Yorkshire & Humber Pan-Network Neonatal Clinical Guideline

Title: **Management of Babies at risk of Bronchopulmonary Dysplasia/Chronic Lung Disease of Prematurity**

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This clinical guideline has been developed to ensure appropriate evidence based standards of care throughout the Yorkshire & Humber Neonatal Network (Pan). The appropriate use and interpretation of this guideline in providing clinical care remains the responsibility of the individual clinician. If there is any doubt discuss with a senior colleague.

1. Aim of the guideline

1.1. Guidance for the management of babies at risk of Bronchopulmonary dysplasia (BPD) / Chronic Lung disease of prematurity (CLD).

1.2. Scope – this guideline applies to the management of babies below 32 weeks gestation at risk of developing BPD including prevention strategies, considerations for babies severely affected and around preparation for discharge. It does not apply to babies with chronic respiratory conditions due to other underlying causes such as congenital heart disease, genetic abnormalities such as cystic fibrosis or other specific lung pathologies

1.3. Recommendations in this guideline include evidence based strategies and some areas of accepted good practice which have not been so easy to clearly reference. However, they represent a group view of reasonable aspects to consider when managing babies at risk of CLD.

2. Summary of recommendations

2.1. Risk factors for CLD should be identified and recognised[1,2]

2.2. Strategies for management of early respiratory care, caffeine administration and fluid management should be in place in all Neonatal units to minimise the risk of development and severity of BPD

2.3. Opportunities for use of early hydrocortisone and postnatal steroids should be actively identified[2,3,15]

2.4. Nutritional strategies should include regular review of growth and adjusted accordingly with as few and as short breaks in nutrition as possible

2.5. Associated complications of prematurity are often more pronounced in babies with significant BPD – metabolic bone disease, adrenal suppression from repeated or prolonged course of steroids, gastro-oesophageal reflux and patent ductus arteriosus

2.6. Preparation for discharge should include consideration for home oxygen and assessment of cardiac function and pulmonary hypertension. https://www.networks.nhs.uk/nhs-networks/yorkshire-humber-neonatal-odn/guidelines-1/guidelines-new/respiratory

Summary Flow chart for Management at birth of Babies at risk of CLD as per ODN Early care guideline

DELAY CORD CLAMPING 1-3 MINUTES

THERMAL CARE: Plastic bag, transwarmer and hat.

CPAP: Start Facial CPAP at 5-6 cm H_2O (If <30 wks or resp distress)

ASSESS: **Heart rate, respiratory rate**, tone, saturations

Persistent Apnoea
Bradycardic despite airway support

Respiratory effort and HR >100

RISK FACTORS FOR RDS/CLD
- No antenatal steroids
- Chorioamnionitis
- PROM
- Oligohydramnios/ Pulmonary hypoplasia
- Congenital anomaly

Inflation breaths via face mask at 25/5
Ventilation breaths if required
Reassess respiratory effort
Titrate oxygen to saturation level

KEEP THE PEEP

Titrate oxygen to saturation levels

PROTECTIVE FACTORS;
- Antenatal steroids

FiO2 >50% and rising @ >10 mins
Poor respiratory effort

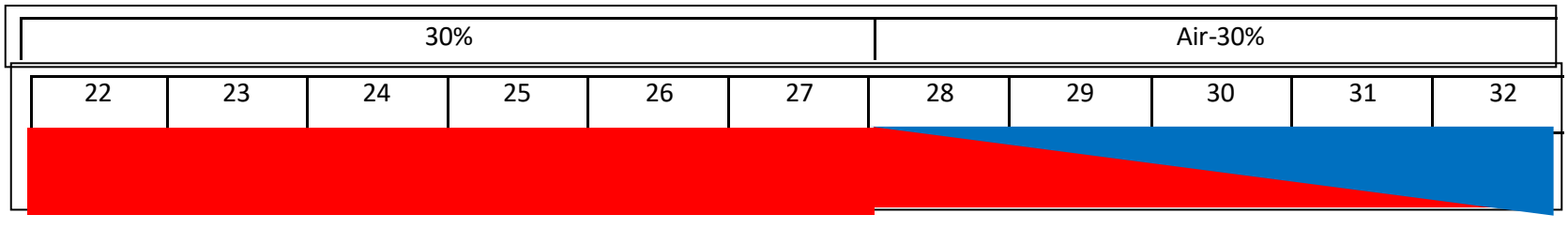
FiO2 <50% (or > 50% & falling) @ >10 mins
Good resiratory effort

Consider Intubation for curosurf @ **200 mg/Kg**

Transfer to NNU ventilated

Transfer to NNU on nasal CPAP

Starting FiO2 on blender



100% Intubated

'99%' CPAP

1. Background

Bronchopulmonary dysplasia (BPD) is a lung disease affecting predominantly preterm babies. It is a lung development disorder characterised by fewer alveoli which are susceptible to injury. Periods of mechanical or non-invasive ventilation can lead to diffuse airway damage and subsequent inflammation and fibrosis. Chronic lung disease of prematurity (CLD) is defined as a requirement for additional oxygen for at least 28 postnatal days[1] and is often a consequence of BPD. The severity is defined by the amount of supplemental oxygen the baby requires at 36 weeks CGA or discharge, if discharge is before 36 weeks.

CLD is associated with increased mortality, poor neurodevelopmental outcome, significant long term cardiorespiratory sequelae including pulmonary hypertension, decreased lung volume in the neonatal period, poor airway function and limited exercise tolerance in later childhood and adulthood.

Severity	Oxygen at 28 days	Supplementary oxygen required at 36 weeks CGA
Mild / Resolved	Yes	Self-ventilating in FiO2 0.21
Moderate	Yes	FiO2 0.22-0.29 (low flow O2)
Severe	Yes	FiO2 ≥0.30 or continuous positive pressure, high flow O2 or mechanical ventilation

2. Risk Factors

Recognised risk factors for bronchopulmonary dysplasia include:

- Demographic factors including
  - Lower gestational age
  - Lower birthweight
  - Small for gestational age (SGA)
  - Male sex
- Admission temp <35C
- Early and prolonged invasive ventilation
- Sepsis
- PDA
- CPR at birth
- Formula feeding

3. Early Respiratory Care

It is important to consider management strategies in early neonatal care to reduce modifiable risk factors for the development of CLD.
https://www.networks.nhs.uk/nhs-networks/yorkshire-humber-neonatal-odn/early-care-framework-resources/early-care-framework-for-preterm-infant/view
https://www.nice.org.uk/guidance/ng124

3.1. Thermoregulation

Maintaining normothermia has been shown to be beneficial in a range of neonatal outcomes including CLD. Please refer to local guidelines on Thermoregulation.

3.2. Surfactant Use

3.2.1. Surfactant should be given to all infants requiring intubation for stabilisation at 200mg/kg[1]. Please refer to local or network guideline for this. Yorkshire & Humber Neonatal ODN — NHS Networks

3.2.2. Minimally invasive surfactant administration techniques should be considered in babies who do not require invasive ventilation but do require surfactant. LISA is the preferred route of administration but in delivery suite intubation may be required. Use of a laryngeal mask to give surfactant is not recommended.

3.2.3. Rescue surfactant should be administered to infants requiring ≥30% oxygen on CPAP ≥ 6 cm H2O at ≥ 2 hours of age or who are ventilated and have not received surfactant in the delivery room

3.2.4. Additional doses of surfactant should be given if there is ongoing evidence of RDS such as persistent high oxygen requirement and other problems have been excluded

3.3. Ventilation

3.3.1. Oxygen

Supplemental oxygen can be delivered using low flow nasal cannula or ambient incubator oxygen.

Higher flow rates above 1 L/min via nasal cannula should be humidified.

Oxygen saturations should be between 90 and 94% and achieved by setting alarm limits between 89 and 95%

3.3.2. Non-invasive Ventilation

Nasal CPAP or high flow humidified oxygen as primary mode of respiratory support provides good lung inflation in infants at risk of atelectasis or respiratory fatigue and may prevent the need for ventilation. For infants requiring surfactant, early use of non-invasive support provides opportunities for LISA.

3.3.3. Invasive ventilation

3.3.3.1. Synchronised volume targeted ventilation (VTV) should be used as the primary mode of respiratory support for preterm infants requiring invasive ventilation, with escalation to high frequency oscillation (HFOV) as the next step.[4] Volume targeted HFOV may reduce CO2 variability and allow smaller tidal volumes to be used but does not remove the need for careful CO2 monitoring. It is also dependant on accurately functioning flow sensors and may be difficult in very small babies. Use of volume targeted HFOV even if brief can assist with estimates of required delta P.

3.3.3.2. If VTV or HFOV are not appropriate, other synchronised modes such as SIMV (intermittent mandatory ventilation) can be considered.

3.3.3.3. Synchronised pressure-limited ventilation, such as AC, SIPPV, PTV, PSV and STCPLV, should be avoided as there is evidence of an increased mortality before discharge, longer invasive ventilation and pneumothorax compared with HFOV and VTV[4].
https://www.nice.org.uk/guidance/ng124/chapter/Recommendations#respiratory-support-for-preterm-babies

3.3.3.4. Units should have regular review of ventilated infants throughout a 24 hour period and senior oversight to ensure ventilation periods are kept to a minimum. Consideration of weight, respiratory drive, pressures requirements and other comorbidities are all important factors for successful extubation. Weaning should start as soon as spontaneous respiration is well established. Caffeine therapy, postnatal steroids and avoiding the overuse of sedation can assist with earlier extubation.

3.4. Pharmacological Treatments

3.4.1. Caffeine

Consider early caffeine as soon after the point of admission for all infants <30/40 as it has been shown to reduce the risk of CLD (due to the anti-inflammatory properties) and improve neurodevelopmental outcomes. Caffeine should be considered for more mature babies if respiratory drive is poor.

Caffeine should be stopped at 33-35 weeks' if the baby is clinically stable.[4]

3.4.2. Diuretics

There is some limited evidence that preterm infants > 3 weeks of age with evolving CLD or ventilator dependence may benefit in the short-term from the administration od diuretics.[15] In these cases a trial dose followed by a short (2-4 week) trial of diuretics, with furosemide/chlorothiazide in combination with spironolactone are commonly considered. It is important to monitor for side effects, including electrolyte imbalance, metabolic bone disease, renal dysfunction and nephrocalcinosis. If no benefit is seen within 2 to 3 days, diuretics should not be continued.

When used, diuretics should ideally be reduced after 4 weeks in babies with moderately severe BPD and signs of metabolic bone disease should be monitored carefully.

Babies with severe BPD may require longer courses if clinically indicated.

3.4.3. Postnatal Steroids

3.4.3.1. Early hydrocortisone

Prophylaxis of early adrenal insufficiency with low dose hydrocortisone significantly decreases BPD and mortality in extreme preterm infants[2,3].

Please refer to ODN early hydrocortisone guideline for further details.

Respiratory — NHS Networks

3.4.3.2. Dexamethasone

Multiple RCTs of dexamethasone compared to placebo in preterm infants on respiratory support, have shown a clinically significant reduction in BPD at 36/40 corrected gestational age (CGA)[16].

Up to date evidence has not demonstrated a significant difference in the risk of cerebral palsy and neurodevelopmental impairment associated with postnatal steroid use.

Early use

Early (<7 days of age) dexamethasone use has been shown to significantly increase the risk of gastrointestinal perforation, and is therefore **NOT** recommended

Dexamethasone should also not be used simultaneously with anti-inflammatory drugs (NSAIDs) for this reason

Optimal time of use

Dexamethasone should be considered in preterm infants who are ventilator dependant beyond 8 days of age, have a significantly increased oxygen requirement or high ventilatory requirements and where other treatments have been ineffective[4]. Discussion with tertiary neonatologist/respiratory specialist is required before use in local units.

Dosage regime

Tertiary centres in the region use various different dosing regimens of dexamethasone, such as Maxi-Dex, Mini-Dex or DART, depending on local guidelines and individual baby's clinical circumstances.

Repeat Courses

Infants who initially respond well to dexamethasone, but later deteriorate or relapse, may need repeated courses, or a prolonged wean off of steroids.

Consider discussion with respiratory specialist/ tertiary neonatologist for infants >36/40 CGA with CLD dependent on non-invasive ventilation, who may benefit from dexamethasone to mitigate detrimental effects on neuro-development and facilitate discharge home.

Adrenal Suppression and other side effects

Longer courses or repeated courses of dexamethasone may result in adrenal suppression and babies should be evaluated carefully for effective adrenal function after prolonged use of dexamethasone to ensure replacement hydrocortisone is not required.

Other side effects of dexamethasone should be monitored and include hyperglycaemia, hypertension, infection, poor growth and rarely, hypertrophic cardiomyopathy.

Discuss benefits and side effects of steroid use with parents prior to starting treatment

3.4.3.3. Nebulised Budesonide

There is very little evidence to support the routine use of nebulised budesonide in the treatment of RDS and BPD

3.4.3.4. Sildenafil

Babies with severe CLD should undergo echocardiography assessment after 36 weeks for the possibility of pulmonary hypertension.

All babies being discharged in oxygen should have echocardiography assessment before discharge.

Where echocardiography confirms the presence of pulmonary hypertension

treatment with sildenafil may improve symptoms[5]. The treatment decision should be made in conjunction with cardiology. Dose regimes usually start at 250micrograms/kg QDS and are increased over the first week. Repeat assessment at 7 days is indicated. Where improvement is shown, a 3 month course is appropriate with further assessment at the end of this period.

3.4.4. Others

Other treatments such as Vitamin A, Bronchodilators, pulmonary vasodilators and anti-urea plasma antibiotics currently have limited evidence of benefit in preventing CLD, and are **NOT** recommended for routine use in early respiratory care targeted at managing respiratory distress syndrome (RDS) in the absence of other pathologies. Babies should be considered for recruitment to suitable multi centre trials for prevention of CLD. The outcome for the Aztec trial is awaited.

3.5. Nutrition

BPD is associated with a low lean mass and low functional residual capacity is associated with intrauterine growth restriction.

Parenteral nutrition should be started at the earliest opportunity for babies born < 30 weeks or with a birth weight below 1.25Kg to support introduction of enteral feeding. Standard TPN solutions should be available to use as first maintenance fluids for these babies.

Refer to local/network guidelines on optimising nutrition/feeding.

3.5.1 Gastroesophageal reflux (GOR)

Early assessment and management of gastroesophageal reflux is often required. Management may include pharmacological therapies such as gaviscon and omeprazole but prolonged courses should be avoided where possible. Consider a trial of nasojejunal feeding if simple measures are not effective. This may provide stability until babies are sufficiently mature for further investigations of GOR or careful reintroduction of nasogastric or oral feeding.

3.6. Fluid

3.6.1. Avoid early fluid overload as higher cumulative fluid balance in the first 10 days of life is associated with increased risks of death and BPD in infants <29/40.

3.6.2. In babies who are deemed hypovolaemic and fluid boluses are required, the decision to give a second or subsequent fluid boluses should be discussed and made with the duty consultant.

3.6.3. Maintain strict fluid input/output balances in the early stages of respiratory care especially when the risk of PDA is high

3.6.4. All units should have local guidelines on fluid management of preterm infant.

3.7. Patent Ductus Arteriosus (PDA)

The presence of a PDA and a high fluid intake are associated with an increased risk of BPD likely due to pulmonary fluid overload. Early prophylactic treatment is not recommended. The recently performed Baby OSCAR study did not show benefit in the routine use of prophylactic ibuprofen. (in press)

Consider appropriate management of clinically significant PDA according to local/network guidelines. Asymptomatic patent ducts do not require active steps for pharmacological closure.

https://www.networks.nhs.uk/nhs-networks/yorkshire-humber-neonatal-odn/guidelines-1/guidelines-new/cardiovascular

4. Oximetry for monitoring oxygen therapy in babies with BPD

4.1. The pan network guideline can be accessed by the following link: https://www.networks.nhs.uk/nhs-networks/yorkshire-humber-neonatal-odn/guidelines-1/guidelines-new/respiratory

4.2. This guideline specifically details the requesting of, setting up and interpretation of neonatal oximetry for babies with suspected and confirmed bronchopulmonary dysplasia. It does not cover specific disease management.

4.3. Providing supplemental oxygen to maintain adequate saturations has been shown to:

- Reduce pulmonary vasoconstriction (pulmonary hypertension)[6]
- Reduce mortality[1]
- Reduce risk of adverse neurodevelopmental outcomes[7]
- Reduce frequency of Brief Resolved Unexplained Events (BRUEs) [8]
- Improve growth[9]

4.4. When to do an oximetry

4.4.1. An oximetry study should be requested for those infants ≥36+0 weeks with a confirmed diagnosis of CLD, requiring O2 to maintain target oxygen saturations and who are approaching discharge. Some units may use this for routine care in SCBU and may require oximetry to be performed earlier than immediately pre discharge.

4.4.2. It is recommended that the following baseline investigations are considered:

- Echocardiogram for babies with moderate to severe CLD (to assess for pulmonary hypertension). Where this is not possible, consider an ECG to look for signs of right ventricular hypertrophy with referral for OP cardiac assessment
- Chest X- ray (within last 1-2 weeks, to check is consistent with BPD and not alternative diagnosis)
- Blood gas within 2 weeks

5. Discharge Planning

5.1. A multidisciplinary approach should be taken to discharge planning and the process should begin well in advance of the potential discharge date.

5.2. Early in the process suitability for home oxygen should be assessed by Neonatal or Paediatric specialists.

5.3. Referral to therapy services at discharge if not available on the unit in order to access early therapy intervention. The goal of early intervention is "to promote child health and well-being, enhance emerging competencies, minimise developmental delays, remediate existing or emerging disabilities, prevent functional deterioration and promote adaptive parenting and overall family function" [17,18]

5.4. A discharge check list should be complete (appendix)

1. Patient Assessment

1.1. Babies with CLD may be fit for discharge from the neonatal unit when their oxygen requirement is stable with mean saturations of >93% and without frequent episodes of desaturation[10].

1.2. The following criteria should also be met before discharge

- Over 36 weeks gestation
- Competent care givers and appropriate home environment
- Clinically stable or improving
- Gaining weight appropriately on current management- ideally responsive feeding.

1.3. If babies will not be monitored at home it is important to ensure the monitors are removed for 48 hours before discharge or as soon as a satisfactory overnight oximetry trace has been obtained.

2. Car Seat Challenge

2.1. Some units will assess a baby prior to going home on oxygen with a car seat challenge for a minimum of 30 minutes. For this the baby is placed in their own car seat and oximetry carried out under direct observation.

2.2. Acceptable results are obtained once saturations are 94% or above for the whole time of the study. Repositioning and increased oxygen flow rates are allowed to achieve an acceptable study.

2.3. Safety advice should be offered to all parents to avoid prolonged time in the car seat (>30minutes) whilst there is still respiratory compromise.

3. Discharge Check List

3.1. The Discharge Checklist should be completed prior to discharge (see Appendix A)

4. After Discharge

4.1. Follow up after discharge should include visits from community nurses, oximetry studies intermittently to aid weaning , weight and growth assessments and hospital follow-up within 4-6 weeks of discharge ideally with a consultant who has experience of CLD.
Respiratory — NHS Networks

4.2. Failure to reduce oxygen supplementation as expected should lead to a paediatric respiratory specialist review to rule out concomitant conditions.

4.3. The oxygen equipment can be removed from the home after 3 months if not required, if this is in the winter period it is usually left until the end of winter.

4.4. Other consideration

4.4.1. Infants with CLD should not fly within 6 months of stopping supplemental oxygen as cabin pressures provides FiO2 equivalent to 15% at sea level.

4.4.2. Most CLD infants will be off oxygen by 6 months corrected age and if not a discussion with a respiratory consultant should take place.

4.4.3. If an infant with CLD is still in oxygen at 6 months post term, other conditions should be considered and a referral to a tertiary centre made. Earlier referral for joint respiratory/neonatal follow up may be appropriate in babies with significant disease.

Appendix 1

Example Checklist for Discharge

Topics	Date	Signature
Referral to outreach team		
4-6 week follow-up OPA arranged		
Car seat test passed		
HOOF initiated		
First Palivizumab injection given		
GP aware to give flu vaccination IM after 6 months		
Open access organised		
The following to be discussed/ done with parents		
Reasons for home oxygen		
Signs of illness and recognition of respiratory difficulty		
Use of nasal cannulas including skin care and use of creams		
BLS training		
Medication- how to administer		
Medication- how to order at home		
Prevention of respiratory infections, immunizations and Palivizumab		
Safe storage and handling of oxygen equipment		
Fire safety in the home		
Safe use of oxygen		
Insurance for car and home		
Holidays		
Electricity repayment		
Portable oxygen. Travelling with pram/car/bus		
Supplies and ordering of oxygen		
Problem solving and who to contact		
Ongoing oxygen use, monitoring and weaning process		
DLA and family fund		
Information leaflets		

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