Conclusion: In Canadian NICUs, we observed a higher risk of severe neurologic injury or death among preterm infants of <27 weeks' gestation following a change in practice to initiating resuscitation with either room air or an intermediate oxygen concentration.
**ASSISTED-VENTILATION DEVICES**

Effective ventilation can be achieved with either a flow-inflating or self-inflating bag or with a T-piece mechanical device designed to regulate pressure.\textsuperscript{60–63}

Kattwinkel, Pediatrics 2010

---

**Neonatal Stabilization: Key Points**

- Antenatal care
- Temperature control
- Supplemental oxygen
- **Respiratory support (CPAP, PPV, surfactant)**
- Umbilical cord clamping
- Monitoring

---

**Relationship between \(O_2\)-flow and \(O_2\) concentration**

\[\text{[PIP 25cmH}_2\text{O; RR 40–60/min]}\]


---

**Intubation & Surfactant Prophylaxis**

Nasal-CPAP
**SUPPORT Trial (18-22 months CA)**

<table>
<thead>
<tr>
<th></th>
<th>CPAP Early intubation</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wheezing and cold</td>
<td>47.9%</td>
<td>31.0%</td>
</tr>
<tr>
<td>Wheezing without cold</td>
<td>28.9%</td>
<td>36.5%</td>
</tr>
<tr>
<td>Respiratory illness diagnosed by doctor</td>
<td>47.5%</td>
<td>55.2%</td>
</tr>
<tr>
<td>Physician or emergency room visits for breathing problems</td>
<td>68.0%</td>
<td>72.9%</td>
</tr>
</tbody>
</table>

**Conclusion**

Treatment with early CPAP rather than intubation/surfactant is associated with less respiratory morbidity by 18-22 months CA. Longitudinal assessment of pulmonary morbidity is necessary to fully evaluate the potential benefits of respiratory interventions for neonates.

Stevens TP et al. J Pediatr 2014

---

**Use of CPAP in DR (2002 vs. 2011)**

<table>
<thead>
<tr>
<th></th>
<th>2002</th>
<th>2011</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Use of CPAP</td>
<td>67</td>
<td>86</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>No CPAP</td>
<td>43</td>
<td>14</td>
<td></td>
</tr>
</tbody>
</table>

Trevisanuto et al. Resuscitation 2014

---

**Guidelines 2015**

- **CPAP**

  - We suggest… in favor...

  Wyckoff MH et al. 2015 AHA Guidelines
  Wyllie J et al. 2015 ERC Guidelines

---

**McCarthy L et al. Pediatrics 2013**

---

**Mardegan V et al. ADC F & N Ed 2015**
**Gestational age:** 24 wks  
**Birth weight:** 410 g

<table>
<thead>
<tr>
<th>Controlled, accurate PIP</th>
<th>Controlled, accurate PEEP</th>
<th>Prolonged I.T.</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

### What is a Sustained Inflation?
- **Lindner 2005:** 15 s
- **Harling 2002:** 5 s
- **Te Pas 2007:** 10 s
- **Lista 2015, Mercadante 2016:** 15 s
- **Schwaberger 2015:** 15 s

### Available RCT evidence

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>n</th>
<th>Gestation</th>
<th>Control</th>
<th>Primary Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lindner</td>
<td>2005</td>
<td>61</td>
<td>25-28†</td>
<td>IPPV + PEEP</td>
<td>Intubation in first 48 hours</td>
</tr>
<tr>
<td>Harling</td>
<td>2005</td>
<td>52</td>
<td>&lt;31</td>
<td>IPPV + PEEP</td>
<td>Cytokines in BAL</td>
</tr>
<tr>
<td>Te Pas</td>
<td>2007</td>
<td>207</td>
<td>25-32†</td>
<td>IPPV + no PEEP</td>
<td>Intubation in first 72 hours</td>
</tr>
<tr>
<td>Lista</td>
<td>2015</td>
<td>291</td>
<td>25-28†</td>
<td>CPAP (IPPV + PEEP)</td>
<td>Intubation in first 72 hours</td>
</tr>
<tr>
<td>Schwaberger</td>
<td>2015</td>
<td>40</td>
<td>28-33†</td>
<td>CPAP (IPPV + PEEP)</td>
<td>Cerebral blood volume</td>
</tr>
<tr>
<td>Mercadante</td>
<td>2016</td>
<td>184</td>
<td>34-36†</td>
<td>Routine care</td>
<td>Any respiratory support</td>
</tr>
</tbody>
</table>

### Sustained Lung Inflation (SLI)

**Available RCT evidence**

**TABLE 2** Primary and Secondary Outcomes

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Control Group (n = 140)</th>
<th>SU Group (n = 140)</th>
<th>Unadjusted Odds Ratio 95% CI</th>
<th>p</th>
<th>Adjusted Odds Ratio 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary outcome</td>
<td>85 (60)</td>
<td>78 (55)</td>
<td>0.62 (0.40-0.96)</td>
<td>0.04</td>
<td>0.52 (0.33-0.82)</td>
</tr>
<tr>
<td>Cerebral blood</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>volume</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Lista G. et al. Pediatrics 2015
**Guidelines 2015**

Sustained lung inflation

- We suggest... against...

Wyckoff MH et al. 2015 AHA Guidelines
Wyllie J et al. 2015 ERC Guidelines

---

**Sustained Lung Inflation (SLI)**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Control Group</th>
<th>SLI Group</th>
<th>Unadjusted Odds Ratio (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adverse events</td>
<td>14 (97%)</td>
<td>13 (93%)</td>
<td>0.69 (0.25-1.84)</td>
<td>25</td>
</tr>
<tr>
<td>Respiratory failure</td>
<td>2 (13%)</td>
<td>1 (7%)</td>
<td>4.57 (0.87-21.20)</td>
<td>06</td>
</tr>
<tr>
<td>Meningitis</td>
<td>2 (13%)</td>
<td>1 (7%)</td>
<td>3.00 (0.72-17.10)</td>
<td>09</td>
</tr>
<tr>
<td>Pharmacological treatment of PDA</td>
<td>74 (93%)</td>
<td>16 (22%)</td>
<td>1.53 (0.76-2.32)</td>
<td>07</td>
</tr>
<tr>
<td>Surgical closure of PDA</td>
<td>8 (9%)</td>
<td>5 (3%)</td>
<td>0.58 (0.19-1.65)</td>
<td>26</td>
</tr>
<tr>
<td>IMH</td>
<td>26 (32%)</td>
<td>37 (47%)</td>
<td>1.27 (0.79-2.00)</td>
<td>27</td>
</tr>
<tr>
<td>Grade ≥ 3</td>
<td>8 (9%)</td>
<td>12 (16%)</td>
<td>1.40 (0.56-3.70)</td>
<td>30</td>
</tr>
<tr>
<td>SCL</td>
<td>5 (6%)</td>
<td>1 (1%)</td>
<td>0.19 (0.02-1.65)</td>
<td>00</td>
</tr>
<tr>
<td>NEC</td>
<td>4 (5%)</td>
<td>7 (9%)</td>
<td>1.75 (0.40-8.02)</td>
<td>30</td>
</tr>
<tr>
<td>COP*</td>
<td>16 (41%)</td>
<td>1 (4%)</td>
<td>0.09 (0.03-0.40)</td>
<td>06</td>
</tr>
<tr>
<td>Grade ≥ 3</td>
<td>12 (9%)</td>
<td>14 (10%)</td>
<td>1.14 (0.51-2.56)</td>
<td>75</td>
</tr>
</tbody>
</table>

*p<0.01

Centres performing Sustained Lung Inflation [2011]

<table>
<thead>
<tr>
<th>Year</th>
<th>North</th>
<th>Center</th>
<th>South</th>
</tr>
</thead>
<tbody>
<tr>
<td>2002</td>
<td>68.7</td>
<td>68.4</td>
<td>61.1</td>
</tr>
<tr>
<td>2011</td>
<td>75.4</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*p<0.01

Centres performing Sustained Lung Inflation [2011]


**Neonatal Stabilization: Key Points**

- Antenatal care
- Temperature control
- Supplemental oxygen
- Respiratory support (CPAP, PPV, surfactant)
- Umbilical cord clamping
- Monitoring
“Would you like to cut the cord?”

Treatment Recommendation
Delay in umbilical cord clamping for at least 1 minute is recommended for newborn infants not requiring resuscitation.

Perlman JM et al. Pediatrics, 2010

Guidelines 2015
Delayed cord clamping

“*We suggest* delayed umbilical cord clamping for preterm infants NOT requiring immediate resuscitation after birth. (Weak recommendation, very low quality of evidence).”

“There is insufficient evidence to recommend an approach to cord clamping for preterm infants who do receive resuscitation immediately after birth, as many babies who were at high risk of requiring resuscitation were excluded from or withdrawn from the studies.”

Wyckoff MH et al. 2015 AHA Guidelines
Wyllie J et al. 2015 ERC Guidelines

WHAT THIS STUDY ADDS: Healthy self-breathing neonates in a low-resource setting are more likely to die if cord clamping occurs before or immediately after onset of spontaneous respirations. The risk of death/admission decreases by 20% for every 10-second delay in clamping after breathing.

Ersdal H et al. Pediatrics 2014

WHAT THIS STUDY ADDS: Healthy self-breathing neonates in a low-resource setting are more likely to die if cord clamping occurs before or immediately after onset of spontaneous respirations. The risk of death/admission decreases by 20% for every 10-second delay in clamping after breathing.

Bhatt S et al. J Physiol 2013

Wyckoff MH et al. 2015 AHA Guidelines
Wyllie J et al. 2015 ERC Guidelines

68% GA < 25 w

During the delay, the infant was held in a sterile towel located approximately 10 to 15 inches below the mother’s introitus at vaginal delivery or below the level of the incision at cesarean section.

Delayed cord clamping (30-45s) (n=17)
Immediate cord clamping (<10s) (n=20)

- Higher hematocrits during the first 72 h
- Fewer blood transfusions first 28 days of life
- Severe IVH 20% (ICC) vs 6% (DCC) (p 0.34)
- No difference in safety measures

J Perinatol 2015
Conclusions and Relevance

Umbilical cord milking was associated with some benefits and no adverse effects in the immediate postnatal period in preterm infants (GA, <33 weeks). However, further studies are warranted to assess the effect of UCM on neonatal and long-term outcomes.

UCM vs Control (Immediate or Delayed Cord Clamping)

- 68 preterm infants (24-32 weeks gestation)
- DCC 30s vs Milking
- Follow-up at 2 y (n. 39) and 3.5 y (n. 29)

In this small number of participants followed up at 2 and 3.5 years of age, milking of the cord 4 times did not have any long-term adverse effect on neurodevelopmental outcome, suggesting that cord milking could be used as an alternative to delayed cord clamping.

Neurodevelopmental Outcomes at 2 and 3.5 Years for Very Preterm Babies Enrolled in a Randomized Trial of Milking the Umbilical Cord versus Delayed Cord Clamping

Heike Raber A, Alexandre Sawyer A, Philip Amess A, Susan Ayers A for the Brighton Perinatal Study Group

- 208 preterm infants (24-31 wks)
- DCC 30-45s + 1 milking vs ICC
- Follow-up at 18 months (n. 161)

Our protocol of a brief delay in cord clamping followed by 1 milking of the cord is safe. DCC may provide an advantage in reducing rates of poor motor performance at 18-22 months corrected age.

Figure 2. Logistic regression analyses showing risk factors for motor composite score < 85. AT, actual treatment used for the sensitivity analysis; BPD, bronchopulmonary dysplasia; ITT, intention-to-treat analysis.
Australian Placental transfusion study

RCT
Infants<30 weeks' gestation n. 1600
Clamping time: <10 sec. vs. >60 sec.
Primary Outcome: Composite death and/or major morbidity at 30 weeks post menstrual age
Secondary Outcomes: Death or severe disability (for example cerebral palsy, blindness, deafness, problems with language or speech or a positive score for developmental delay) at 24 months age corrected for gestation

UK Cord Pilot Trial
RCT (8 centers)
Infants <32 weeks' gestation
N° 100-110
Clamping time <20 sec. vs >120 sec.
Bedside neonatal resuscitation in DCC
Primary Outcome: feasibility study

Guidelines 2015

Cord milking

Treatment Recommendation
“We suggest against the routine use of cord milking for infants born at less than 29 weeks of gestation because there is insufficient published human evidence of benefit.”

“Cord milking may be considered on an individualized basis or in a research setting as it may improve initial mean blood pressure, hematological indices and intracranial hemorrhage. There is no evidence for improvement or safety in long-term outcomes. (Weak recommendation, low level of evidence).”

Perlman J et al. Circulation 2015

Neonatal Stabilization: Key Points

- Antenatal care
- Temperature control
- Supplemental oxygen
- Respiratory support (CPAP, PPV, surfactant)
- Umbilical cord clamping
- Monitoring

Assessment in DR

- Color
- Umbilical cord palpation
- HRusculation
- Chest excursions
- Inaccurate

- Pulse oximetry
- ECG
- CO2 detector
- Recommended

Wyckoff MH et al. 2015 AHA Guidelines
Wyllie J et al. 2015 ERC Guidelines
Assessment in DR

- Respiratory Function Monitoring
  - ETCO₂
  - NIRS

News

1 Hooper SB. PlosOne 2013
2 Schmolzer GM. J Pediatr 2012
3 Hawkes GA. ADC F&N Ed 2016
4 Finn D. J Pediatr 2013
5 vanVonderen JJ. Frontiers in Pediatrics 2016

Conclusions

Lights
- Biology and antenatal history are important
- Prevent hypothermia seems to have a role in decreasing mortality and morbidity
- CPAP instead of intubation is suggested
- Delayed cord clamping (after breathing) seems to be the best choice
- Pulse oxymetry, ECG and CO₂ detector are recommended

Shadows
- Low Oxygen concentrations (21-30%) seem reasonable, but more evidence is necessary
- SLI needs more data to be recommended
- Milking instead of DCC seems to work, but long term outcomes are needed
- Respiratory Function Monitoring, ETCO₂, NIRS appear reasonable, but more evidence is needed

Table 1
Characteristics of centres in the two study periods.

<table>
<thead>
<tr>
<th></th>
<th>2002 (n. 76)</th>
<th>2011 (n. 98)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participating centres</td>
<td>64</td>
<td>64</td>
</tr>
<tr>
<td>Total births at surveyed centres</td>
<td>126,897</td>
<td>137,504</td>
</tr>
<tr>
<td>Total VLBWI born at surveyed centres</td>
<td>2796</td>
<td>3608</td>
</tr>
<tr>
<td>Total ELBWI born at surveyed centres</td>
<td>1168</td>
<td>1388</td>
</tr>
<tr>
<td>Births/centre</td>
<td>1560 (1278–2594)</td>
<td>1850 (1349–2564)</td>
</tr>
<tr>
<td>ELBWI admitted</td>
<td>17 (10–23)</td>
<td>19 (13–27)</td>
</tr>
<tr>
<td>Physicians</td>
<td>9 (7–12)</td>
<td>11 (9–12)</td>
</tr>
<tr>
<td>Nurses</td>
<td>26 (17–30)</td>
<td>27 (21–34)</td>
</tr>
<tr>
<td>Ratio physicians/ELBWI</td>
<td>0.61 (0.40–0.80)</td>
<td>0.57 (0.41–0.78)</td>
</tr>
<tr>
<td>Ratio nurses/ELBWI</td>
<td>1.51 (1.18–2.29)</td>
<td>1.45 (1.03–1.96)</td>
</tr>
<tr>
<td>Team leader for neonatal resuscitation:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pediatrician/Neonatologist</td>
<td>59 (92.1)</td>
<td>62 (96.8)</td>
</tr>
<tr>
<td>Anesthesiologist</td>
<td>5 (7.9)</td>
<td>2 (3.2)</td>
</tr>
</tbody>
</table>

Data expressed as n (%) or *median (IQR).

Trevisanuto D et al. Resuscitation 2014

Thank you!!!

daniele.trevisanuto@gmail.com