Ashford and St. Peter's Hospitals
NHS Foundation Trust

Prevention and Management of Chronic Lung Disease of Prematurity

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Guideline History		
Date	**Comments**	**Approved By**
Jan 22	New guideline incorporating previous guidance on Budesonide use	

Patients first • Personal responsibility • Passion for excellence • Pride in our team

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Prevention of Chronic Lung Disease

Chronic Lung Disease (CLD) by definition is the persistent need for oxygen in a neonatal patient beyond 28 days of life or 36 weeks corrected gestation. For simplicity in our unit we only classify these infants as CLD at 36 weeks corrected, before which they are “evolving” CLD.

CLD is also referred to as Bronchopulmonary Dysplasia (BPD). This is a specific histological diagnosis typically referring to lung disease caused by surfactant deficiency and mechanical ventilation.

CLD infers increased morbidity and mortality to our patients and their families, from the milder end of the spectrum going home on nasal cannula oxygen; to ongoing need for invasive long term ventilation with a very prolonged hospital stay.

Many of our commonplace practices are geared towards a reduction in CLD. With an increasingly immature population of premature infants surviving to discharge, it is timely to review these and make plain our wish to reduce all cause CLD.

Strategy to prevent BPD

1. Where possible, prevent preterm birth.
2. If preterm birth is inevitable, ensure antenatal optimisation including delivery in centre with a tertiary NICU; the timely use of antenatal steroids; appropriate management of chorioamnionitis. See KSS ODN Management at the Threshold of Viability.
3. At delivery, offer optimal cord clamping. Avoid positive pressure ventilation where possible. If the baby is making respiratory effort, stabilise using humidified high flow. See delayed cord clamping and extreme preterm guidelines.
4. Keep the baby’s temperature within the normal range throughout stabilisation and admission. See thermoregulation guideline.
5. Offer rescue surfactant in any infant who’s oxygen requirement is approaching 30% or who demonstrates increased work of breathing on optimised respiratory support. Consider earlier in the smallest babies (<25%). Use a Less Invasive approach to surfactant delivery in non-ventilated patients. See respiratory guidelines.
6. Start all preterm infants <30 weeks gestation on caffeine regardless of ventilation status.
7. If mechanical ventilation is required, use a patient triggered mode with volume guarantee (such as PC-AC VG, Drager *SLE). See respiratory guidelines.
8. Aim to minimise the duration of mechanical ventilation.
9. Do not routinely use morphine for sedation in ventilated preterm babies.

10. In the absence of sepsis, commence nebulised budesonide in all preterm infants <25 weeks regardless of FiO2, and in all infants 25-32 weeks gestation requiring oxygen.

11. Adopt a targeted approach to PDA management in the infants at greatest risk of CLD. See PDA guideline.

12. Optimise nutrition and growth. See nutrition and PN guidelines.

13. If the baby is likely to remain mechanically ventilated beyond 14 days of life, consider the need for steroid treatment (Dexamethasone).

Inhaled Budesonide in Preterm Babies

There is evidence that inhaled steroids reduce BPD in preterm babies, and despite a recent large study raising concerns about a slight (non-significant) increase in mortality, the latest meta-analysis data of 17 studies in 1807 babies shows no significant change in mortality and a RR of BPD of 0.79 p=0.0002 (1). A 20% reduction in risk of BPD is significant. BPD is a multifactorial disease, and whilst lung damage is a clear risk factor, others such as PDA may need to be simultaneously addressed.

- Start nebulised budesonide in babies in oxygen 25-32 weeks.
- Start nebulised budesonide in babies <25weeks on respiratory support, regardless of oxygen delivery
- Consider the use of budesonide in babies with respiratory insufficiency requiring prolonged respiratory support at any gestation

In the majority this will be delivered via the ultrasonic nebulised attachment for the Vapotherm Precision Flow, but in ventilated babies should be administered via the inspiratory ventilator tubing. Budesonide is continued until the baby has been in air for 1-2 weeks or comes off the High Flow. The decision to stop is a clinical one.

Care of the preterm lung is paramount, so early use of surfactant and non-invasive ventilation are important co-strategies. Inhaled budesonide is generally considered to be safe in children, with minimal systemic absorption anticipated. For example we have not seen any blood glucose derangements from using inhaled budesonide. Minimising sepsis is also critical. If there are objective concerns regarding sepsis, withhold budesonide until the episode is settling/under control.

If a baby has inhaled steroids stopped and then develops an oxygen requirement, it may be reasonable to restart them at the discretion of the attending/baby's consultant.

Postnatal steroids to facilitate extubation from mechanical ventilation

In any baby who requires ongoing mechanical ventilation beyond the first 14 days of life, consider the need for dexamethasone to assist coming off the ventilator.

Consider other causes of ongoing need for ventilation e.g. haemodynamically significant PDA. Exclude sepsis prior to starting.

Use the DART regime:

West of Scotland ORAL/ OTHER ROUTE Drug Monographs

Dexamethasone

****All doses expressed as Dexamethasone Base****

Neonatal

FORM Oral Solution 400micrograms/ml (2mg/5ml)
(Oral solution 100microgram/ml available on request for small doses)

INDICATION
1. Bronchopulmonary Dysplasia (BPD) / Facilitating Extubation in a pre term infant
2. Cerebral Oedema
3. Treatment of post intubation laryngeal oedema

DOSE RANGE
1. BPD / facilitating Extubation in a preterm infant

LOW DOSE SCHEDULE (DART regimen)

Day of treatment (inclusive)	DOSE	FREQUENCY	ROUTE
1 to 3	60 micrograms/kg/dose	2 times daily	Oral
4 to 6	40 micrograms/kg/dose	2 times daily	Oral
7 to 8	20 micrograms/kg/dose	2 times daily	Oral
9 to 10	8 micrograms/kg/dose	2 times daily	Oral

HIGH DOSE SCHEDULE (Consultant authorisation only)

Day of treatment (inclusive)	DOSE	FREQUENCY	ROUTE
1 to 3	200 micrograms/kg/dose	3 times daily	Oral
4 to 7	200 micrograms/kg/dose	2 times daily	Oral
8 to 14	200 micrograms/kg/dose	ONCE daily	Oral

Day 15 onwards- if the response is good the course may be stopped. If the response is less than adequate, then the course should be continued at 200micrograms/kg/dose ONCE daily or on alternative days

ADDITIONAL DOSING INFORMATION
- For both dose schedules, the weight to be used to calculate the doses prescribed is to be the baby's weight at the start of therapy, unless the consultant instructs otherwise
- Regimens can be lengthened/ shortened/ repeated as clinically indicated
- The decision about the length of each section will be the responsibility of a Consultant Neonatologist/ Paediatrician
- If doses of 300micrograms/kg/day are given for more than 7 days OR doses of 150micrograms/kg/day are given for more than 14 days, LIVE vaccinations must be delayed until three months after stopping treatment as per the guidance in the green book.

Counsel parents as to the risks of postnatal steroids:

- Potential impact on neurodevelopment
- Risk of gut injury
- Growth decline during treatment

- Hypertension
- Potential impact on blood sugar

Caffeine for the prevention of CLD

Apnoea of prematurity is defined as periods over 20 seconds of apnoea or less if associated with bradycardia and desaturation. Apnoea of prematurity is common but infants should be assessed to exclude other causes of apnoea such as sepsis, anaemia, NEC, encephalopathy, respiratory illness or apnoea secondary to medication.
Methyl xanthines (Caffeine, aminophylline and theophylline) are used as respiratory stimulants to prevent apnoea and facilitate extubation. They stimulate the respiratory centre and increase the basal metabolic rate.
Caffeine has a long half-life of around 100 hours, thus it can be safely given once daily and has less toxicity than the other methyl xanthines. It has a wider therapeutic to toxic ratio and has reliable enteral absorption.

Potential Benefits:
- Reduction in apnoea
- Reduction in chronic lung disease
- Improvement in extubation failure within 7 days
- Prevention of postoperative apnoea
- Diuretic effect.
- Reduction, although not statistically significant, in the incidence of severe retinopathy of prematurity.
- Improved rate of survival without neuro-developmental disability at 18-21months corrected. This statistically significant improvement has not been shown to persist at 5 years, although there was a continuing reduction in severity of motor impairment
- Improved white matter structure on MRI

Potential Risks/Disadvantages:
- Tachycardia, agitation, tachypnoea, tremors, vomiting, jitteriness and seizures (symptoms of Caffeine toxicity).
- Potential to worsen gastro-oesophageal reflux.
- Transient decreased weight gain (first 3 weeks of life).
- No significant difference in death rate, severe hearing loss or necrotising enterocolitis but some studies have suggested a reduction in intestinal and cerebral blood flow.
- Possible association with nephrocalcinosis, particularly in conjunction with diuretic therapy

Recommendations
- Give caffeine to all infants <30 week gestation, and/or <1500g

- Consider the need for caffeine in any infant 30-34 weeks requiring respiratory support or demonstrating recurrent apnoea (other causes excluded)
- Give a loading dose of 20mg/kg
- Standard maintenance dose is 5mg/kg OD
- In some circumstances increased maintenance caffeine may be given, up to 20mg/kg in divided doses (eg 7.5mg/kg BD for a total maintenance of 15mg/kg)
- Consider stopping caffeine between 32-34 weeks gestation in a clinically stable baby.
- Babies receiving Caffeine should have saturation and ECG monitoring. This can be discontinued 48 hours after stopping caffeine.

Management of established CLD

CLD can variously be grouped into severity depending on age and requirement for respiratory support. The important thing for us as clinicians is to recognise infants at increased risk of severe CLD, and tailor their holistic treatment accordingly.

Risks suggestive of evolving severe CLD in an infant born <27 weeks

1. Ongoing need for mechanical ventilation beyond 30 weeks gestation
2. Ongoing need for non-invasive ventilation beyond 34 weeks gestation (including high flow)
3. Early and persistent chest film abnormalities

These are not mandatory or exclusive risks for consideration of evolving severe CLD.

Approach to management should be multidisciplinary. The aim is to protect against further lung damage whilst supporting lung repair and optimising function.

Ventilation

Aim for extubation to non-invasive support

Optimise recruitment - pCO2 as a marker

Aim for O2 >93% >95% of the time

Medication

Consider the role of diuretics

Consider higher dose steroids

Feeding

Nutrition and growth paramount

Organise a pH study and treat any GORD

Reduce risk of aspiration - SLT review early (before 34 weeks)

Review evidence of metabolic bone disease

Cardiac

Review blood pressure (hypertension sequalae of CLD and steroid use)

Echo to review for pulmonary hypertension

Neurodevelopment

Refer for physio input

Consider ND needs if swaddling

Specialist Input

ENT review +/- MLB to review malacia/cords/SGS

CT chest

LTV team for specialist respiratory input

Diuretics

There is little evidence for a role for diuretics in the management of BPD. Theoretically their use can lead to a transient improvement in cardiopulmonary mechanics. In some cases, they may offer a superadded effect with other medication/ventilation strategies.
Diuretic use is associated with electrolyte abnormalities and a risk of nephrocalcinosis. They can negatively impact on growth.

Sildenafil

There is little evidence for the role of sildenafil in the management of BPD, though these infants are at increased risk of pulmonary hypertension. Echocardiographic review should be undertaken for any infant in persisting oxygen >36 weeks corrected gestation. Pulmonary hypertension may not be clearly identified by echocardiographic parameters, as shunting may occur at intrapulmonary level. A trial of sildenafil (or alternative) therapy may therefore be suggested. Sildenafil can worsen reflux or lead to feed intolerance.

Gastro-oesophageal Reflux Disease (GORD)

GORD is almost physiological in preterm babies. In babies with respiratory disease, they are at disproportionately increased risk of GORD and micro-aspirations which can lead to lung inflammation and damage. Babies with a persisting oxygen requirement >36 weeks should have been fully assessed for reflux, including the use of a pH study.
Conservative measures such as slow, smaller volume feeds should be considered.
Medication can be considered. First line treatment is with omeprazole. Be aware of the side effects of bone demineralisation (increasing risk of metabolic bone disease) and the impact on the gut microbiome by reducing gastric acid production.
Second line medications include domperidone (conduct an ECG prior to starting, and after 2 weeks) or erythromycin to promote gastric emptying.
In some cases gaviscon may be trialled, particularly for an infant who is bottle feeding.
Carobel is not routinely used in the treatment of GORD. It is a thickener with no role in acid suppression or gastric emptying; though anecdotally it may help reduce vomiting by keeping milk in the stomach.
Some infants may require continuous feeds via nasojejunal tube to overcome GORD and/or as a lung protective strategy.
Consider other causes of GORD such as cow's milk protein intolerance where there is family history or typical symptoms.

Oral feeding

Typically infants develop their suck/swallow/breathe co-ordination from around 34 weeks gestation. In extremely preterm infants this is very likely to be delayed.

Refer early for SLT input for any high risk infant:

- Ongoing need for respiratory support beyond 32 weeks gestation
- Any infant born <25 weeks

For infants with ongoing respiratory support it is particularly important to both avoid oral aversion, and to maintain airway safety/avoid aspiration. In these infants therefore the goal of oral feeding is not to necessarily get to full oral feeds, but to learn skills and enjoyment around feeding.

Being on HHFNC (vapotherm) is not an absolute contraindication to oral feeding, however at flows of >6LPM the suck swallow co-ordination can become more difficult. This is even more so on a background of lung disease and developmental delay.

Management of infants on ongoing invasive ventilation >36 weeks

1. Optimise ventilation strategy according to underlying pathology. Older infants may require a different approach, with a prolonged iT (or inversed i:e) and high PEEP in order to improve oxygenation.
2. Consider appropriate sedation. Wherever possible this should be non-pharmacological (swaddling) or oral medication. See below.
3. Consider the impact of procedures which may cause destabilisation. Procedures should be carried out by experienced personnel with adequate preparation and sedation as warranted; and sufficient assistants.
4. Infants with significant chronic lung disease may benefit from higher dose steroids, or repeated courses. Discuss with respiratory service for advice.
5. Infants may benefit from nasal rather than oral endotracheal fixation. This may reduce the incidence of unplanned extubation; however it can only be carried out as an elective procedure in the main.
6. Consider need for further investigations to identify the reason for ongoing ventilation.
    - Genetics including respiratory insufficiency panel (congenital surfactant deficiency, alpha 1 antitrypsin, cystic fibrosis)
    - Airway investigations – MLB. Discuss with ASPH ENT Mr Kiran Varadharajan
    - CT chest. Possible to do at ASPH.
7. Refer early for tertiary respiratory support (Paediatric Respiratory Team at St George's Hospital). Not all infants will be a candidate for long term ventilation.
8. Ongoing important role for physio, SLT and dietetic input

Options for sedation:

Oral/NG	Sucrose Oramorph (titrate from IV dose as per formulary) Clonidine
PR	Chloral (use only for isolated events eg pre-procedure, not regularly)
IV	Morphine Clonidine Midazolam Fentanyl

Paralytic agents including suxamethonium, pancuronium, vecuronium should only be considered in extremis to support improving oxygenation as a temporary measure; or to support success of a critical procedure such as long line insertion.

Pain relief: sucrose, paracetamol, morphine, fentanyl

2. Supporting References

Shinwell ES. Are inhaled steroids safe and effective for prevention or treatment of bronchopulmonary dysplasia? Acta Paediatr. 2018 Apr;107(4):554-556.

West of Scotland Neonatal Formulary

NICE guidance Neonatal Respiratory Care

South West ODN Neonatal Guideline on Caffeine Use

Bamat NA, Nelin TD, Eichenwald EC, Kirpalani H, Laughon MM, Jackson WM, Jensen EA, Gibbs KA, Lorch SA. Loop Diuretics in Severe Bronchopulmonary Dysplasia: Cumulative Use and Associations with Mortality and Age at Discharge. J Pediatr. 2021 Apr;231:43-49.e3. doi: 10.1016/j.jpeds.2020.10.073. Epub 2020 Nov 3. PMID: 33152371; PMCID: PMC8005411.

Michael Z, Spyropoulos F, Ghanta S, Christou H. Bronchopulmonary Dysplasia: An Update of Current Pharmacologic Therapies and New Approaches. Clinical Medicine Insights: Pediatrics. January 2018. doi:10.1177/1179556518817322

3.Parent resources

What is BPD and what causes it? | British Lung Foundation (blf.org.uk)

Chronic lung disease (CLD) | Bliss

4. Supporting relevant trust guidelines

Management of extreme prematurity

Neonatal stabilisation

Thermoregulation

Neonatal respiratory guideline

5. Guideline Governance

a. Scope

This guideline in relevant to all staff caring for babies across neonatal intensive care, transitional care and maternity.

b. Purpose

i. This guidelines aims to facilitate a common approach to the management of babies admitted under neonatal care. At times deviation from the guideline may be necessary, this should be documented and is the responsibility of the attending consultant.

ii. This guideline is subject to regular review to ensure ongoing evidence based practice.

c. Duties and Responsibilities

What is expected from the health care professionals using this guideline to look after infants.

d. Approval and Ratification

This guideline will be approved and ratified by the Neonatal Guidelines Group.

e. Dissemination and Implementation

i. This guideline will be uploaded to the trust intranet 'Neonatal Guidelines' page and thus available for common use.
ii. This guideline will be shared as part of ongoing education within the Neonatal Unit for both medical and nursing staff.
iii. All members of staff are invited to attend and give comments on the guideline as part of the ratification process.

f. Review and Revision Arrangements

a. This policy will be reviewed on a 5 yearly basis.
b. If new information comes to light prior to the review date, an earlier review will be prompted.
c. Amendments to the document shall be clearly marked on the document control sheet and the updated version uploaded to the intranet. Minor amendments will be ratified through the Neonatal Guidelines Group. A minor amendment would consist of no major change in process, and includes but is not limited to, amendments to documents within the appendices.

g. Equality Impact Assessment

Background • Who was involved in the Equality Impact Assessment
Neonatal Guidelines Group
Methodology • A brief account of how the likely effects of the policy was assessed (to include race and ethnic origin, disability, gender, culture, religion or belief, sexual orientation, age) • The data sources and any other information used • The consultation that was carried out (who, why and how?)
All patient and staff groups were considered
Key Findings • Describe the results of the assessment • Identify if there is adverse or a potentially adverse impacts for any equalities groups
No evidence of discrimination
Conclusion • Provide a summary of the overall conclusions
No evidence of discriminaton
Recommendations • State recommended changes to the proposed policy as a result of the impact assessment • Where it has not been possible to amend the policy, provide the detail of any actions that have been identified • Describe the plans for reviewing the assessment
Guideline ratified for use, review as per guidance 3 yearly

h. Document Checklist

To be completed (electronically) and attached to any document which guides practice when submitted to the appropriate committee for approval or ratification.

Title of the document:

Policy (document) Author:

Executive Director:

		Yes/No/ Unsure/NA	Comments
1.	**Title**		
	Is the title clear and unambiguous?	**Y**	
	Is it clear whether the document is a guideline, policy, protocol or standard?	**Y**	
2.	**Scope/Purpose**		
	Is the target population clear and unambiguous?	**Y**	
	Is the purpose of the document clear?	**Y**	
	Are the intended outcomes described?	**Y**	
	Are the statements clear and unambiguous?	**Y**	
3.	**Development Process**		
	Is there evidence of engagement with stakeholders and users?	**Y**	
	Who was engaged in a review of the document (list committees/ individuals)?	**Y**	**Neonatal guidelines group**
	Has the policy template been followed (i.e. is the format correct)?	**Y**	
4.	**Evidence Base**		
	Is the type of evidence to support the document identified explicitly?	**Y**	
	Are local/organisational supporting documents referenced?	**Y**	
5.	**Approval**		
	Does the document identify which committee/group will approve/ratify it?	**Y**	
	If appropriate, have the joint human resources/staff side committee (or equivalent) approved the document?		
6.	**Dissemination and Implementation**		

		Yes/No/ Unsure/NA	Comments
	Is there an outline/plan to identify how this will be done?	**Y**	
	Does the plan include the necessary training/support to ensure compliance?	**N/A**	
7.	**Process for Monitoring Compliance**		
	Are there measurable standards or KPIs to support monitoring compliance of the document?	**N/A**	
8.	**Review Date**		
	Is the review date identified and is this acceptable?	**Y**	
9.	**Overall Responsibility for the Document**		
	Is it clear who will be responsible for coordinating the dissemination, implementation and review of the documentation?	**Y**	
10.	**Equality Impact Assessment (EIA)**		
	Has a suitable EIA been completed?	Y	

Committee Approval (Neonatal Guidelines Committee)			
If the committee is happy to approve this document, please complete the section below, date it and return it to the Policy (document) Owner			
Name of Chair	**M. S. Edwards**	**Date**	**26 Sept 22**
Ratification by Management Executive (if appropriate)M. S.			
If the Management Executive is happy to ratify this document, please complete the date of ratification below and advise the Policy (document) Owner			
Date: n/a			