## Women and Babies: Surfactant in Preterm Infants

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<td>RPA Newborn Care</td>
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<td>A/Prof David Osborn, Senior Staff Specialist</td>
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Women and Babies: Surfactant in Preterm Infants

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SLHD - RPA Women and Babies: Surfactant in Preterm Infants

1. **Introduction**

Need for mechanical ventilation is almost universal for infants born <27 weeks gestation)\(^1\) with rapidly reducing rates for very preterm (28 to <32 weeks) \(^1\) and late preterm (33 to <37 weeks) infants \(^2-4\). Recognising risk allows appropriate targeting of treatments for prevention and minimisation of respiratory morbidity, including surfactant treatment. A substantial proportion of ventilated preterm infants have surfactant deficiency \(^5\). Surfactant strategies for improving outcomes of infants born preterm include prophylactic \(^6\) or early rescue surfactant use \(^7\), and repeat surfactant use where indicated \(^8\). Early use of thin catheter surfactant administration has been shown to reduce need for mechanical ventilation in extremely premature \(^9\) and very preterm infants \(^10\). Recent systematic reviews and meta-analysis found that strategies designed to minimise mechanical ventilation (including thin catheter surfactant and InSurE technique) are likely to be associated with better outcomes (including death and chronic lung disease) than strategies involving intubation, surfactant and continued ventilation.

2. **The Aims / Expected Outcome of this Guideline**

- Risk of surfactant deficiency will be identified and early surfactant replacement treatment given where appropriate.

3. **Risk Statement**

SLHD Enterprise Risk Management System (ERMS) Risk # 106 Recognising and Responding to Clinical Deterioration in Acute Health Care

- Clinical risk of respiratory distress syndrome and ventilation in preterm infants.

4. **Guideline Statement**

Exogenous surfactant treatment should be given to preterm infants with surfactant deficiency based on best evidence for treatment.

5. **Scope**

- RPA Newborn Care

6. **Resources**

- None required

7. **Implementation**

- Distribution and notification of this Guideline via usual means (email, relevant management and ward meetings) and via
- Notification on the SLHD RPAH Policies/Guidelines Intranet.

8. **Key Performance Indicators and Service Measures**

- Surfactant use and time to surfactant in ventilated preterm infants.
- Mortality, chronic lung disease (36 weeks corrected gestation), duration of mechanical ventilation, duration of oxygen, duration of respiratory support and use of home oxygen of infants born at preterm gestations.
9. Guidelines

9.1 Summary

Infants born extremely premature <28 weeks:

- Should be considered for enrolment in the EPINIST trial
- Unless Respiratory Distress Syndrome RDS seems clinically unlikely e.g. good postnatal respiration in low oxygen, there should be a low threshold for delivery room surfactant. The preferred technique outside the EPINIST trial is endotracheal intubation, surfactant administration and brief mechanical ventilation (goal to extubation within 1 hour).

Surfactant available at RPAH

- Poractant alfa (Curosurf ®) 120mg/1.5mL Intrantracheal Susp 1
- Poractant alfa (Curosurf ®) 240mg/3mL Intrantracheal Susp 1

Beractant (Survanta Surfactant ®) 200mg/8mL is not usually available.

Infants born very premature 28 to 31+6 weeks gestation:

- If intubated in the delivery room, should receive surfactant immediately after intubation and resuscitation.
- Infants not needing intubation and with respiratory distress should be managed with nasal continuous positive airways pressure (nCPAP) titrated up to 8 cmH2O. If infants should be considered for surfactant treatment if:
  - FiO₂ ≥0.25-0.35 in the 1st 24 hours or
  - FiO₂ > 0.3 to 0.4 after 1st 24 hours
- The threshold should be individualised but generally a lower threshold within the cited ranges could be used for infants < 30 weeks’ gestation at high risk of RDS with increasing oxygen requirements, and the x-ray is consistent with RDS, particularly if using thin catheter surfactant. Infants at high risk of RDS include those of increasing prematurity, no or incomplete antenatal corticosteroids use (<48 hours) and those born after caesarean section without labour.
- Infants with nCPAP titrated up to 8 cmH2O and meeting criteria for surfactant replacement may, according to clinical judgement, receive surfactant either by intubation and brief ventilation or, in the first 24 hours, early rescue thin catheter surfactant with a goal to avoiding mechanical ventilation.

Infants born premature 32 to 36 weeks gestation:

- If intubated in delivery room should be considered for surfactant, after resuscitation, if (RDS) is considered likely.
- Infants with respiratory distress should be managed with (nCPAP) titrated up to 8-10 cmH₂O. Infants should be considered for surfactant treatment if:
  - FiO₂ ≥0.3 to 0.4 in the first 24 hours or
  - FiO₂ > 0.35 to 0.45 after 1st 24 hours
- The threshold should be individualised but generally a lower threshold within the cited ranges could be used for less mature babies at high risk of RDS with increasing oxygen requirements and the x-ray is consistent with RDS, particularly if using thin catheter surfactant. Infants at high risk of RDS include those of increasing prematurity, no or incomplete antenatal corticosteroids use (<48 hours) and those born after caesarean section without labour.
- Infants with nCPAP titrated up to 8-10 cmH₂O and meeting criteria for surfactant replacement may, according to clinical judgement, receive surfactant either by intubation
and brief ventilation or, in the first 24 hrs, early rescue thin catheter surfactant with a goal to avoiding mechanical ventilation.

Treatment of respiratory distress syndrome:

- Give Poractant alfa (Curosurf ®) 200 mg/kg then 100 mg/kg every 6 to 12 hours until extubated to a maximum of 4 doses depending on respiratory compliance.

Repeat doses of surfactant:

- Repeat doses of surfactant should be given via thin catheter or ETT if the infant continues to meet criteria for thin catheter surfactant, or for ventilated infants, until the infant’s lung compliance allows for extubation.

Late surfactant (>24 hours)

- Response to delayed surfactant particularly after 24 hours age is likely to be suboptimal with reports limited to clinical response with improvement in respiratory status in babies 24-48 hrs old and tolerance in infants towards the end of the first week with severe respiratory disease or evolving bronchopulmonary dysplasia but no change in neonatal or long term outcomes reported.13-17
Figure 1: Summary of recommended surfactant treatment strategies for preterm infants.

**Preterm infants born <28 weeks**
- Eligible for the Extreme preterm infant non-invasive surfactant trial [EPINIST] - see protocol
- Delivery room endotracheal intubation and surfactant unless RDS is considered clinically unlikely.
  - Curosurf 200 mg/kg
- Repeat surfactant every 6-12 hours if reduced lung compliance until extubated.
  - Curosurf 100 mg/kg.
  - Maximum total 4 doses.

**Preterm infants born 28+0 to 31+6 weeks**
- If intubated in the delivery room, should receive surfactant immediately after intubation and resuscitation.
  - Curosurf 200 mg/kg
- Infants with respiratory distress should be managed with nCPAP titrated up to 8 cmH₂O.
- Consider Surfactant if
  - FiO₂ is 0.25-0.35 <24hrs
  - FiO₂ is 0.3-0.4 >24hrs
- Administration strategy:
  - EITHER, if <24 hrs, consider thin catheter strategy:
  - OR: Endotracheal intubation and brief ventilation strategy:
    - Curosurf 200 mg/kg
- Repeat surfactant every 6-12 hours if reduced lung compliance until extubated.
  - Curosurf 100 mg/kg.
  - Maximum total 4 doses.

**Preterm infants born ≥32 weeks**
- If intubated in delivery room, consider giving surfactant immediately after resuscitation if at high risk for RDS.
  - Curosurf 200 mg/kg
- Infants with respiratory distress could be managed with nCPAP titrated up to 8-10 cmH₂O.
- Consider Surfactant if
  - FiO₂ is 0.3-0.4 <24hrs
  - FiO₂ is 0.35-0.45 >24 hrs
- Administration Strategy
  - EITHER, if <24 hrs, consider thin catheter surfactant
  - OR: Endotracheal Intubation and brief ventilation strategy.
    - Curosurf 200 mg/kg
- Repeat surfactant every 6-12 hours if reduced lung compliance until extubated.
  - Curosurf 100 mg/kg.
  - Maximum total 4 doses.
Incidences

Need for mechanical ventilation is almost universal for infants born extremely premature (<28 weeks gestation) which reflects infant immaturity and with rapidly reducing rates for very preterm (28 to <32 weeks) and late preterm (33 to <37 weeks) infants.

Table 1: Reports the risk of serious respiratory morbidity or mechanical ventilation in NSW/ACT population cohort of extremely preterm and very preterm infants 2007 to 2011.

<table>
<thead>
<tr>
<th>Gestation (weeks)</th>
<th>Overall survival %</th>
<th>Mechanical ventilation %</th>
<th>Surfactant treatment %</th>
<th>Chronic lung disease (36 weeks) postmenstrual age %</th>
<th>Home oxygen %</th>
</tr>
</thead>
<tbody>
<tr>
<td>23</td>
<td>25</td>
<td>&gt;95</td>
<td>95</td>
<td>25</td>
<td>10</td>
</tr>
<tr>
<td>24</td>
<td>60</td>
<td>&gt;95</td>
<td>96</td>
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<td>20</td>
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<td>25</td>
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<td>95</td>
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<td>61</td>
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<td>29</td>
<td>97</td>
<td>55</td>
<td>44</td>
<td>10</td>
<td>&lt;1</td>
</tr>
<tr>
<td>30</td>
<td>98</td>
<td>40</td>
<td>31</td>
<td>&lt;5</td>
<td>&lt;1</td>
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<td>31</td>
<td>99</td>
<td>30</td>
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</tr>
</tbody>
</table>

Table 2: Risk of serious respiratory morbidity or mechanical ventilation in population cohorts of preterm infants, including risk according to presence of labour versus no labour.

<table>
<thead>
<tr>
<th>Years</th>
<th>Mechanical ventilation %</th>
<th>Gestation (weeks)</th>
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<tbody>
<tr>
<td>1992-1999³</td>
<td>All</td>
<td>3102</td>
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<tr>
<td></td>
<td>Labour</td>
<td></td>
</tr>
<tr>
<td></td>
<td>No labour (elective caesarean)</td>
<td></td>
</tr>
<tr>
<td>1997-2006²</td>
<td>Mechanical ventilation %</td>
<td></td>
</tr>
<tr>
<td>1990-1998⁴</td>
<td>Serious respiratory morbidity %</td>
<td></td>
</tr>
</tbody>
</table>

9.2 Aetiology and Risk Factors

Premature infants are at high risk of RDS (hyaline membrane disease or surfactant deficiency) and congenital pneumonia. Clinical presentations associated with...
increasing prematurity increase the likelihood of lung immaturity (RDS) and infection, preterm rupture of membranes or clinical chorioamnionitis increase the likelihood of infection. Infants born by elective caesarean section are at much higher risk of RDS and mechanical ventilation.

A risk of mechanical ventilation greater than 10% exists for infants born after established labour below 34 weeks gestation, but is below 36 weeks gestation for infants born by elective caesarean (no labour).

9.3 Diagnosis
Infants born preterm or by caesarean section not in labour are at high risk of surfactant deficiency (see table 1 and table 2). The diagnostic accuracy of a chest x-ray diagnosis of RDS (fine granularity, air bronchograms and low lung volume) has not been reported. Surfactant deficiency or inactivation may diagnosed with high sensitivity and positive predictive value by performing the click test or stable microbubble test on a tracheal aspirate as soon as possible after intubation of any infant with respiratory distress. However, given the benefits of early surfactant and relatively low cost, surfactant treatment should be given within 15 minutes to any infant meeting early criteria for treatment.

9.4 Consequences (prognosis)
Table 1 reports the risk of serious respiratory morbidity or mechanical ventilation in NSW/ACT population cohort of extremely preterm and very preterm infants 2007 to 2011.

9.5 Intervention
• Prevention:
  Use of antenatal corticosteroids prior to preterm birth reduces the risk of neonatal mortality, RDS and intraventricular haemorrhage. Australian and New Zealand Clinical Practice Guidelines recommend for women at risk of early preterm, imminent birth use a single course of antenatal corticosteroids (betamethasone 24 mg in divided doses):
  • when gestational age is 34 weeks’ and 6 days or less,
  • when preterm birth is planned or expected within the next seven days, even if birth is likely within 24 hours,
  • regardless of the reason the woman is considered at risk of preterm birth.

Repeat courses of antenatal corticosteroids reduce the incidence of RDS and mechanical ventilation. Treatment with multiple (≥4) repeat doses of corticosteroid is associated with a reduction in mean birth weight. The Australian and New Zealand Clinical Practice Guidelines 2015 recommend:
  • Use of a repeat dose of antenatal corticosteroid (12 mg betamethasone) in women at risk of early preterm birth when gestational age is 32 weeks and 6 days or less, and
  • Preterm birth is planned or expected within the next 7 days, even if birth is likely within 24 hours.
  • The repeat dose should not be less than 7 days following a single course of antenatal corticosteroids and should be given regardless of the reason the woman is considered at risk of preterm birth.
  • It is recommended that up to a maximum of three, single, repeat doses only be used in view of growth concerns.
9.6 Treatment

Prevention of intubation: non-invasive surfactant:

There are several potential methods for non-invasive surfactant delivery including intra-amniotic surfactant prior to delivery (no RCTs found)\(^32\), intrapartum pharyngeal surfactant administration (no RCTs found)\(^33\), nebulised surfactant administration (single small RCT reporting no evidence of benefit)\(^34\), laryngeal mask airway surfactant administration (single small RCT reporting no evidence of benefit)\(^35\) and thin catheter-delivered surfactant.

Thin catheter surfactant:

6 trials\(^9, 10, 36-39\) including 839 infants assessed the effect of thin catheter-delivered surfactant in infants with respiratory distress. No trial has assessed the effect of prophylactic thin catheter surfactant.

- Three trials compared use of rescue thin catheter-delivered surfactant to later intubation and rescue surfactant in infants born extremely premature (23-26 weeks\(^9\) and 26-28 weeks gestation\(^10\)), and very premature infants (28–32 weeks\(^39\)) on CPAP with respiratory distress. Criteria for thin catheter surfactant included a FiO\(_2\) > 0.3. Meta-analysis found rescue thin catheter surfactant reduced need for mechanical ventilation (3 trials, 521 infants; RR 0.71, 95% CI 0.62, 0.81) and incidence of pneumothorax (RR 0.43, 95% CI 0.20, 0.91) with no significant effect on mortality (3 trials, 521 infants; RR 1.18, 0.62, 2.25), chronic lung disease or mortality (3 trials, 521 infants; RR ) and chronic lung disease (3 trials, 489 infants; RR 0.74, 0.52, 1.08).

- A systematic review\(^40\) found 6 RCTs enrolling a total of 895 infants assessing the efficacy of the LISA technique compared to other strategies of endotracheal intubation and surfactant. The review found it reduced the composite outcome of death or bronchopulmonary dysplasia (BPD) at 36 weeks (RR 0.75, 95% CI 0.59 to 0.94; p=0.01), BPD36 among survivors (RR 0.72, 0.53 to 0.97; p=0.03), need for mechanical ventilation within 72 hours of birth (RR 0.71, 0.53 to 0.96; p=0.02) and need for mechanical ventilation anytime during the neonatal intensive care unit stay (RR 0.66, 0.47 to 0.93; p=0.02). There were no differences noted for the outcome of death and other neonatal morbidities. Procedure failure rate on the first attempt and the need for additional doses of surfactant were not different between the intervention groups. CONCLUSIONS: LISA technique for surfactant delivery results in a lesser need for mechanical ventilation in infants with RDS, reduction in the composite outcome of death or BPD at 36 weeks, and BPD36 among survivors.

- A network meta-analysis\(^41\) of 7 ventilation strategies for preterm infants including nasal continuous positive airway pressure (CPAP) alone, intubation and surfactant administration followed by immediate extubation (INSURE), less invasive surfactant administration (LISA), noninvasive intermittent positive pressure ventilation, nebulized surfactant administration, surfactant administration via laryngeal mask airway, and mechanical ventilation found the use of LISA was associated with the lowest likelihood of the composite outcome of death or BPD at 36 weeks’ postmenstrual age. The findings were limited by the overall low quality of evidence and lack of robustness in higher-quality trials.

Intubation and surfactant:

Early Versus Delayed Surfactant:

Early surfactant treatment for neonatal RDS reduces mortality, rates of chronic lung disease and pneumothorax compared to delayed selective surfactant treatment.\(^7\)
Early surfactant administration with brief ventilation:
In preterm infants with RDS, early surfactant administration with brief ventilation (aim to extubate within 1 hour) reduced need for mechanical ventilation (6 trials, 664 infants; RR 0.67 95 % CI 0.57, 0.79), pneumothorax and chronic lung disease at 28 days compared to selective surfactant and continued mechanical ventilation.

Prophylactic versus delayed selective surfactant:
For trials without routine use of CPAP in the control arm, meta-analysis found a reduction in mortality (8 trials, 2761 infants; RR 0.69, 95 % CI 0.56, 0.85) from routine intubation for prophylactic surfactant compared to delayed intubation and selective surfactant administration.
In contrast, meta-analysis of trials with routine use of CPAP found no significant difference in mortality or chronic lung disease, and a significant increase in combined mortality and chronic lung disease for infants treated with intubation and prophylactic surfactant.

Timing of surfactant:
Pre- Versus Post-ventilatory Surfactant in Preterm Infants:
A single randomised controlled trial including 651 infants reported no significant difference in mortality, chronic lung disease, pneumothorax or air leak or chronic lung disease for infants given endotracheal surfactant prior to initiation of positive pressure ventilation. There is no proven benefit from endotracheal surfactant prior to resuscitation of the newborn infant.

Surfactant dose:
The optimal initial dose of surfactant is unclear. Meta-analysis of trials of higher initial dose (Poractant alpha 200mg/kg) versus lower initial dose (Beractant (Survanta Surfactant ®) or Poractant alpha (Curosurf ®)100mg/kg) found reduced mortality (5 trials, 2546 infants; RR 0.89, 0.77, 1.03) and reduced need for repeat dosing of surfactant (4 trials, 2441 infants; RR 0.87, 0.83, 0.92).

How many doses?
Multiple versus Single Doses of Exogenous Surfactant in Preterm Infants:
Repeated dosing of surfactant in ventilated preterm infants improved oxygenation and ventilatory support parameters and reduced mortality (3 trials, 1220 infants; RR 0.59, 95 % CI 0.44, 0.78) and rates of pneumothorax.

Intubation / sedation:
Newborn infants should receive analgesic premedication for endotracheal intubation, except for emergency intubations during resuscitation or infants in whom instrumentation of the airway is likely to be extremely difficult [See Intubation/sedation drugs guideline http://www.slhd.nsw.gov.au/rpa/neonatal/protocols.html].
9.7 Summary

An overview of systematic reviews of prophylactic and early surfactant provides evidence for the earliest possible administration of surfactant especially in extremely premature infants. However, the optimal strategy is unclear, particularly in infants with adequate antenatal corticosteroid cover managed with CPAP. Two recent systematic reviews concluded a less invasive surfactant technique results in a lesser need for mechanical ventilation in infants with RDS, reduction in the composite outcome of death or BPD at 36 weeks, and BPD36 among survivors; and among preterm infants, the use of less invasive surfactant technique was associated with the lowest likelihood of the composite outcome of death or BPD at 36 weeks' postmenstrual age.

There is increasing evidence becoming available regarding the relative safety of less invasive methods of surfactant administration.

Table 3: Postnatal respiratory support and surfactant strategies for avoiding mechanical ventilation

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Outcome</th>
<th>Trials / participants</th>
<th>Effect RR [95%CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rescue thin catheter surfactant versus delayed intubation with selective surfactant in preterm infants on CPAP</td>
<td>Mortality</td>
<td>2 / 431</td>
<td>1.12 [0.58, 2.18]</td>
</tr>
<tr>
<td></td>
<td>Chronic lung disease (36 weeks)</td>
<td>2 / 399</td>
<td>0.72 [0.49, 1.07]</td>
</tr>
<tr>
<td></td>
<td>Mortality or chronic lung disease</td>
<td>2 / 431</td>
<td>0.83 [0.60, 1.13]</td>
</tr>
<tr>
<td></td>
<td>Intubation / mechanical ventilation</td>
<td>2 / 431</td>
<td>0.71 [0.62, 0.81]</td>
</tr>
<tr>
<td></td>
<td>Pneumothorax</td>
<td>2 / 431</td>
<td>0.43 [0.20, 0.91]</td>
</tr>
<tr>
<td>Rescue thin catheter surfactant versus rescue InSure technique in preterm infants on CPAP</td>
<td>Mortality</td>
<td>4 / 408</td>
<td>0.96 [0.53, 1.72]</td>
</tr>
<tr>
<td></td>
<td>Chronic lung disease (36 weeks)</td>
<td>4 / 368</td>
<td>0.66 [0.37, 1.16]</td>
</tr>
<tr>
<td></td>
<td>Intubation / mechanical ventilation</td>
<td>3 / 318</td>
<td>0.79 [0.59, 1.07]</td>
</tr>
<tr>
<td></td>
<td>Pneumothorax / air leak</td>
<td>3 / 370</td>
<td>0.86 [0.42, 1.76]</td>
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</table>
Table 4: Surfactant strategies for preventing or minimising mechanical ventilation

| Study Description                                                                 | Mortality        | RR  
|-----------------------------------------------------------------------------------|------------------|------
| Early versus delayed selective surfactant treatment for neonatal RDS \(^7\) [trials 1992-2002] | Mortality        | RR  
|                                                                                   | 6 / 3577         | 0.84 [0.74, 0.95] |
|                                                                                   | Chronic lung disease | 0.69 [0.55, 0.87] |
|                                                                                   | Pneumothorax / air leak | 0.69 [0.59, 0.82] |
|                                                                                   | 8 / 2761         | 0.69 [0.56, 0.85] |
|                                                                                   | Chronic lung disease (36 weeks) | 1.30 [0.77, 2.17] |
|                                                                                   | Pneumothorax / air leak | 0.79 [0.63, 0.98] |
| Prophylactic versus selective use of surfactant in preterm infants \(^6\) Studies with routine application of CPAP [trials 2010-2011] | Mortality        | RR  
|                                                                                   | 2 / 1746         | 1.24 [0.97, 1.58] |
|                                                                                   | Chronic lung disease (36 weeks) | 1.12 [0.99, 1.26] |
|                                                                                   | Mortality or chronic lung disease | 1.12 [1.02, 1.24] |
|                                                                                   | Pneumothorax / air leak | 1.08 [0.73, 1.60] |
| Early surfactant administration with brief ventilation versus selective surfactant and continued mechanical ventilation for preterm infants with or at risk for RDS \(^42\) [1994-2005] | Mortality        | RR  
|                                                                                   | 6 / 396          | 0.52 [0.17, 1.56] |
|                                                                                   | Chronic lung disease (28 days) | 0.51 [0.26, 0.99] |
|                                                                                   | Intubation / mechanical ventilation | 0.67 [0.57, 0.79] |
|                                                                                   | Days mechanical ventilation | -0.36 [-0.81, 0.10] |
|                                                                                   | Pneumothorax / air leak | 0.52 [0.28, 0.96] |
| Pre- versus post-ventilatory surfactant in preterm infants \(^43\)                | Mortality        | RR  
<p>|                                                                                   | 1 / 651          | 1.20 [0.90, 1.60] |
|                                                                                   | Chronic lung disease | 1.35 [0.93, 1.94] |
|                                                                                   | Pneumothorax / air leak | 1.02 [0.60, 1.71] |</p>
<table>
<thead>
<tr>
<th>Chronic lung disease (36 weeks)</th>
<th>1 / 505</th>
<th>RR 1.42 [0.99, 2.02]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multiple versus single doses of exogenous surfactant for the prevention or treatment of neonatal RDS (^a) [trials 1990-1995]</td>
<td>Mortality</td>
<td>3 / 1220</td>
</tr>
<tr>
<td>Chronic lung disease</td>
<td>3 / 1221</td>
<td>RR 1.13 [0.83, 1.54]</td>
</tr>
<tr>
<td>Pneumothorax / air leak</td>
<td>3 / 1220</td>
<td>RR 0.70 [0.52, 0.94]</td>
</tr>
</tbody>
</table>

**Key Points**

<table>
<thead>
<tr>
<th>Key points</th>
<th>Level of evidence; Grade of recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infants born extremely premature &lt;28 weeks gestation should receive delivery room surfactant unless RDS is considered unlikely.(^6,,7)</td>
<td>LOE I GOR B</td>
</tr>
<tr>
<td>Infants who are intubated in the delivery room and are likely to have RDS should receive endotracheal tube surfactant after resuscitation and within 15 minutes where possible.(^43)</td>
<td>LOE I GOR B</td>
</tr>
<tr>
<td>Infants born (\geq 28) weeks on nCPAP should receive early surfactant treatment if moderate or severe respiratory distress or FiO(_2) (\geq 0.35) or earlier.(^6,,7)</td>
<td>LOE I GOR A</td>
</tr>
<tr>
<td>Thin catheter surfactant administration is an option for preterm infants on nCPAP with a FiO(_2) (\geq 0.3) or earlier.(^9,,10,,36-41) This reduces need for mechanical ventilation with evidence for safety.</td>
<td>LOE I GOR B</td>
</tr>
<tr>
<td>The initial dose of Poractant alpha (Curosurf ®) should be 200 mg/kg.(^44-48) This reduces need for additional doses and may reduce mortality.</td>
<td>LOE II GOR B</td>
</tr>
<tr>
<td>Repeat doses of surfactant should be administered to infants with reduced lung compliance until extubation.(^8) This reduces mortality and airleak.</td>
<td>LOE I GOR A</td>
</tr>
<tr>
<td>The goal of treatment of preterm infants with respiratory distress should either be avoidance of mechanical ventilation, or surfactant with thin catheter or INSUrE or with brief mechanical ventilation (aiming for extubation where possible within 1 hour).(^40-42,,50)</td>
<td>LOE I GOR B</td>
</tr>
</tbody>
</table>
Infants >24 hours may benefit from delayed surfactant administration although the threshold of administration is unclear.  

Newborn infants should receive analgesic premedication for endotracheal intubation, except for emergency intubations during resuscitation or infants in whom instrumentation of the airway is likely to be extremely difficult.

<table>
<thead>
<tr>
<th>Respiratory distress syndrome</th>
<th>LOE IV</th>
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<tbody>
<tr>
<td>Newborn infants should receive analgesic premedication for endotracheal intubation, except for emergency intubations during resuscitation or infants in whom instrumentation of the airway is likely to be extremely difficult.</td>
<td>GOR C</td>
</tr>
</tbody>
</table>

### 10. Definitions

**Respiratory distress syndrome (RDS)**

Presence of early onset respiratory distress in an infant with a typical chest x-ray (fine granularity, air bronchograms, low lung volume) and/or evidence of surfactant deficiency (e.g. negative or equivocal click or stable microbubble test).

**nCPAP**

Nasal continuous positive airway pressure

### 11. Consultation

RPA Newborn Care Guideline Meeting: Multi-disciplinary group of senior neonatologists and nurses within RPA Newborn Care

### 12. References


35. Abdel-Latif ME, Osborn DA. Laryngeal mask airway surfactant administration for prevention of morbidity and mortality in preterm infants with or at risk of respiratory distress syndrome. The Cochrane database of systematic reviews. 2011:CD008309.


42. Stevens TP, Harrington EW, Blennow M, Soll RF. Early surfactant administration with brief ventilation vs. selective surfactant and continued mechanical ventilation for preterm infants with or at risk for respiratory distress syndrome. The Cochrane database of systematic reviews. 2007:CD003063.


12.1 National Safety and Quality Health Service (NSQHS) Standards

- Standard 1, Governance for Safety and Quality in Health Service Organisations
- Standard 4, Medication Safety
- Standard 9, Recognising and Responding to Clinical Deterioration in Acute Health Care