CPAP use in the newborn

What is the evidence?
Clinical uses
- For primary treatment of RDS
- As InSurE strategy for RDS
- Delivery room/Very early CPAP
- Post-extubation
- Apnea of Prematurity

CPAP interfaces
- CPAP generators—continuous flow vs variable flow
CPAP for primary treatment of RDS

- Decreased mortality
- Decreased need for ventilation
- Decreased need for transfer to higher level unit

Ho 2002 (Cochrane review)
Early CPAP group had reduction in MV use [RR 0.55 (95% CI 0.32, 0.96)], no effect on mortality
**Early CPAP + surfactant (InSurE) vs. Selective surfactant and mech. vent**

### Need for mechanical ventilation

**Stevens 2007 (Cochrane review)**

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Early Surfactant n/N</th>
<th>Selective Surfactant n/N</th>
<th>Risk Ratio M-H, Fixed, 95% CI</th>
<th>Weight</th>
<th>Risk Ratio M-H, Fixed, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 FIO2 at Study Entry &lt;= 0.45</td>
<td>13/32</td>
<td>18/30</td>
<td>10.0%</td>
<td>0.68 [0.41, 1.13]</td>
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</tr>
<tr>
<td>Vermont Oxford 2003</td>
<td>54/138</td>
<td>65/132</td>
<td>35.9%</td>
<td>0.79 [0.61, 1.04]</td>
<td></td>
</tr>
<tr>
<td>Dani 2004</td>
<td>0/13</td>
<td>6/14</td>
<td>3.4%</td>
<td>0.08 [0.01, 1.33]</td>
<td></td>
</tr>
<tr>
<td>Reininger 2005</td>
<td>26/52</td>
<td>37/53</td>
<td>19.8%</td>
<td>0.72 [0.52, 0.99]</td>
<td></td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td>235</td>
<td>229</td>
<td><strong>69.0%</strong></td>
<td><strong>0.72 [0.59, 0.87]</strong></td>
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</tr>
</tbody>
</table>

| 2 FIO2 at Study Entry > 0.45 | 15/35 | 28/33 | 15.6% | 0.51 [0.34, 0.76] |
| Texas Research 2004       | 17/65 | 29/67 | 15.4% | 0.60 [0.37, 0.99] |
| **Subtotal (95% CI)**     | 100 | 100 | **31.0%** | **0.55 [0.40, 0.77]** |

| **Total (95% CI)**        | 335 | 329 | **100.0%** | **0.67 [0.57, 0.79]** |

Test for overall effect:
- **Favours early**
- **Favours selective**
- Decreased need for MV
- Decreased air leaks
- Decreased BPD

**Increased surfactant use**

*Stevens 2007 (Cochrane review)*
% of VLBW babies surviving at 28 days

100%

MV users vs CPAP user

5 cms CPAP to all RD, 50% in LR, PaCO2 < 60

(Avery, 1987)
CPAP vs MV: Observational studies

- **Avery 1987**
  - Boston vs New York: BPD 22% vs 4%; MV 75% vs 29%

- **Van Marter 2000**

- **Ammari 2005**
  - Retrospective chart review: Lower mortality, surfactant use, BPD and IVH in CPAP grp vs MV grp

- **Gagliardi 2011**
  - BPD and MV rates higher in units with high delivery room intubation rates in a comparison of 14 NICUs from northern Italy
CPAP vs MV: RCTs

- 25-28 wks, 610 infants with resp distress
- At 5 min of life—CPAP 8 cm H$_2$O vs MV
- Decreased risk of death or oxygen requirements at 28 days of life in CPAP grp but no difference at 36wks
- 46% of the CPAP grp required intubation in first 5 d
- Surfactant use decreased by 50%
- Best benefits for 27-28 weekers
- Increased pneumothorax (9% vs 3%)
CPAP vs MV: RCTs

- SUPPORT trial 2010
- 24 to 27 weeks, 1316 infants
- Intubation & Surfactant (within 1 hour) vs CPAP in delivery room
- No differences in death or BPD (48% vs 51%)
- CPAP group—less frequent use of intubation, postnatal steroids and shorter duration of ventilation
CPAP vs MV: RCTs

- Dunn 2011 (VON-DRM trial)
- 26-29 wks gestation, 648 infants
- 3 groups: CPAP alone (selective INSURE) vs CPAP + surfactant (Prophylactic INSURE) vs MV + surfactant
- No differences in mortality, BPD and other complications of prematurity
Non-invasive vs Invasive resp support
—a systematic review

Schmolzer 2013

- Included 4 RCTs (2782 participants)
- Significant benefit for the combined outcome of death or BPD at 36 weeks (RR 0.91; 95% CI 0.84 to 0.99)
- Significantly decreased need for surfactant (RR 0.40; 95% CI 0.23 to 0.70)
- Significantly decreased need for MV (RR 0.56; 95% CI 0.32 to 0.97)
Can CPAP alone be good enough?

Sandri 2010 (CURPAP trial)

- 25-28 weeks, 208 spontaneously breathing infants
- Intervention - Prophylactic INSURE (Prophylactic surfactant + nCPAP) vs Early selective INSURE (Early nCPAP + selective SRT f/b ext to nCPAP)
- Curosurf (200mg/k used)
- About half of selective INSURE required - SRT
- One-third required MV
- Median time to SRT - 4 hrs
Rojas-Reyes 2012 (Cochrane review)

- Included SUPPORT and VON-DRM trials
- Studies without routine application of CPAP: Decreased mortality and decreased air leaks
- Studies with routine application of CPAP (SUPPORT and VON-DRM trials): Trend towards increased mortality or CLD if prophylactic surfactant used as against early CPAP and selective use.

Conclusion: Benefits of prophylactic surfactant in terms of decreased air leaks and decreased mortality no longer hold true in the era of high antenatal steroid coverage and early routine CPAP application
Studies using early rescue surfactant in presence of RDS

- **Rojas 2009**
  - 27-32 weeks, 279 infants with RDS
  - NCPAP + early rescue surfactant vs NCPAP
  - Decreased need for MV, air-leaks and BPD with early rescue use of surfactant

- **Kandaraju 2013**
  - 28-33 weeks, 153 infants with RDS
  - NCPAP + Early rescue vs NCPAP + Late rescue (FiO₂ > 0.5)
  - Decreased need for MV and trend towards decreased air-leaks with early rescue
When CPAP is applied very early (delivery room) in infants < 28 weeks, before RDS ‘manifests’, ‘prophylactic’ surfactant increases mortality and CLD.

When CPAP is applied early in infants 27-33 weeks with RDS, early rescue surfactant decreases the need for MV, air leaks and BPD.

Hence, an early rescue strategy of surfactant is beneficial.
Post-extubation

Analysis 1.1. Comparison of Nasal CPAP vs Headbox, Outcome: Failure

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>NCPAP n/N</th>
<th>Headbox n/N</th>
<th>Risk Ratio M-H,Fixed,95% CI</th>
<th>Weight</th>
<th>Risk Ratio M-H,Fixed,95% CI</th>
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<tbody>
<tr>
<td>Annibale 1994</td>
<td>15/40</td>
<td>17/42</td>
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<tr>
<td>Chan 1993</td>
<td>19/60</td>
<td>22/60</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Davis 1998</td>
<td>16/47</td>
<td>27/45</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dimitriou 2000</td>
<td>15/75</td>
<td>25/75</td>
<td></td>
<td></td>
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<tr>
<td>Engelke 1982</td>
<td>0/9</td>
<td>6/9</td>
<td></td>
<td></td>
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<tr>
<td>Higgins 1991</td>
<td>7/29</td>
<td>23/29</td>
<td></td>
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<tr>
<td>Peake 2005</td>
<td>16/49</td>
<td>24/48</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>So 1995</td>
<td>4/25</td>
<td>13/25</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tapia 1995</td>
<td>7/29</td>
<td>2/30</td>
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</tbody>
</table>

Total (95% CI) 363 363

Total events: 99 (NCPAP), 159 (Headbox)
Heterogeneity: Chi² = 17.93, df = 8 (P = 0.02); I² = 55%
Test for overall effect: Z = 4.58 (P < 0.00001)

Davis 2007 (Cochrane review)
Post-extubation

*Davis 2007 (Cochrane review)*

- Decreased incidence of respiratory failure (apnea, respiratory acidosis and increased oxygen requirements)
  
  RR 0.62 (0.51, 0.76)  
  RD −0.17 (−0.23, −0.10)  
  NNT 6

- No difference in BPD
Apnea of Prematurity

- Used as a ‘safe’ and ‘effective’ therapy for more than 35 years
- Enhances functional residual capacity, reduces the work of breathing, improves oxygenation, decreases bradycardia
- Opens airway, splints and stabilizes chest wall
- No RCTs
Patient interfaces for CPAP

- Short bi-nasal Hudson’s prongs
- RAM’s cannula
- Bi-nasopharyngeal prongs
- Short bi-nasal Argyle prongs
- Nasal mask
Which interface?

- Short bi-nasal devices are more effective at preventing re-intubation when compared with single nasal prong devices:
  - RR 0.59 (0.41, 0.85),
  - RD −0.21 (−0.35, −0.07)
  - NNT 5 (3, 14)
  
  *(De Paoli AG et al, Cochrane 2008)*

- Lesser resistance, Decreased work of breathing, Better oxygenation, More successful weaning with short bi-nasal prongs
Nasal masks

RCT in < 31 weeks gest. showed decreased intubation rates within 72 h when CPAP was administered with nasal mask vs binasal prongs (28% vs 52%) *(Kieran 2012)*

RAM’s cannula

Binasal prong like oxygen prongs but with a wider diameter, easy application and connection to CPAP/ventilator circuit
Techniques of CPAP generation

- Expiratory flow valve (conventional ventilator) (V-CPAP)
- Underwater tube ‘bubble’ CPAP (B-CPAP)
- Variable flow CPAP (Infant Flow Driver-IFD)
- Heated Humidified High Flow Nasal cannulae (HHHFNC)
Lung recruitment with 3 types of CPAP

- Variable flow
- Constant Flow
- Nasal cannula
Pressure delivery with Bubble CPAP

Kahn 2007
• Courtney 2007

26 babies on CPAP from a bubbling bottle, received vigorous, high amplitude, or slow bubbling for 30 minutes. Pulse oximetry, TcCO2 and RR were not different.
Clinical studies of B-CPAP vs V-CPAP

- Lee 1998
  - Reduction in RR but no difference in blood gas
- Tagare 2010
  - Success rate of B-CPAP vs V-CPAP similar in primary treatment of RDS
- Courtney 2011
  - Cross-over trial of B-CPAP vs V-CPAP in VLBW
  - No difference in WOB, TV, RR, HR
  - TcO2 higher in B-CPAP
- Bahman 2011
  - Higher success and survival with B-CPAP
- Yadav 2012
  - Extubation failure rate lower with B-CPAP vs V-CPAP
- Tagare 2013
  - Higher success rate with B-CPAP vs V-CPAP (83% vs 63%) in primary treatment of RDS
Variable flow CPAP

- Decreased work of breathing
- More stable pressures
- Better lung recruitment

- Is it clinically better?
In primary treatment of RDS


- Bober 2012
  - Multi-centric RCT of 276 infants ≤ 32 wks and 750-1500 g
  - IFD vs V-CPAP
  - Two scenarios: Post-extubation and as Primary treatment for RDS
  - Overall, treatment failure rates within 3 days were similar. In post-extubation grp, infants on IFD had lower failure rates but pneumothorax occurred more frequently. Severe nasal injury occurred significantly less often with IFD in both scenarios.
Clinical studies of IFD in post-extubation setting: IFD vs V-CPAP

- Trials enrolled 36 to 162 infants and compared IFD to V-CPAP delivered through nasophayngeal route, single nasal prong or binasal prongs.

- Two trials (Roukema 1999, Sun 1999) found lower extubation failures with IFD but the more recent trials (Kavvadia 2000, Stefanescu 2003) found no differences or any short term advantages of IFD over V-CPAP.
Clinical studies of IFD in post-extubation setting: IFD vs B-CPAP

- 140 infants, 24-29 weeks, 600-1550 gms
- Rates of successful extubation similar with both devices
- No differences in CLD and other complications
- Those ventilated for ≤ 14 days----Bubble CPAP had high rates of successful extubation
- Median duration of CPAP support shorter with Bubble CPAP

Gupta 2009
Physiological advantages of variable flow CPAP over constant flow CPAP have been documented.

Clinical superiority of variable flow CPAP has not been demonstrated.

Pressure generated by B-CPAP is flow dependent and is usually higher than set pressure. This may account for some of the additional benefits of B-CPAP.
How much CPAP pressure?

- 23-30 wks, 500-1000g infants (n=93) being extubated for the first time and needing FiO2 ≥ 0.25
- Intervention: CPAP pressure 7-9 (high) vs 4-6 cm H2O (low)
- Rates of extubation failure 24% vs 43%
- Rates of reintubation 17% vs 38%
- Differences mainly because of strikingly different results in 500-750g infants
Infants who have their CPAP pressure weaned to a predefined level and then taken off completely have less total time on CPAP and shorter durations of O2 and hospital stay compared to those who have CPAP removed for a predetermined hours each day.
Strategies of weaning from CPAP

- **Abdel-Hady 2011**
  - Weaned to nasal cannula (NC) O2 @ 2LPM when FiO2 < 0.30 vs no NC when FiO2 = 0.21
  - No differences in success of weaning
  - No-NC group had fewer days on O2 and resp support

- **Todd 2012**
  - OFF CPAP vs Cycled ‘OFF’ and ‘ON’ vs Cycled to NC 0.5 LPM and ON
  - OFF CPAP approach had shortened weaning time, CPAP and O2 duration and BPD rates

- **O’Donnell 2013**
  - CPAP to sp breathing on room air vs CPAP to NC 1 LPM air
  - No benefit of low flow room air by NC. Weaning success similar
Strategies of weaning from CPAP

- Abrupt cessation of CPAP, once predefined stability criteria (usually FiO2 = 0.21) have been met, is the best weaning strategy rather than trying to wean to nasal cannula OR cycling OFF and ON.
Key Messages

- Avoiding intubation is of great benefit
- Earlier the CPAP is started, the better it is -- extreme preterms benefit from very early CPAP started right from delivery room table
- Use early rescue surfactant (INSURE)
  Prophylactic surfactant increases mortality / CLD
- Short soft binasal prongs are the best interface. New generation nose masks may offer similar efficacy with less trauma
- IFD vs B-CPAP vs V-CPAP---no clear superiority
“There is perhaps nothing more dangerous for the preterm lung than an anxious physician with an endotracheal tube and a bag”.

Dr. Alan H. Jobe, editor of “The Journal of Pediatrics”
Optimal Strategy to Protect the Preterm Lungs in 21st century?

No Intubation!!
No BPD!