator or an equivalent device. After transfer to the NICU, CPAP was given using a ventilator, a purpose-built flow driver or a bubble CPAP circuit.

The primary outcome of the study was death or bronchopulmonary dysplasia (using physiologically-defined criteria), and the prespecified secondary outcome was bronchopulmonary dysplasia (defined as the need for supplemental oxygen at 36 weeks). Infants were stratified into two groups based on gestational age: 24 weeks to 25 weeks 6 days (n=565), and 26 weeks to 27 weeks 6 days (n=751).

This study also compared the effects of two different target ranges for oxygen saturation, but these results were presented in a separate publication [NEJM 2010 May 27; 362 (21):1959-1969].

RESULTS:
Interventions and outcomes in the two treatment groups are reported in the table (next page). A greater number of infants in the CPAP group were alive and free from the need for mechanical ventilation by day 7 compared with the surfactant group (p=0.01). The adjusted mean number of days of mechanical ventilation required was significantly lower in the early CPAP versus early surfactant group (24.8 vs 27.7 days; p=0.03). There were no significant differences between the early CPAP and early surfactant groups with respect to the need for supplemental oxygen, the number of patients with any air leak in the first 14 days, the incidence of necrotizing enterocolitis requiring treatment, the incidence of grade 3 or 4 intraventricular hemorrhage and the incidence of severe retinopathy of prematurity.
95% CI = 95% confidence intervals; PPV = positive pressure ventilation; CPAP = continuous positive airway pressure; NICU = neonatal intensive care unit; BPD = bronchopulmonary dysplasia; NS = not significant.

<table>
<thead>
<tr>
<th>Patients</th>
<th>Early CPAP</th>
<th>Early Surfactant</th>
<th>Relative risk with CPAP (95% CI)</th>
<th>Adjusted P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Interventions</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PPV in delivery room</td>
<td>435/662 (65.7%)</td>
<td>606/652 (92.9%)</td>
<td>0.71 (0.67, 0.75)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CPAP in delivery room</td>
<td>538/663 (81.1%)</td>
<td>146/653 (22.4%)</td>
<td>3.66 (3.16, 4.25)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Intubation in delivery room:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>For any reason</td>
<td>227/660 (34.4%)</td>
<td>609/652 (93.4%)</td>
<td>0.37 (0.34, 0.42)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>For resuscitation</td>
<td>215/660 (32.6%)</td>
<td>176/652 (27.0%)</td>
<td>1.21 (1.02, 1.43)</td>
<td>0.02</td>
</tr>
<tr>
<td><strong>Surfactant treatment</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>In delivery room</td>
<td>93/660 (14.1%)</td>
<td>335/652 (51.4%)</td>
<td>0.28 (0.23, 0.34)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>In delivery room or NICU</td>
<td>443/660 (67.1%)</td>
<td>646/653 (98.9%)</td>
<td>0.67 (0.64, 0.71)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Epinephrine in delivery room</td>
<td>13/660 (2.0%)</td>
<td>27/653 (4.1%)</td>
<td>0.48 (0.25, 0.91)</td>
<td>0.02</td>
</tr>
<tr>
<td><strong>Outcomes</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BPD or death by 36 weeks:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Physiological definition</td>
<td>317/663 (47.8%)</td>
<td>333/653 (51.0%)</td>
<td>0.95 (0.85, 1.05)</td>
<td>0.30</td>
</tr>
<tr>
<td>Oxygen requirement definition</td>
<td>323/663 (48.7%)</td>
<td>353/653 (54.1%)</td>
<td>0.91 (0.83, 1.01)</td>
<td>0.07</td>
</tr>
<tr>
<td>BPD by 36 weeks:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Physiological definition</td>
<td>223/569 (39.2%)</td>
<td>219/539 (40.6%)</td>
<td>0.99 (0.87, 1.14)</td>
<td>0.92</td>
</tr>
<tr>
<td>Oxygen requirement definition</td>
<td>229/569 (40.2%)</td>
<td>239/539 (44.3%)</td>
<td>0.94 (0.82, 1.06)</td>
<td>0.32</td>
</tr>
<tr>
<td>Death by 36 weeks:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infants born at 24 weeks to 25 weeks 6 days of gestation</td>
<td>57/285 (20.0%)</td>
<td>82/280 (29.3%)</td>
<td>0.68 (0.5, 0.92)</td>
<td>0.01</td>
</tr>
<tr>
<td>Infants born at 26 weeks to 27 weeks 6 days of gestation</td>
<td>37/378 (9.8%)</td>
<td>32/373 (8.6%)</td>
<td>1.12 (0.72, 1.75)</td>
<td>0.61</td>
</tr>
<tr>
<td>Death during hospitalisation:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infants born at 24 weeks to 25 weeks 6 days of gestation</td>
<td>23.9%</td>
<td>32.1%</td>
<td>0.74 (0.57, 0.98)</td>
<td>0.03</td>
</tr>
<tr>
<td>Infants born at 26 weeks to 27 weeks 6 days of gestation</td>
<td>10.8%</td>
<td>10.2%</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Survival without need for high-frequency or conventional ventilation at 7 days</td>
<td>362/655 (55.3%)</td>
<td>318/652 (48.8%)</td>
<td>1.14 (1.03, 1.25)</td>
<td>0.01</td>
</tr>
<tr>
<td>Postnatal corticosteroid therapy for BPD</td>
<td>47/649 (7.2%)</td>
<td>83/631 (13.2%)</td>
<td>0.57 (0.41, 0.78)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
DISCUSSION:
Early surfactant treatment has been shown to reduce the risk of chronic lung disease in preterm infants. In addition, there is increasing evidence that early use of CPAP might decrease the rate of intubation and mechanical ventilation in very preterm infants with respiratory distress. The initial strategy of early CPAP compared with early intubation and surfactant treatment was chosen for this study on the basis that it would provide clinically relevant results. Further analysis to compare 18- to 22-month survival without neurodevelopmental impairment in the two treatment groups is underway. The results showing a significant reduction in the risk of death in infants in the CPAP group born at 24 to 25 weeks 6 days of gestation, but not in those born at a later gestational age, should be interpreted with caution because of the post-hoc nature of the analysis and the number of secondary analyses performed on the data.

CONCLUSION:
Based on the results of this study, CPAP could be considered as an alternative to routine intubation and administration of surfactant in preterm infants.

KEY POINTS:
• There is no difference between an early CPAP strategy and an early intubation and surfactant strategy for the combined endpoint of death or bronchopulmonary dysplasia in preterm infants with respiratory distress.
• In preterm infants with respiratory distress, lower rates of intubation, reduced corticosteroid use and a shorter duration of mechanical ventilation are associated with use of early CPAP compared with early intubation and surfactant.
• CPAP can be considered as an alternative to routine intubation and administration of surfactant in preterm infants with respiratory distress.
Early bubble CPAP and outcomes in ELBW preterm infants

AIM:
To determine whether early use of bubble nasal continuous positive airway pressure (CPAP) could improve respiratory outcomes in extremely low birth weight (ELBW) infants.

METHOD:
Respiratory outcomes for ELBW infants (401–1,000 grams) treated with bubble CPAP from 1 July 2000 to 10 October 2001 at a neonatal tertiary care unit in Cincinnati, OH, USA were compared with those of a historical control group of ELBW infants who received standard treatment without nasal CPAP between 1 January 1998 and 31 December 1999.

Standard treatment for ELBW infants with moderate-to-severe respiratory distress syndrome consisted of intermittent positive pressure ventilation with bag and mask in the delivery room, early intubation, surfactant administration and intermittent mandatory ventilation. Bubble CPAP at 5 cmH₂O was delivered via Hudson nasal prongs and initiated immediately after the initial steps of drying and stimulation in all spontaneously-breathing infants. The fraction of inspired oxygen (FiO₂) was adjusted based on pulse oximetry to maintain saturation at 92–96%. If intubation and surfactant therapy were required, infants were weaned aggressively back to CPAP as early as possible.

RESULTS:
Demographics and non-pulmonary outcomes were similar in infants treated with nasal CPAP (n=79) and historical controls (n=92), apart from mean weight at 36 weeks’ corrected gestational age, which was higher in the nasal CPAP group (2,134 vs 1,917 grams; p<0.05). Respiratory outcomes that improved significantly in infants treated with early bubble CPAP are shown in the table. There were no significant differences between treatment groups in the proportion of infants who received surfactant or invasive mechanical ventilation, were diagnosed with respiratory distress syndrome, had chronic lung disease at 36 weeks, or received antenatal corticosteroids; the rate of death or chronic lung disease also did not differ significantly between the nasal CPAP and control groups.

<table>
<thead>
<tr>
<th>Respiratory outcomes</th>
<th>Historical controls (n=92)</th>
<th>Bubble nCPAP (n=79)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intubation in delivery room, % patients</td>
<td>59.8</td>
<td>31.6^</td>
</tr>
<tr>
<td>Mean time on invasive mechanical ventilation, days</td>
<td>28</td>
<td>13^</td>
</tr>
<tr>
<td>Mean time on nCPAP, days</td>
<td>4</td>
<td>16^</td>
</tr>
<tr>
<td>Postnatal steroids, % patients</td>
<td>42.4</td>
<td>13.9^</td>
</tr>
<tr>
<td>nCPAP use at 24 hours, % patients</td>
<td>10.9</td>
<td>46.8^</td>
</tr>
</tbody>
</table>

^ p<0.05 vs historical controls.

CONCLUSION:
Early use of bubble CPAP in ELBW infants reduced the need for intubation in the delivery room, improved weight gain, and was safe and inexpensive.
KEY POINTS

- Early use of bubble CPAP in ELBW infants is safe, effective and inexpensive.
- Early use of bubble CPAP in ELBW infants reduces the need for intubation the delivery room.
- Early use of bubble CPAP in ELBW infants improves weight gain.
Is chronic lung disease in low birth weight infants preventable? A survey of eight centers

AIM:
To investigate potential reasons for differences in rates of chronic lung disease of prematurity between eight US centers after birth weight, race and sex have been taken into account.

METHOD:
This retrospective analysis included 1,625 infants weighing 700–1,500 grams at birth from eight major neonatal intensive care units in the USA. Data were collected for a ≥12-month period between 1 January 1982 and 31 December 1984. Chronic lung disease of prematurity was defined as oxygen dependency at 28 days of age. Data collected included sex, birth weight, race, and information about general nursery practices (e.g. use of tocolytics, prenatal corticosteroids, resuscitation, muscle relaxants, intubation, mechanical ventilation, desired levels of blood gas values and fluid intake, type of incubator and staffing levels).

RESULTS:
Overall survival rates were relatively similar across centers, ranging from 78% to 84%. In contrast, there was much more variability in survival rates without oxygen at 28 days. As expected, survival without added oxygen at 28 days was significantly higher in heavier versus lighter infants (p<0.01), in females versus males (p<0.01) and non-White versus White infants (p<0.01). On multivariate analysis, birth weight, sex and race were significant predictors of chronic lung disease, in the anticipated directions.

Even after adjusting for birth weight, sex and race, one center (Columbia) had a much lower rate of chronic lung disease than the other centers. Analysis showed two significant differences between practices at this center and all the others. Firstly, Columbia instituted continuous positive airway pressure (CPAP) at ≈5 cmH₂O with nasal prongs soon after birth in all infants showing signs of respiratory distress; only 42% of infants went on to require intubation and mechanical ventilation. This is in contrast with the two centers that had the highest rates of chronic lung disease where nasal CPAP was either infrequently or never used. Secondly, muscle relaxants were almost never used at Columbia, where infants were allowed to breathe spontaneously with minimal but adequate ventilator settings.
CONCLUSION:
Differences between large US centers in the rate of chronic lung disease of prematurity may be due to differential use of early nasal CPAP and muscle relaxants. Early intervention with nasal CPAP could facilitate the maintenance of an adequate functional residual capacity and improve gas exchange, while the associated reduction in intubation reduces the risks associated with this invasive procedure.

KEY POINTS
• Birth weight, sex and race cannot account for all differences between neonatal care facilities in the rate of chronic lung disease of prematurity.
• Centers that use nasal CPAP early after birth in premature infants with respiratory distress may have lower rates of chronic lung disease of prematurity compared with those that don't use early nasal CPAP.
Bubble CPAP versus ventilator CPAP in preterm neonates with early onset respiratory distress – a randomized controlled trial

AIM:
To compare the efficacy and safety of bubble continuous positive airway pressure (CPAP) with ventilator-derived CPAP (CPAP) in preterm neonates with moderate-to-severe respiratory distress.

METHOD:
A randomized controlled trial of 145 neonates born at <37 weeks’ gestation who developed respiratory distress. Within the first 6 hours of life, these neonates had Silverman Anderson (SA) scores ≥4 and requirement for oxygen at >30% and were randomized to receive oxygen therapy with Bubble CPAP (Fisher & Paykel Healthcare) [n=57] or ventilator CPAP (Bear Cub 750 PSV ventilator; Bear Medical Systems) [n=57]. Both therapies were delivered via appropriately-sized nasal prongs, and started at 6 cmH₂O and 40% oxygen, with adjustments made as clinically indicated to maintain oxygen saturation at 88–93%. Success of CPAP therapy was defined as stoppage of CPAP after reduction in pressure (<4 cmH₂O) and oxygen (<30%) requirements, clinical improvement (SA score ≤3) and no requirement for CPAP or mechanical ventilation over the next 72 hours. Failure was defined as the presence of any of the following: worsening SA score; increase in pressure (>8 cmH₂O) and oxygen (>60%) requirements; ≥2 episodes of apnea requiring positive pressure ventilation; shock. Arterial blood gases for determination of the arterial to alveolar oxygenation (a/A) ratio were analyzed within 30 minutes of randomization.

RESULTS:
The success rate was significantly higher in neonates treated with Bubble CPAP versus ventilator CPAP (see table). The difference in success rate between Bubble CPAP and ventilator CPAP was greatest in neonates with a gestational age of >30 weeks or a birthweight of >1500g. Failure of CPAP was significantly more likely in neonates who had a higher SA score and a lower a/A ratio. A significantly higher number of patients treated with ventilator CPAP required surfactant (n=18 vs 9 with Bubble CPAP; p<0.05). In addition, a higher proportion of neonates who failed CPAP required surfactant therapy.
### Patients (%)

<table>
<thead>
<tr>
<th></th>
<th>Ventilator CPAP (n=52)</th>
<th>Bubble CPAP (n=57)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of CPAP, h [median (range)]</td>
<td>30 (2–160)</td>
<td>36 (2–160)</td>
<td>NS</td>
</tr>
<tr>
<td>Outcome of CPAP, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Success</td>
<td>36 (63.2)</td>
<td>47 (82.5)</td>
<td>0.03</td>
</tr>
<tr>
<td>Morbidity</td>
<td>33 (57.9)</td>
<td>37 (64.9)</td>
<td>NS</td>
</tr>
<tr>
<td>Mortality</td>
<td>5 (8.8)</td>
<td>4 (7.0)</td>
<td>NS</td>
</tr>
<tr>
<td>Morbidities associated with CPAP device, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dislodgement</td>
<td>28 (49.1)</td>
<td>26 (45.6)</td>
<td>NS</td>
</tr>
<tr>
<td>Dilation of nares</td>
<td>12 (21.1)</td>
<td>17 (29.8)</td>
<td>NS</td>
</tr>
<tr>
<td>Nasal septal injury</td>
<td>4 (7.0)</td>
<td>12 (21.1)</td>
<td>0.03</td>
</tr>
<tr>
<td>Abdominal distension</td>
<td>3 (5.3)</td>
<td>8 (14.0)</td>
<td>NS</td>
</tr>
<tr>
<td>Skin erosion</td>
<td>1 (1.8)</td>
<td>2 (3.5)</td>
<td>NS</td>
</tr>
<tr>
<td>Air leak</td>
<td>2 (3.5)</td>
<td>0 (0)</td>
<td>NS</td>
</tr>
<tr>
<td>Secondary pneumonia</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>NS</td>
</tr>
</tbody>
</table>

NS, not significant.

**CONCLUSION:**

Nasal CPAP has a well-established role in the management of neonates with respiratory distress. In this study, one of only a few comparing ventilator CPAP and Bubble CPAP as primary respiratory support, Bubble CPAP was significantly more successful than ventilator CPAP in preterm neonates with early-onset, moderate-to-severe respiratory distress. It has been suggested that Bubble CPAP is more effective in cases of milder respiratory distress syndrome, in addition data from this study suggests that the magnitude of difference between treatments in favor of Bubble CPAP was greatest in neonates with a gestational age of >30 weeks or a birth weight of >1500g. Overall, those with more severe disease were more likely to fail CPAP therapy; these findings were significant. The simplicity and low cost of Bubble CPAP compared with ventilator CPAP make it a particularly attractive treatment option, particularly in settings where resources including referral to tertiary care centers are limited. A larger trial is required to validate the findings of this study and confirm the safety and effectiveness of Bubble CPAP for the treatment of early respiratory distress in preterm neonates.
KEY POINTS

• The success rate of Bubble CPAP in preterm neonates with respiratory distress is higher than that of ventilator CPAP.

• The advantage of using Bubble CPAP over ventilator CPAP is greatest in neonates with a gestational age >30 weeks or a birthweight of >1500g.

• Data from larger trials are required to confirm the safety and effectiveness of Bubble CPAP for the treatment of early respiratory distress in preterm neonates.

• Attractive features of Bubble CPAP include its simplicity and low cost.
Bubble and ventilator-derived nasal continuous positive airway pressure in premature infants: work of breathing and gas exchange

AIM:
To compare work of breathing (WOB) and other short-term respiratory outcomes between bubble nasal continuous positive airway pressure (nCPAP) and ventilator-derived NCPAP (nCPAP) at equivalent nasal prong pressures in preterm infants.

METHOD:
This crossover study enrolled preterm infants with a birth weight of <1500 g who required nasal CPAP for mild respiratory distress (fraction of inspired oxygen [FiO2] ≤0.40). Infants received both Bubble nCPAP and ventilator nCPAP; the order of device was randomized. Ventilator nCPAP was given by a calibrated VIP Bird infant ventilator [VIASYS HealthCare] using the positive end-expiratory pressure (PEEP) control. For Bubble nCPAP, the expiratory limb of ventilator tubing was submerged in a purpose-built water chamber [Airways Development LLC] to the desired level of nasal CPAP (cm H2O); this system was similar to commonly used Bubble nCPAP systems and enabled easy conversion from ventilator nCPAP to Bubble nCPAP. Hudson prongs were used for all infants on both nasal CPAP devices. Intraprong pressure was measured using a calibrated pressure transducer [Validyne DP45-28].

Calibrated respiratory inductance plethysmography [Respiband Plus and Respitrace; SensorMedics] was used to record abdominal and chest wall movements, and pleural pressure was measured with an oesophageal balloon catheter [Ackrand Laboratories]. Each infant was studied at pressures of 3, 5, 7, 4 and 2 cm H2O while on each nasal CPAP device. Data were collected continuously after 5 minutes of stabilization at each setting.

RESULTS:
Eighteen preterm infants (mean birthweight 1101 g; mean gestational age 28 weeks; mean age at study 13 days) were included in the study. Nasal prong pressures on Bubble nCPAP and ventilator nCPAP were nearly identical, allowing for meaningful comparisons between the two devices. There were no statistically significant differences between Bubble nCPAP and ventilator nCPAP for WOB (inspiratory, elastic and resistive WOB). Tidal volume, respiratory rate, phase angle, minute ventilation and lung compliance were also not significantly different between the two nasal CPAP devices. Likewise, heart rate, oxygen saturation and transcutaneous (Tc) CO2 were not significantly different between Bubble nCPAP and ventilator nCPAP, but TcO2 was significantly higher with Bubble nCPAP (p=0.01 vs ventilator nCPAP).

DISCUSSION:
Nasal CPAP is effective for the management of respiratory distress syndrome in preterm infants. However, preterm infants have variable responses to nasal CPAP. It has previously been shown that Bubble nCPAP has prominent oscillations in airway pressure at the nasal prong level, which are diminished at the alveolar level. This study found that most short-term respiratory outcomes were comparable between Bubble nCPAP and ventilator nCPAP, with the exception of TcO2, which was significantly higher with Bubble nCPAP. High-frequency oscillations in intraprong pressure were substantially greater with Bubble nCPAP than ventilator nCPAP, but measurement devices were not sensitive enough to accurately reflect oscillations at the chest/abdomen and intrapleural level.
CONCLUSION:
WOB and most other short-term respiratory outcomes are similar between Bubble nCPAP and ventilator nCPAP with equivalent delivered airway pressure. Improved TcO₂ with Bubble nCPAP suggests that the greater oscillations in airway pressure may lead to improved oxygenation compared with ventilator nCPAP.

KEY POINTS:
• WOB and most other short-term respiratory outcomes are similar between Bubble nCPAP and ventilator nCPAP with equivalent delivered airway pressure.
• TcO₂ is significantly higher with Bubble nCPAP compared with ventilator nCPAP, suggesting that greater oscillations in airway pressure may lead to improved oxygenation.
A Randomized Controlled Trial of Post-extubation Bubble Continuous Positive Pressure Versus Infant Flow Driver Continuous Positive Airway Pressure in Preterm Infants with Respiratory Distress Syndrome

**AIM:**
To compare the efficacy and safety of post-extubation management with bubble continuous positive airway pressure (CPAP) and Infant Flow Driver (IFD) CPAP in preterm infants with respiratory distress syndrome (RDS).

**METHOD:**
One hundred and forty preterm infants (24-29 weeks' gestation or birth weight 600-1500g) were randomized to receive bubble CPAP [Fisher & Paykel Healthcare] or IFD CPAP [Electro Medical Equipment] after extubation. Readiness for extubation was determined objectively using the minute ventilation test (MVT).

CPAP was delivered at 6 cm H2O and was decreased by 1 cm H2O if the infant was stable over the preceding 12 hours, to a minimum of 4 cm H2O. Conversely, if the reduction in CPAP was not tolerated, increases of 1 cm H2O, to a maximum of 6 cm H2O were permitted. For bubble CPAP, a fixed flow rate of 6 L/min was used and for IFD CPAP the flow rate was adjusted to deliver the appropriate CPAP pressure. CPAP was delivered using short binasal prongs provided by the device manufacturers. Discontinuation of CPAP was attempted when the infant had been stable for 12 hours and the oxygen requirement was <30%.

Patients were stratified on the basis of the duration of mechanical ventilation: ≤14 days or >14 days. The primary endpoint of the study was successful extubation maintained for at least 72 hours; secondary endpoints were maintenance of successful extubation for 7 days, total duration of CPAP support, and the incidences of chronic lung disease and complications of prematurity.

**RESULTS:**
Data for the primary and secondary endpoints are reported in the table. In infants mechanically ventilated for ≤14 days (n=127), the extubation failure rate in the first 72 hours was significantly lower in infants on bubble CPAP compared with IFD CPAP. There was no significant difference in extubation failure between the 2 devices in infants ventilated for >14 days (n=13). The overall extubation failure rate in the first 72 hours was 21.3% in infants ventilated for ≤14 days compared with 30.8% in those ventilated for >14 days (p=0.484).
## Data at the end of 3 weeks' treatment

<table>
<thead>
<tr>
<th></th>
<th>Type of CPAP</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Bubble (n=71)</td>
<td>IFD (n=69)</td>
<td>P value</td>
<td></td>
</tr>
<tr>
<td>Failed extubation (patients)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>16.9%</td>
<td>27.5%</td>
<td>0.130</td>
<td></td>
</tr>
<tr>
<td>Within first 72 hours in patients ventilated for ≤14 days</td>
<td>14.1%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(n=64)</td>
<td></td>
<td>28.6%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(n=63)</td>
<td></td>
<td>0.046</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Within first 72 hours in patients ventilated for &gt;14 days</td>
<td>42.9%</td>
<td>16.7%</td>
<td>0.308</td>
<td></td>
</tr>
</tbody>
</table>

### Median duration of CPAP [days (95% CI)]

<p>| | | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Excluding deaths</td>
<td>2 (1-3)</td>
<td>4 (2-6)</td>
<td>0.031</td>
</tr>
<tr>
<td>Including deaths</td>
<td>3 (1.5-4.5)</td>
<td>4 (2.1-5.7)</td>
<td>0.754</td>
</tr>
</tbody>
</table>

## Complications of prematurity (patients)

<p>| | | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic lung disease at 36 weeks</td>
<td>20%</td>
<td>30%</td>
<td>NS</td>
</tr>
<tr>
<td>Survival without bronchopulmonary dysplasia</td>
<td>75%</td>
<td>66%</td>
<td>NS</td>
</tr>
<tr>
<td>Patent ductus arteriosis requiring treatment</td>
<td>17%</td>
<td>25%</td>
<td>NS</td>
</tr>
<tr>
<td>Severe IVH/periventricular leukomalacia</td>
<td>15.6%</td>
<td>13.5%</td>
<td>NS</td>
</tr>
<tr>
<td>Necrotizing enterocolitis (Bell stage ≥2)</td>
<td>7.0%</td>
<td>4.3%</td>
<td>NS</td>
</tr>
<tr>
<td>Retinopathy of prematurity requiring treatment</td>
<td>5.6%</td>
<td>7.2%</td>
<td>NS</td>
</tr>
<tr>
<td>Death before discharge</td>
<td>5.6%</td>
<td>0</td>
<td>NS</td>
</tr>
<tr>
<td>Pneumothorax</td>
<td>0</td>
<td>0</td>
<td>NS</td>
</tr>
</tbody>
</table>

CI = confidence interval; IVH = intraventricular haemorrhage; NS = not significant.
**DISCUSSION:**
The use of CPAP in preterm infants helps to facilitate extubation, thus reducing the risks associated with prolonged intubation and ventilation. IFD CPAP has a dedicated flow driver and generator with a unique fluidic flip mechanism which adjusts gas flow throughout the breathing cycle. IFD CPAP has been shown to provide stable pressure delivery, improve functional residual capacity, reduce thoracoabdominal asynchrony and decrease work of breathing (WOB). Bubble CPAP uses a fixed gas flow and a column of water in the expiratory limb and has been shown to improve gas exchange and protect against lung injury. No previous controlled clinical trials have directly compared these two devices in preterm infants. The shorter duration of CPAP in the bubble device group may be a result of some unknown physiological advantage, but this cannot be determined in the current unblinded study. Despite previous theoretical concerns about an increased risk of necrotizing enterocolitis during bubble CPAP, this was not observed in this trial. Additional data on long-term clinical outcomes are required to more fully elucidate any differences between CPAP devices for the post-extubation management of preterm infants.

**CONCLUSION:**
Bubble and IFD CPAP have similar effectiveness for the post-extubation management of preterm infants with RDS. For infants ventilated for ≤14 days, bubble CPAP was associated with a significantly higher successful extubation rate. In addition, the median duration of CPAP support was significantly shorter than that of IFD CPAP.

**KEY POINTS:**
- Bubble and IFD CPAP have similar effectiveness for the post-extubation management of preterm infants with RDS.
- In preterm infants mechanically ventilated for ≤14 days, bubble CPAP is associated with a significantly higher successful extubation rate than IFD CPAP.
- The duration of CPAP support after extubation in mechanically ventilated preterm infants is significantly shorter when bubble CPAP versus IFD CPAP is used.
A comparison of underwater bubble continuous positive airway pressure with ventilator-derived continuous positive airway pressure in premature neonates ready for extubation

AIM:
To investigate whether vibrations produced by bubble continuous positive airway pressure (CPAP) contribute to gas exchange compared with conventional ventilator-driven CPAP in premature neonates.

METHOD:
Premature neonates admitted to the Regional Perinatal Unit at Women's College Hospital in Toronto, Ontario, Canada weighing 750–2000 grams who were endotracheally intubated and ready for extubation (oxygen requirement 21% and ventilator rate ≤10) were included in this crossover study. Infants were randomised to receive CPAP in the following sequences for 15 minutes each (total treatment time of 1 hour): ventilator to bubble to ventilator to bubble; or bubble to ventilator to bubble to ventilator. CPAP circuits (Baxter) were almost identical for ventilator-driven and bubble therapy. Gas flow at 8 L/min was provided by a continuous source and humidified using a heated humidifier (Fisher & Paykel Healthcare). The expiratory seal for ventilator-driven CPAP was delivered by a Bear Cub or Sechrist ventilator at 5 cmH₂O, and for bubble CPAP was an underwater seal created by immersing a Fisher & Paykel Healthcare underwater column in a reusable glass suction bottle filled with sterile water. With this set-up, vibration frequency was approximately 15–30 Hz and the amplitude of the waveform was 2–4 cmH₂O. In each 15-minute treatment block, tidal volume (TV), minute ventilation (VE), respiratory rate, heart rate, oxygen saturation (SpO₂) and transcutaneous pressure of carbon dioxide (tcPCO₂) were measured four times, three minutes apart after a six-minute stabilisation period and the values were averaged.

RESULTS:
A total of 10 infants were enrolled (mean weight 1350 grams, mean corrected gestational age 30.7 weeks); recruitment was then stopped when an interim analysis yielded a p-value for minute ventilation (VE) of <0.005 between the two forms of CPAP. No significant carryover effects were observed and all infants tolerated CPAP. Key respiratory parameters are shown in the table. There was no difference between the ventilator-driven and bubble CPAP groups with respect to tcPCO₂ and SpO₂.
<table>
<thead>
<tr>
<th>Variable</th>
<th>CPAP</th>
<th>Difference (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Ventilator-driven</td>
<td>Bubble</td>
<td></td>
</tr>
<tr>
<td>VE, mL/min</td>
<td>340±72 (306–374)</td>
<td>205±67 (177–239)</td>
<td>135 (101, 163)</td>
</tr>
<tr>
<td>Corrected VE, mL/kg/min</td>
<td>253±37 (236–270)</td>
<td>157±48 (134–179)</td>
<td>96 (76, 116)</td>
</tr>
<tr>
<td>TV, mL</td>
<td>6.8±2.0 (5.8–7.7)</td>
<td>6.2±2.3 (5.1–7.2)</td>
<td>0.6 (0.1, 1.2)</td>
</tr>
<tr>
<td>Corrected TV, mL/kg</td>
<td>4.9±0.7 (4.6–5.2)</td>
<td>4.5±1.1 (4.0–5.0)</td>
<td>0.4 (0.03, 0.8)</td>
</tr>
<tr>
<td>Heart rate, beats/min</td>
<td>145±17 (137–153)</td>
<td>149±14 (142–156)</td>
<td>−4 (−7, −11)</td>
</tr>
<tr>
<td>Respiratory rate, breaths/min</td>
<td>59±8 (56–63)</td>
<td>55±8 (52–59)</td>
<td>4 (2, 6)</td>
</tr>
</tbody>
</table>

Values are mean ± standard deviation (range).

**CONCLUSION:**

The physiologic effect of bubble CPAP was associated with significant reductions in MV and respiratory rate in premature neonates, without any change in alveolar ventilation. Although not specifically measured in this study, it is possible that the vibrations associated with bubble CPAP simulate high-frequency ventilation and contribute to gas exchange and decreased work of breathing.

**KEY POINTS**

- When all other settings are equal, bubble CPAP reduces VE and respiratory rate to a greater extent than ventilator-driven CPAP in premature neonates.
- The greater reduction in VE observed during bubble versus ventilator-driven CPAP may be the result of vibration-related improvements in gas exchange.
AIRWAY RESISTANCE
A measure of the impedance to ventilation caused by the movement of gas through the airways. This measurement is calculated as the change in pressure along a tube divided by flow.

APGAR SCORE
The evaluation of an infant’s physical condition performed at one and five minutes after birth. The testing is based on a rating of five categories including heart rate, breathing effort, muscle tone, response to stimulation and color to reflect the infant’s ability to adjust to life outside the uterus.

ARterial to Alveolar Oxygenation Ratio (a/A)
A measure of the difference between the alveolar concentration of oxygen and the arterial concentration of oxygen.

BRonchopulmonary Dysplasia (BPD) or Chronic Lung Disease
A form of chronic lung disease that develops in premature neonates treated with oxygen and positive-pressure ventilation.

Bubble Continuous Positive Airway Pressure (BCPAP)
Continuous positive airway pressure therapy delivered via a bubble generator.

Continuous Positive Airway Pressure (CPAP)
A technique of respiratory therapy in which airway pressure is maintained above atmospheric pressure throughout the respiratory cycle by pressurization of the ventilatory circuit.

Continuous Distending Pressure (CDP)
Continuous pressure applied to the lungs to expand them. Can be applied using continuous positive or negative airway pressure to create a partial vacuum.

DEAD SPACE
Volume in the airway path that is common to both the inspiratory and expiratory passages. Volume of gas that does not participate in gas exchange. It is ventilated but NOT perfused by the pulmonary circulation.

• Alveolar dead space: Volume of gas ventilating unperfused alveoli that has no blood perfusion (shunt or pulmonary embolism).
• Anatomic dead space: Volume of gas within the conducting zone of the lungs and upper airway. (Amount of volume that does not enter the alveoli.)
• Mechanical dead space: Expired air that is re-breathed through connecting tubing.
• Physiologic dead space: Anatomic and alveolar dead space.

Endotracheal Tube (ETT)
A tube inserted through the mouth or nose into the trachea to maintain an unobstructed airway.

Extubation
Withdrawing an endotracheal tube (ETT) from a patient’s airway.

Fraction of Inspired Oxygen (FIO₂)
The proportion of oxygen in the air that is inspired.

Insure Protocol
A technique involving intubation to administer surfactant before extubation to CPAP.

Intubation
The insertion of an ETT or tracheostomy tube into the trachea.

Low Birth Weight (LBW)
Birth weight less than 2500g.

Lung Compliance
The ability of the lungs to stretch during a change in volume relative to an applied chamber pressure.

Mechanical Ventilation (MV)
The use of an invasive artificial airway to mechanically assist or replace spontaneous breathing, when patients cannot do so on their own.

Minute Ventilation (VE)
The volume of gas that moves in and out of the lungs in one minute; it is calculated by multiplying the exhaled tidal volume by the respiratory rate.

Nasal Oxygen Cannula
A small, half-moon shaped plastic tube, the ends of which fit into the nostrils of a patient, which is used to deliver oxygen at a concentration higher than that in ambient air.

Neonatal Intensive Care (NICU)
A hospital facility providing intensive nursing and medical care for critically ill newborn infants.

Oxygen Saturation by Pulse Oximetry (SpO₂)
Oxygen saturation as measured by pulse oximetry.

Partial Pressure of Carbon Dioxide (PCO₂)
The part of total blood gas pressure exerted by carbon dioxide gas; a measure of how much carbon dioxide is dissolved in the blood and how well carbon dioxide is able to move out of the body.

Partial Pressure of Oxygen (PaO₂)
The part of total blood gas pressure exerted by oxygen gas; a measure of how much oxygen is dissolved in the blood and how well oxygen is able to move from the airspace of the lungs into the blood.

Positive End Expiratory Pressure (PEEP)
The amount of pressure above atmospheric pressure present in the airway at the end of the expiratory cycle during mechanical ventilation.
POSITIVE END INSPIRATORY PRESSURE (PIP)
The highest pressure applied to the lungs during inspiration.

POSITIVE PRESSURE VENTILATION (PPV)
Administration of oxygen under pressure during mechanical ventilation.

PRETERM
An infant born before 37 weeks gestation regardless of their weight. Usually the preterm infant are found in the NICU of the hospital on some form of respiratory support. They can be further divided into:

- Moderate to late preterm 32 to <37 weeks gestation
- Very preterm 28 to <32 weeks gestation
- Extremely preterm <28 weeks gestation

RESPIRATORY DISTRESS SYNDROME (RDS)
Lung disease of the newborn, most frequently occurring in premature infants, that is caused by abnormally high alveolar surface tension as a result of a deficiency in lung surfactant; also called hyaline membrane disease.

RESPIRATORY RATE
The amount of breaths over a specified time period.

SILVERMAN ANDERSON (SA) SCORE
A scoring system used in newborns to assess the degree of respiratory distress; it evaluates five parameters and assigns a numerical score for each parameter. Scores range from 0 (normal) to 10 (severely depressed respiratory function).

TIDAL VOLUME (VT)
The volume inspired or expired per breath.

TRANSCUTANEOUS CARBON DIOXIDE PRESSURE (tcPCO₂)
The partial pressure of carbon dioxide in arterial blood measured using a transcutaneous sensor.

VENTILATOR CONTINUOUS POSITIVE AIRWAY PRESSURE (VCPAP)
Continuous positive airway pressure therapy delivered via a ventilator.

VERY LOW BIRTH WEIGHT (VLBW)
Infants with birth weight less than 1500g.

WORK OF BREATHING (WOB)
The force required to expand the lung against its elastic properties.