Chronic Lung Disease of Prematurity, Management of - Paediatric Full Clinical Guideline - Joint Derby and Burton

Reference no.: NIC RC 14

Target health care professionals:	Staff of the Neonatal unit at Derbyshire Children's Hospital
Patients to whom this applies:	All infants at risk of or with chronic lung disease on the neonatal unit
Key words:	Chronic Lung Disease, Mechanical ventilation, fluid regime, Patent Ductus Arteriosus, Respiratory Distress Syndrome

1. Introduction

1.1 **Aim and Purpose:** To ensure a standard approach to the management of babies with chronic lung disease (CLD) based on:

- Evidence
- Increase awareness of the risk factors contributing to CLD
- Develop strategies to minimise the incidence of CLD in at risk babies
- Awareness of short and long-term management strategies
- Standardise post discharge care for babies with CLD

1.2 **Background:** Up to 70% of extremely low gestational age newborns (ELGANs) still ventilated after 7 days of age will develop chronic lung disease. CLD is associated with long-term respiratory morbidity, neurodevelopmental abnormalities and death.

1.3 Incidence of CLD

- 501-750g (34%), 751-1,000g (20%), 1,001-1,250g (5%) 1,251-1,500g (3%)
- <32 weeks GA: No BPD 52.3%, Mild BPD 16.9% and Significant BPD 30.9%[1]

1.4 Definition of chronic lung disease

- CLD, often interchanged with Bronchopulmonary dysplasia (BPD), is defined as oxygen requirement or respiratory support at 36 weeks PMA[1].
- National Neonatal Audit Programme criteria: gestational age at birth <32 weeks

Key points

1. The incidence of CLD in ELGANs still ventilated on day 7 of life is high
2. CLD is associated with significant long term morbidity and mortality
3. CLD is oxygen dependence or respiratory support at 36 weeks PMA

2 Causes of chronic lung disease (CLD)

ELGANs are born in the late canalicular/early saccular phases of lung development prior to alveolarization. Exposure to higher oxygen concentrations at birth and in the first week of life is associated with oxidative stress strongly linked with BPD and poor outcome.

2.1 **Risk Factors:** Many factors contribute to the development and worsening of CLD; they trigger systemic and pulmonary inflammatory response. The factors include:

a) Prematurity, infection and antenatal steroids
b) Birth weight <1000gms and intrauterine growth failure
c) Surfactant deficiency
d) Pulmonary oedema from fluid over load and Patent ductus arteriosus
e) Barotrauma and volutrauma from ventilation
f) Supplemental oxygen use

2.2 Clinical Features

Pathology: Initially there are areas of atelectasis and emphysema, hyperplasia of airway epithelium and interstitial oedema. Later changes include interstitial fibrosis and smooth muscle hypertrophy.

- **Oxygen dependence ≥ 36 weeks PMA.** Severity of CLD is based on the degree of respiratory support and or oxygen requirement.

Severity	Oxygen requirement or respiratory support
Mild	Oxygen >day 28 but self-ventilating in air at 36 weeks PMA
Moderate	<30% oxygen at 36 weeks PMA or discharge
Severe	>30% oxygen +/- CPAP/High flow at 36 weeks PMA or discharge

- **CXR shows changes due to inflammation and fibrosis**

Type	CXR changes
Type 1	Homogenous opacifications of lung fields beyond the first week of life
Type 2	Coarse streaky opacities with cystic changes in lung fields

- **Pulmonary hypertension and Cor-pulmonale** can be late features

Key points
1. Risk factors of CLD are multifactorial
2. Some risk factors may be iatrogenic and potentially modifiable

3 Prevention and managing risk factors of CLD

3.1 Antenatal

- **Prevent preterm birth:** liaise with maternity team on strategies to prevent preterm birth and appropriate use of tocolysis
- **Antenatal steroids**: at least one dose given to mothers who delivers between 24-34 weeks gestation.

3.2 **Infection prevention and treatment**: may induce early inflammatory cytokines causing chronic inflammation and neonatal lung injury.

- Early detection and treatment of infection; consider *Ureaplasma sp* colonisation
- No contraindication for immunisation; BCG should be delayed in babies on steroids.

3.3 **Caffeine**: In the CAP trial[2] VLBW, <30 weeks GA babies caffeine commenced within first 10 days of life had lower BPD and better neurodevelopmental outcome. Start caffeine prior to extubation, or within 3 days in <30weeks GA babies and continued until 34 to 36 weeks PMA.

3.4 **Minimise oxygen toxicity:** free oxygen radical is toxic and contribute to lung injury and retinopathy of prematurity.[3] To reduce this, we suggest

a) In the delivery suite
   - initiate resuscitation in blended oxygen starting with air
   - avoid excessive pressure and tidal volume in the first few bagging after birth
   - apply **oximetry** as indicated (see NLS algorithm in 1st 10 mins of life)

b) Post-delivery, keep saturation around 88-92%. After 36 weeks PMA keep saturation > 95% to prevent pulmonary hypertension

3.5 **Patent Ductus Arteriosus (PDA) and CLD:** See PDA guideline on:

- Avoiding high fluid intake in the presence of a PDA[4]
- Early identification and treatment of PDA

3.6 **Natural surfactant replacement therapy:** Early surfactant replacement reduces the risk of acute lung injury if requiring ventilation; consider dose, administration, timing of prophylactic or rescue surfactant on clinical ground. *See Surfactant guideline.* Early surfactant, with or without immediate extubation to CPAP, compared to delayed treatment, is associated with a significantly lower incidence of CLD [5]

If surfactant is administered, aim to extubate to BiPAP/CPAP as early as possible[6] minimal or less invasive [7-11] surfactant therapy with ongoing non-invasive ventilation (BiPAP/CPAP) under expert hands only.

a) **Prophylaxis (within 15mins of birth):** surfactant therapy and intubation followed by early extubation to non-invasive support as clinically indicated
   - **≤26 weeks gestation:** routinely offer prophylaxis
   - **>26-28 weeks gestation:** offer prophylaxis if ventilated
   - **≥28-32 weeks gestation:** offer prophylaxis if
     - Mother had no or incomplete antenatal steroid
     - intubated at birth as part of resuscitation

b) **Early Rescue**:
   - **≥ 28-32 weeks:** give surfactant therapy if oxygen requirement >30%
   - **>32-34weeks**: give surfactant therapy if oxygen requirement >40%

3.7 Strategies to minimise barotrauma and volutrauma

- Avoid routine intubation solely for surfactant administration >26 weeks gestation
- Offer BiPAP/CPAP if the baby has good respiratory drive in ≥26 week GA
- Use volume targeted/volume guarantee with pressure limited ventilation in ventilated surfactant deficient preterms, 3-4mls/kg is recommended
- Permissive hypercapnoea may reduce time on the ventilator
- Higher PEEP eg 6cm H_2O
- Avoid High flow (HF) <32weeks GA; documented clinical exemptions

3.8 **Adequate nutrition:** 110-135 kcal/kg/day[12] is required for normal growth. Babies with BPD have increased work of breathing and energy consumption; optimise calorie intake but avoid fluid overload.

- **Optimise calories** at 140-160kcal/kg/day with emphasis on calories not volume; fluid volume and calorie requirements are not interchangeable
- **Dietetic** input if growth is inadequate
- **Breast milk fortifier** if on ≥150mls/kg/day of maternal EBM
- **High energy** milk in reduced volumes may avoid fluid overload eg SMA High Energy 130mls/kg/day or Infatrini 120 mls/kg/day has same calories as 150mls/kg/day of preterm formulae

- **Vitamin A:** There is enough Vitamin A in TPN or breast milk fortifier; not enough evidence to support giving additional Vitamin A

3.9 **Fluid and sodium management:** judicious fluid use will avoid fluid overload.

- Avoid aggressive intravenous fluid administration or boluses.
- Limit total intravenous fluid or parenteral nutrition to 120mls/kg/day.
- Accept mild hyponatremia (>130mmol/L) in preterms, it is common in the first week of life, is tolerated well and not an indication to ↑ Na+ intake.
- Fluid restrict rather than add more Sodium if Na ≤125mmol/L

Key points

1. Adopt strategies to minimise or prevent risk factors of CLD
2. In liaison with maternity, prevent preterm birth and offer timely antenatal steroids
3. Avoid routine intubation ≥ 26 weeks GA; if ventilated offer early surfactant and extubate to Bi/CPAP at the earliest
4. Minimise oxygen toxicity and barotrauma/volutrauma
5. Avoid fluid overload but optimise calories/nutrition
6. Offer caffeine in VLBW babies by day 3 of life

4 Treatment of established chronic lung disease

4.1 **Respiratory support:** mortality is high, up to 25%, in babies with CLD requiring mechanical ventilation beyond 36 weeks PMA.

- Only offer mechanical ventilation if other modalities fail.
- Permissive hypercapnoea if pH >7.25
- Allow higher FiO_2 up to 80% on non-invasive support if good respiratory drive

4.2 **Steroids:** Steroids are not routinely indicated in CLD and rarely have lasting benefit; avoid in the first week of life except life threatening.

- **Indication:** should be used only in very severe CLD
  - infant on high O_2 and high ventilator settings who is worsening
  - ventilator depended at >2 weeks of age
  - after multi-disciplinary team and consultant discussion with parents
- **Goal:** facilitate extubation from the ventilator.
- **Regime and timing:** Optimum regime unknown but use minimum effective dose and shortest possible duration. Timings include **early** (<96hrs old), **Intermediate** (7-14days) and **late** (>3 weeks) [13-15]
- **Dosage: Dexamethasone:**
  Lower dose regimen (DART trial schedule):[16]
  - 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
- If no response, consider repeating above course or use the higher dose regime
  Higher dose regime
  - 0.5mg/kg/day 12 hourly for 3 days
  - 0.3mg/kg/day 12 hourly for 3 days
  - 0.2mg/kg/day 12 hourly for 2 days
  - 0.1mg/kg/day 12 hourly for 2 days
  - 0.05mg/kg/day 24 hourly for 4 days
- Consider shortening course if there is a good early response
- Consider a longer course if they deteriorate as the dose is being weaned down.
- **Side effect:** Steroids have significant side effects

- **Short term** adverse effect include hypertension, hyperglycaemia, myocardial hypertrophy, infection, adrenal suppression, gastrointestinal perforation/ haemorrhage. Please discuss with neonatal consultant
- **Long term** increased risk of poor neurological outcome

4.3 **Diuretics:** decision to start is consultant led; it may improve lung compliance and oxygenation[17,18]

- **Furosemide** solely for CLD should be avoided except with rapid weight gain and fluid oedema despite restricted fluid intake and adequate Na+ supplement. Alternate day furosemide may be effective with less side effect.
- **Chlorothiazide and spironolactone** for long term use in CLD but if no improvement by 1 week stop; consider stopping before discharge if effective
- **Side effects:** are common like hypercalciuria (leading to osteopenia & nephrocalcinosis), metabolic alkalosis (due to Cl- loss) and hypokalemia
- **Monitoring:** Babies on diuretics should be monitored closely for electrolyte imbalance, alkaline phosphatase and serum phosphate

4.4 **Severe CLD:** Discuss with tertiary paediatric respiratory consultant

- Pulsed methylprednisolone
- Hydroxychloroquine
- Azithromycin

Key points

1. Accept relative hypercapnoea and higher FiO_2 on non-invasive ventilation
2. Diuretics and steroids are not routinely indicated in CLD:
    a. they do not provide long term benefit
    b. side effects are common
    c. particular concerns on neurodevelopment outcome with steroid use
3. In severe CLD with failed 2 courses of steroids, seek paediatric respiratory consult

5 Discharge and follow up

5.1 **Counselling** of parents: the following should be discussed before discharge

- Chronic lung disease and its medical implications
- Natural history of CLD
- Early signs of respiratory decompensation and when 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 counselling
- Prevention of infection (Handwashing, avoiding persons with respiratory illness)

5.2 **Home Oxygen and sleep studies** (refer to Home Oxygen Therapy guideline)

5.3 Discharge planning for babies with CLD going home on oxygen

- Counselling parents (see 5 above)
- MDT meeting (see Home oxygen Therapy guideline)
- 12 lead ECG prior to discharge looking for pulmonary hypertension (PHT)
- Echocardiogram if suspected cardiac abnormality or ECG suggestive of PHT

5.4 Follow up

- **RSV immunization**: liaise with neonatal outreach nurse, offer RSV prophylaxis as per guidance except in those with confirmed RSV positive bronchiolitis.
- **Seasonal Influenza** vaccination after 6months chronological age
- **Routine Baby clinic**: arrange as usual with individual named consultant
- **CLD clinic:** on case by case basis as agreed with CLD neonatal lead

- **Mandatory 2-year neuro-development** clinic

Key points
1. Facilitate timely discharge planning and adequate counselling to parents
2. Timely sleep studies and 12 lead ECG before discharge
3. Arrange appropriate follow up

6 Monitoring compliance

4.2 **Audit standards:** to be carried out at least once every 12 month

- 85% of mothers giving birth between 24-34 weeks GA age should receive at least one dose of antenatal steroids
- 100% of babies born 24-32 weeks to have pulse oximetry by 5 minutes of life
- 100% of babies with CLD on steroids should have discussions with parents documented prior to treatment
- 100% of babies with CLD going home on oxygen should have ECG prior to discharge

4.3 Useful data collection

- Number of CLD with significant PDA >1.5mm
- Number of babies > 26-32 weeks GA intubated on arrival to NICU
- Number of babies on diuretics >1 week duration
- Number of babies with CLD given oral steroids
- Number of babies ≥ 28-32 weeks given surfactant when oxygen >30%
- Number of babies >32-34weeks given surfactant when oxygen >40%
- Babies 24-32 weeks GA on >120mls/kg/day of intravenous fluid (except indicated)
- Number of babies born before 32 weeks managed on High flow

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