Neonatal Chronic Lung Disease

INTRODUCTION

Chronic lung disease (CLD) results from the effects of positive pressure ventilation on a structurally and functionally immature lung. Chorioamnionitis and an inflammatory cascade have also been implicated in the pathogenesis of CLD, but their precise role is uncertain. CLD is characterised primarily by prolonged need for ventilatory support, O2 requirements, need for home oxygen and readmission with respiratory illness in the first year of life. CLD was in the past defined as oxygen requirements beyond 28 days with abnormal x-ray. However, a more meaningful definition in the current era is respiratory support (supplemental oxygen or CPAP in air) beyond 36 weeks post-conceptual age, which will be used in this document.

The pathological condition of bronchopulmonary dysplasia (BPD) is frequently used interchangeably with CLD. Pathologists can recognize changes in the lungs of infants soon after birth including airway epithelial necrosis and squamous metaplasia, organisation of hyaline membranes, and fibroblastic proliferation in the lung interstitium. This leads to eventual lung fibrosis and emphysematous changes.

Risk Factors

Perinatal – Controversial

- **Chorioamnionitis ± umbilical vasculitis (CAM).** There is a widely held belief that CAM is associated with an increased risk of CLD, with review articles stating it as if an established fact. Evidence for this belief is largely based on the paper by Watterberg et al who reported on 53 ventilated babies <2000 grams from the late 1980’s who received neither antenatal steroids nor surfactant replacement, and two other small studies. However, babies who develop CLD in the current era are generally a different population, being mainly <28 weeks GA, and receiving both antenatal steroids and surfactant, and experiencing much less mechanical ventilation. Recent studies, with babies more typical of the current era, found that there was either no increase in CLD following CAM, or that CAM was associated with a reduced incidence of CLD.

  Recent research in this department showed that chorioamnionitis alone (OR 0.49, CI 0.31-0.78), or chorioamnionitis plus vasculitis (OR 0.23, CI 0.15-0.25) dramatically reduce the odds of RDS, and therefore the need for and severity of ventilation. It was thus counter-intuitive that CAM would be the cause of worse CLD, and in a further study we have shown that after adjusting for confounders, chorioamnionitis plus vasculitis remains protective of CLD (OR 0.57 CI 0.34-0.96). However, chorioamnionitis alone is also protective (OR 0.69 CI 0.39-1.23) but not significantly. These findings combined with those above cast serious doubt on the assertion that CAM is a risk factor for CLD.

Perinatal - **Definite**

- **Gestational Age.** This is the primary risk factor, and is well demonstrated by data from this Unit in the Figure below.
- **Low birth weight percentile.** At each week of gestation, there is a stepwise increase in risk for lower birth weight percentile categories.
- **Male gender**

Post-natal
- **Resuscitation**: The potential for significant lung damage in the first moments of the resuscitation was dramatically demonstrated in animal studies with lambs in which those subjected to 6 bagging breaths held for 5 seconds with pressures of about 60 cm H2O immediately after birth caused substantial changes in lung architecture compared to controls. In a second study, lambs were ventilated from birth at 5, 10 or 20ml/Kg TV, and the lambs receiving 20ml/Kg had evidence of significant lung injury compared to those with 5ml/Kg.

- **Ventilation (Barotrauma & Volutrauma)**: Infants who receive ongoing ventilation via an endotracheal tube because of respiratory distress syndrome (RDS) or other disorders (particularly when high ventilator pressures and high FiO2 are required) may have a prolonged recovery period with persisting oxygen requirements and coarse reticular changes on chest X-ray. In a comparison of NICUs in New York and Boston, it was concluded that variation in CLD was primarily associated with initiation of mechanical ventilation. In the COIN trial, infants 25-28 weeks gestation were randomized to received either CPAP or mechanical ventilation from birth. At 28 days of age, the CPAP group had significantly lower need for oxygen (OR 0.62, CI 0.44-0.86), but at 36 weeks corrected, there was still a strong trend but no longer significant (OR 0.76, CI 0.54-1.09). The CPAP advantage was probably diluted by the fact that 45% of the infants assigned to CPAP were eventually intubated and ventilated for apnoea or other failure criteria.

- **Oxygen toxicity**

- **RDS**: the association is likely to be the result of the above mechanisms occurring over time.

- **Infection**: the CLD results from the associated need for re-ventilation or prolonged ventilation in septicaemic babies via the above mechanisms as well as from endotoxin and other inflammatory mediators. Infection may also have a role in causation of CLD when it causes re-opening or worsening of PDA via a synergistic effect.

- **PDA**: one may well suspect that there is an association between PDA and CLD due to the need for re-ventilation, or increased ventilation, because of stiff, hyperaemic lungs, and a number of observational studies have reported such a finding. However, meta-analyses of randomized controlled trials of prophylactic indomethacin for prevention of PDA, indomethacin for asymptomatic PDA in preterm infants, and prophylactic surgical ligation of PDA all failed to find that treating PDAs had any significant effect on preventing CLD.

## Incidence

This figure shows the incidence (%) of CLD in babies born at less than 32 completed weeks at RPAH over the years 1994-2004.

## Patterns of CLD

1. The first pattern includes infants who require ventilation via an endotracheal tube because of RDS, particularly when high ventilator pressures and high FiO2 are required. Also included are infants who required ventilation for an episode of acquired infection. Such infants may have a prolonged
recovery period with persisting oxygen requirements and coarse reticular changes on chest X-ray. This pattern is similar to that originally described by Northway et al. Proposed mechanisms of pulmonary injury include3,20.

- Postnatally acquired infection and inflammation
- Barotrauma: pressure induced injury
- Volutrauma: excessive variations in lung volumes producing iatrogenic lung injury. This is supported by animal experiments.
- Oxygen toxicity

2. The second pattern involves very low birthweight infants who may not have classical RDS or even require ventilation. Their initial chest X-ray can be normal. But after days or weeks it takes on a coarse reticular appearance, with continuing or increasing oxygen requirements. Late-onset infection likely plays a significant role. This is similar to the pattern previously described by Wilson & Mikity31. In practice the clinical course is usually a combination of these and may be prolonged with persisting pulmonary insufficiency for many months.

Consequences:

CLD is associated with the following:

1. **Pulmonary consequences:** the pulmonary function status of infants with CLD is characterised by low lung compliance, increased pulmonary resistance and increased energy used for breathing. This may result in:
   - Persistent oxygen and ventilation requirements,
   - Longer stay in hospital,
   - Need for home oxygen,
   - Use of additional therapies: post-natal steroids and diuretics,
   - Pulmonary hypertension if adequate oxygen is not maintained (with subsequent cor pulmonale and death),
   - Exacerbations due to respiratory infections in first year of life, especially with RSV resulting in increased incidence of rehospitalisation.
   - Increased incidence of bronchial hyper-reactivity32,
   - Minimal functional abnormalities at long term follow up33.

2. **Neurodevelopmental sequelae:** since 1990, at least 12 published studies34-45 of premature infants have examined the association between bronchopulmonary dysplasia (BPD) and neurodevelopment as compared to infants without BPD. Although quality and correction for confounding is variable, in general infants with BPD have significantly worse developmental outcomes including poorer cognitive outcomes, more developmental delays and higher rates of learning disabilities even after adjustment for confounding. It is not clear to what extent CLD causes the sequelae, or to what extent the problem leading to CLD (eg infection) caused the sequelae.

3. **Physical growth:** There is an increased incidence of growth failure (weight and stature) as a consequence of increased energy expenditure, abnormal sucking patterns and iatrogenic limitation of fluids32.

Diagnosis:

The two most commonly used definitions are:

- Oxygen requirements beyond 28 days with abnormal x-ray1, or
Respiratory support beyond 36 weeks post-conceptual age.

Using a definition of respiratory support near term increases the specificity but reduces the sensitivity for subsequent significant respiratory morbidity in the 1st 2 years of life. CXR abnormalities as staged by Northway:

Stage 1: Radiographically indistinguishable from severe RDS (1-3 days).
Stage 2: Marked radio-opacity of the lungs (4-10 days).
Stage 3: Clearing of the radio-opacity into a cystic bubbly, pattern (10-20 days).
Stage 4: Hyperexpansion, linear streaks and areas of emphysema with variable cardiomegaly (>1 month).

Interventions:

Prevention

Interventions aimed at reducing the incidence and severity of CLD have been listed in recent quality improvement initiatives: 47-49

1. Give antenatal corticosteroids (ANS) when preterm birth is anticipated. ANS significantly reduce the incidence and severity of RDS, and therefore the need for mechanical ventilation, so a reduction in CLD might also be expected to flow on. Unfortunately, only some of the RCTs in the updated Cochrane meta-analysis of ANS reported CLD as an outcome. The largest of these involved women with PROM > 12 hrs at randomization, and the treated group (betamethasone, two doses) had a reduced incidence of CLD with OR 0.50 [0.33, 0.76]. However, combining the smaller studies gave an overall result with a trend to reduction of CLD: OR 0.86 [0.61-1.22] that was no longer significant. A recent observational study reported that a complete course of ANS was associated with significantly reduced CLD: OR 0.63 [0.45, 0.89]. However, as those who were exposed to ANS may differ significantly from those who were not, despite adjusting for confounders, such results need to be interpreted with caution.

2. Avoid excessive delivery room oxygen and ventilation. Irreversible lung injury may occur if high tidal volumes or pressures are given in the first few moments of bagging after birth, and the aim is to avoid excessive pressure by use of a manometer on bagging circuits and early transfer to a ventilator set up with minimal appropriate tidal volumes. In all but the smallest babies, CPAP alone should be given a trial. The use of blended oxygen and oximetry on all babies avoids inappropriate oxygen exposure.

3. Give surfactant early to infants requiring assisted ventilation. Early surfactant, with or without immediate extubation to CPAP, compared to delayed treatment, is associated with a significantly lower incidence of CLD. For babies born before 28 completed weeks, those requiring intubation should receive prophylactic surfactant as soon as practicable in the delivery room. For those >= 28 weeks who need intubation, prophylactic surfactant would still be appropriate if they show signs of significant RDS, otherwise early targeted surfactant should be applicable.

4. Avoid excessive fluid intakes in preterm infants. While this is conventional wisdom, trials comparing liberal versus restricted water intake in preterm infants found a non-significant trend to more BPD. Also, no increase was found in the NNNI trial in the incidence of oxygen requirements at 37 weeks PMA in infants who received 10mls/kg volume expansion on day 1 and 2 of life.

5. Optimize on-going ventilation
   a. With conventional ventilation:
      - Target normal PaCO2 levels (40-60mmHg). Avoid over-distention of the lung resulting in hypocarbia by using appropriate peak inspiratory pressures and inspiratory times to achieve tidal volumes 3-4mls/kg/min. However, there is no evidence that permissive hypercapnia reduces the incidence of death or chronic lung disease at 36 weeks. (RR
Use of higher rates (60 bpm) and lower inspiratory times (0.3-0.35 seconds) in infants with RDS reduces incidence of air leak compared to conventional ventilation. Synchronized ventilation may decrease time to extubation and shows a non-significant trend to less CLD.

b. With high frequency oscillation ventilation:

- Theoretically, HFOV has the advantage of small tidal volumes which might translate into less volutrauma. The most recent Cochrane meta-analysis of RCTs concludes that HFOV, when used as the initial ventilation strategy, does offer marginal advantage over conventional ventilation for reducing CLD: RR 0.89 [0.81, 0.99], but the evidence is weakened by the inconsistency of this effect across trials and the overall borderline significance. There were no other important differences between the two modes of ventilation. We currently do not use HFOV as our initial mode of ventilation.

- With rescue HFOV, there is a reduction in any new pulmonary air leak, but no difference in the rate of PIE or of gross pulmonary air leak or the use of IPPV at 30 days. The rate of CLD was not reported. The rate of intraventricular hemorrhage (IVH) of any grade is increased in infants treated with rescue HFOV.

6. Target appropriate oxygen levels in preterm infants (see oxygen and ventilation guidelines). In the STOP-ROP trial use of supplemental oxygen at pulse oximetry saturations of 96% to 99% increased the risk of adverse pulmonary events including pneumonia and/or exacerbations of chronic lung disease and the need for oxygen, diuretics, and hospitalization at 3 months of corrected age. The BOOST trial found no difference in growth or development from targeting saturations 95-98% compared to 91-94%, but the higher saturation target group had a statistically significantly longer duration of oxygen, increased rates of chronic lung disease diagnosis and home oxygen.

- Target FiO2 to obtain PaO2 60-80 mmHg (alarms set 50-80) or
- Saturations 90-95% in preterm infants (alarms set 85-95% in acute phase, 83-97% in chronic phase).

7. Post-natal steroids: see below

8. Other potential preventative strategies:

- **Prophylactic jet ventilation:** There is a benefit in pulmonary outcomes in the group electively ventilated with HFJV. Of concern is the significant increase in acute brain injury in one trial, which used lower mean airway pressures when ventilating with HFJV. There are as yet no long term pulmonary or neurodevelopmental outcomes from any of the trials. Until further studies ascertain the most appropriate strategy to routinely ventilate premature infants with HFJV safely, ventilation with HFJV cannot be recommended for preterm infants with RDS.

- **Antioxidants:** There is no evidence that the use of antioxidants (superoxide dismutase) prevents CLD.

- **Vitamin A:** Supplementing very low birthweight infants with vitamin A is associated with a reduction in death or oxygen requirement at one month of age and oxygen requirement among survivors at 36 weeks postmenstrual age, with this latter outcome being confined to infants with birthweight less than 1000 g. Whether clinicians decide to utilise repeat intramuscular doses of vitamin A to prevent chronic lung disease may depend upon the local incidence of this outcome and the value attached to achieving a modest reduction in this outcome, balanced against the lack of other proven benefits and the acceptability of treatment. At RPA we estimated the amount the babies received in TPN or in breast milk fortifier was sufficient.
Prophylactic hydrocortisone: A group led by Watterberg showed babies who developed CLD had lower hydrocortisone levels than those who didn’t, and this led to a pilot RTC (20 patients per arm) of low dose hydrocortisone (0.5mg/Kg/dose 12 hrly for 9 days, given from birth) vs placebo, which found a reduced incidence of CLD (p 0.04). However, the same group then proceeded to a multicentre RCT which unfortunately was stopped at about halfway (360 of 790 planned) because of increased incidence of spontaneous GIT perforation. Overall, there was no decrease in incidence of CLD, and there were no significant differences between the groups for other primary and secondary outcomes. In the subset of patients with placental histology showing chorioamnionitis, hydrocortisone did confer significantly reduced CLD. However, the study was contaminated by up to 40% of patients (majority in placebo group) receiving systemic ‘off-label’ corticosteroids during or after the intervention, which would have reduced the chance of hydrocortisone showing a beneficial effect. A recent review of all trials involving the use of hydrocortisone to prevent CLD concluded there was insufficient evidence to recommend routine use of hydrocortisone. However, in follow-up studies of RCTs including Watterberg’s, hydrocortisone appears to have less potential for neurological injury than dexamethasone.

**Treatment:**

1. **Post-natal steroids**

Postnatal steroids have been the mainstay of treatment. Although there has been a recent shift towards hydrocortisone (see above) or betamethasone, in the large majority of cases, the agent used was dexamethasone. Timing of steroids has been an issue. Early steroids (<96 hours) given to all ventilated infants result in many infants receiving steroids unnecessarily and are associated with an increased rate of intestinal perforation. Intermediate steroids (day 7-14) are given to infants at risk of CLD, are used to facilitate weaning from the ventilator and have been shown to be effective at reducing oxygen dependency at 36 weeks PMA. However, recent long-term follow up studies have created concerns regarding the long-term effects of postnatal corticosteroids. Most recently, the DART trial of low-dose and short course dexamethasone demonstrated that successful extubation was achieved without the short-term side effects of the traditional, higher-dose treatments used in the older trials. The following is summary of the evidence:

a. **Early post-natal steroids (<96 hours):**

- Benefits include earlier extubation, and decreased risks of CLD, and death or CLD at 36 weeks (NNT = 14), PDA and pulmonary air leak.
- There were no differences in the rates of neonatal mortality, infection, severe ROP, severe IVH, PVL, NEC and pulmonary haemorrhage.
- Hypertension, hyperglycaemia, gastrointestinal bleeding, intestinal perforations (NNT = 17), hypertrophic cardiomyopathy and growth failure were important short-term adverse effects.

b. **Intermediate post-natal steroids (7-14 days):** systematic review of RCTs of post-natal steroid found that moderately early steroid treatment (7-14 days of age):

- Reduced mortality at 28 days but not mortality before discharge
- Reduced CLD at 36 weeks (NNT = 5)
- Reduced death or CLD at 36 weeks (RR = 0.63, 95% CI 0.51-0.78; NNT = 4)
- Earlier extubation was facilitated (extubation failure at 7 days post steroids: NNT = 3)
- There was no significant effect on the rates of pneumothorax, severe ROP, and NEC.
- Short-term adverse effects included hypertension, hyperglycaemia, gastrointestinal bleeding, hypertrophic cardiomyopathy and infection.
- Steroid-treated infants were less likely to need late rescue with dexamethasone.

c. **Late post-natal steroids (>3 weeks):**

- Delayed steroid treatment had no effect on mortality. Beneficial effects of delayed
steroid treatment included reductions in failure to extubate by 7 or 28 days, need for late rescue treatment with dexamethasone, chronic lung disease at 36 weeks, death or CLD at 36 wk, and discharge to home on oxygen therapy. There was no increase in risk of infection, necrotising enterocolitis, or gastrointestinal bleeding. Short-term adverse affects included hyperglycemia, glycosuria and hypertension. There was an increase in severe retinopathy of prematurity, of borderline significance in survivors, but no significant increase in blindness.

d. Postnatal corticosteroids and neurodevelopment:

- **<96 hours**: Follow-up studies have been limited, but show increased risks of abnormal neurological examination, developmental delay, cerebral palsy (NNT = 15) and death or cerebral palsy (NNT = 20), but non-significant effects on moderate to severe neurological impairment and death or moderate to severe neurological impairment.

- **7-14 days**: These were reported in only one study, which did not demonstrate increased risks of abnormal neurological examination and death or abnormal neurological examination.

- **3 weeks**: Blindness was not significantly increased. There were increased rates of abnormal neurological examination both overall and in survivors. However, the incidence of moderate to severe neurological impairment both overall and in survivors was not increased. Non-significant effects on the rates of cerebral palsy were noted both overall (NNT = 25) and in survivors (NNT = 16). The combined outcome of death or cerebral palsy was not increased.

In summary, after consideration of the above evidence, we have decided to offer therapeutic postnatal corticosteroids to ventilated preterm infants at high risk of CLD, and that existing data are reassuring concerning long term outcomes of steroids used in a therapeutic manner. Therefore, postnatal corticosteroids should be offered after discussion with parents. The dose used should be the minimum effective dose, and the length of the course no longer than necessary.

e. Indications for steroids

Dexamethasone should be avoided in the first week of life unless life-saving.

Consider giving if:

- Preterm infants with persisting oxygen and ventilation requirements > 7 days of age.

Exclude other possible causes of respiratory deterioration including:

- Infection,
- PDA, or
- ET tube obstruction.

**Dosage: Dexamethasone:**

**Lower dose regimen (same as the DART trial schedule):** Consider shortening course if there is a good early response.

- 0.15 mg/kg/day 12 hourly for 3 days
- 0.10 mg/kg/day 12 hourly for 3 days
- 0.05 mg/kg/day 12 hourly for 2 days
- 0.02 mg/kg/day 12 hourly for 2 days

Consider repeating course or using the following higher dose if there is no response.

- 0.5mg/kg/day 12 hourly for 3 days.
Some babies may need a longer course if they deteriorate as the dose is being weaned down.

**Side Effects (% incidence in trials of intermediate steroid therapy)**:

- Hypertension (9%): This occurs quite commonly. It is unclear whether there are any benefits to treating it.
- Hyperglycemia (44%): Glycosuria occurred only in infants treated with dexamethasone (7 of 27) in the only trial evaluating this outcome. The number needed to treat to produce this harm is 4 (CI 2, 13). If values repeatedly exceed 12mmol/L, an insulin infusion is usually required.
- Gastrointestinal perforation or bleeding (8%): Resuscitation, ranitidine or surgery may be needed.
- Myocardial hypertrophy (23%): Think about this if a murmur appears in association with a respiratory deterioration in a baby on steroids. Following the change to lower dose courses, this is now rarely seen.
- Infection: There is an increased risk of infection: OR 1.35 [1.06, 1.71]. The risk may be reduced if care is taken to exclude sepsis prior to starting steroids, or covering sepsis with antibiotics if time doesn’t permit.
- Adrenal suppression: short courses (7 days) of dexamethasone only transiently suppress adrenal function. Longer courses (45 days) result in lower morning cortisol levels but continuing adrenal responsiveness to ACTH.

Any of these side effects may be an indication to stop the steroids early. This should be done in consultation with the Staff Specialist on call.

2. **Nitric Oxide**

There is currently insufficient evidence to use NO routinely for all preterm infants. In summary, there have been 11 RCTs of inhaled nitric oxide for preterm infants, of which 9 were eligible for inclusion in a Cochrane meta-analysis. However, the studies fell into 2 different groups: firstly, iNO was given in the first 3 days to preterm infants in respiratory failure or severe RDS, and secondly, it was given routinely to any babies requiring mechanical ventilation, or babies deemed to be at risk of CLD at 7 days. The second group clearly contained babies with less severe illness and lower risk of IVH or PVL.

In the first group, while there were short term improvements in oxygenation in treated infants, there was only a trend towards reduced death and/or CLD, and there was a strong trend to more IVH or PVL. By contrast, in the second group, there was significantly reduced IVH/PVL, and a significant reduction in death and/or CLD. Only one study reported long-term neurodevelopmental outcome, and these strongly favoured the iNO group. In summary, in babies who are beyond the period of risk for IVH and of mild-moderate illness severity, the treatment holds promise, but further research is needed.

**Long term Management of CLD:**

**Oxygen (see oxygen policy):** after the acute period, adequate oxygen needs to be provided for as long as necessary to achieve oxygen saturation between 90 and 95%. Targeting higher doses may exacerbate lung disease and does not help long term growth or development.

**Nebulised steroids** (early versus placebo, late versus placebo, or versus systemic steroids). Currently, use of inhaled steroids in this population cannot be recommended. There is no evidence from these meta-analyses that administration of inhaled steroids to ventilated preterm neonates is effective in
reducing the incidence of CLD. In the late (>14 days) group there was improved extubation, and in the early group there was a reduction in the need for systemic steroids.

**Fluids:** In babies with chronic lung disease, lung function may be improved by avoiding fluid overload. There is no evidence that fluid restriction is of any benefit. Care must be taken to ensure adequate caloric intake (carbohydrate, protein and fat) to ensure growth. These babies have high metabolic rates so need more than average calories. Fluid intakes up to 180/kg/day are well tolerated by most babies.

**Diuretics:**

1. Thiazide and spironolactone: in preterm infants > 3 weeks of age with CLD, four-week treatment with thiazide and spironolactone improved lung compliance and reduced the need for furosemide. Thiazide and spironolactone decreased the risk of death and tended to decrease the risk for lack of extubation after 8 weeks in intubated infants who did not have access to corticosteroids, bronchodilators or aminophylline. However, there is little or no evidence to support any benefit of diuretic administration on need for ventilatory support, length of hospital stay, or long-term outcome in patients receiving current therapy.

2. Furosomide: In preterm infants < 3 weeks of age developing CLD, furosemide administration has either inconsistent effects or no detectable effect. In infants > 3 weeks of age with CLD, a single intravenous dose of 1 mg/kg of furosemide improves lung compliance and airway resistance for 1 hour. Chronic administration of furosemide improves both oxygenation and lung compliance.

**Bronchodilators:** Inadequate data and no long-term data exist to recommend the use of beta-agonists, ipratropium bromide or methylxanthines for CLD. Beta-agonists and methylxanthines produce short-term improvements in lung mechanics. Use of bronchodilators is on an individual patient basis in RPA Newborn Care.

**Home oxygen:** A program exists for the provision of home nasal low-flow oxygen to patients residing in our area. Babies with CLD who do not tolerate breathing air, as judged by unsatisfactory overnight oximeter downloads, at a time when they are otherwise ready for discharge, should be considered for this program.

**Respiratory Syncytial Virus Immune Globulin:** The Cochrane review on this topic has been withdrawn due to a possible conflict of interest in one of the authors. Prior to this, it concluded that RSVIG is effective in preventing RSV hospitalizations and admission to the intensive care unit, but not in preventing mechanical ventilation. There was a non-significant trend towards a higher mortality in children given RSVIG. It is not effective as treatment for RSV infection. It should be considered on an individual patient basis for infants with severe chronic lung disease on discharge from hospital.

**Counseling of parents of infants with CLD should focus on:**

- Chronic lung disease and its medical implications.
- Natural history of CLD.
- Early signs of respiratory decompensation so as to seek urgent medical attention.
- Handling of respiratory emergencies.
- Awareness of environmental irritants and minimisation of infection risk.
- Effect of chronic disease on family dynamics and need for support and counseling.
- Prevention of infection (Handwashing, not sharing food and pacifiers, avoiding adults and children with respiratory illness, delay of childcare).

**Keypoints:**

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<th>Key Points</th>
<th>Level of Evidence</th>
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<td>Early targeted surfactant therapy in infants with RDS prevents CLD</td>
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With conventional ventilation: avoid over distention and over ventilation resulting in hypocarbia

HFO: use of a high volume strategy offers a marginal reduction the incidence of CLD (oxygen at 28 days) compared to conventional ventilation. Further results of neurodevelopmental follow up needed before routine use can be recommended.

After day 7, dexamethasone facilitates extubation and reduces CLD. Lowest effective dose should be used.

Indications for steroids in infants with CLD:

- Failure to wean from ventilator, or
- Preterm infants with persisting oxygen and ventilation requirements > 7 days of age.

Use of steroids should be discussed with parents before treatment is given.

Diuretics improve lung mechanics and oxygenation in infant. No long-term benefits have been shown.

Beta-agonists and methylxanthines improve short-term lung mechanics.

Prophylaxis with RSV immune globulin significantly reduces the incidence of RSV infection and need for hospitalisation, but doesn’t prevent ventilation

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Last Updated: July, 2008
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