Management of the Infant with Evolving/Established Bronchopulmonary Dysplasia (BPD)

PEDIATRIC NEWBORN MEDICINE CLINICAL PRACTICE GUIDELINES
Clinical Practice Guideline:
Management of Evolving and Established Bronchopulmonary Dysplasia (BPD)

Points of emphasis/Primary changes in practice:
1. Criteria for extubation from invasive mechanical ventilation
2. Criteria for weaning from non-invasive mechanical ventilation
3. Use of pharmacotherapy to facilitate extubation and weaning from assisted ventilation
4. Nutritional support
5. Feeding and developmental care
6. Discharge planning and follow-up care

Rationale for change:
To optimize and standardize management of infants with evolving and established bronchopulmonary dysplasia using a multidisciplinary team approach

Questions?
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This is a clinical practice guideline. While the guideline is useful in approaching the care of the infant with established bronchopulmonary dysplasia (BPD), clinical judgment and/or new evidence may favor an alternative plan of care, the rationale for which should be documented in the medical record.

I. Purpose

The purpose of this clinical practice guideline is to optimize and standardize the care of infants with evolving and established BPD to improve short-term and long-term outcomes.

II. Scope

Preterm infants born at < 32 weeks’ gestation, who require non-invasive (NIPPV, NCPAP or HFNC > 2 lpm) or invasive mechanical ventilation beyond 28 days of life.

III. Definitions

Evolving BPD is defined as an ongoing need for invasive or non-invasive respiratory support (NIPPV, CPAP, HFNC > 2 lpm) and/or supplemental O₂ in preterm babies (< 32 wks GA) between postnatal day 28 and 36 wks PMA.

Established BPD is defined as an ongoing need for invasive or non-invasive respiratory support (NIPPV, CPAP, HFNC > 2 lpm) and/or supplemental O₂ in preterm babies (< 32 wks GA) older than 36 wks PMA.

IV. Pharmacotherapy

Diuretics: Excessive interstitial and/or alveolar edema occurs commonly in BPD and can lead to decreased pulmonary compliance. Loop diuretics (including furosemide) and thiazide diuretics (including chlorothiazide) transiently improve pulmonary compliance [1, 2]. Infants with clinical and radiographic signs of pulmonary edema may transiently benefit from a single-dose or short

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course of diuretic therapy (up to one week). Generally, furosemide is preferred for short duration therapy. Infants who persistently require and benefit clinically from single-doses or short course of furosemide may benefit from chronic therapy. In this setting, chlorothiazide is preferred due to lower risks of electrolyte imbalance, ototoxicity, nephrocalcinosis, and osteopenia. Chronic therapy after demonstration of benefit in an individual patient should be initiated with a clear clinical endpoint to limit exposure to the adverse effects of diuretic therapies. When utilizing chronic diuretic therapy, careful attention must be paid to serum electrolytes, specifically chloride and potassium [3]. When possible, correction with potassium chloride is preferred over sodium chloride to minimize fluid retention from excessive sodium intake (Appendix 1 & Appendix 2).

**Bronchodilators:** Increased airway resistance due to smooth muscle hypertrophy and hyperreactivity can be associated with severe BPD. Bronchodilators (including the beta2 adrenergic agonist albuterol and anticholinergic ipratropium) transiently improve pulmonary compliance with high inter-individual variation (4% - 25%). However, bronchodilators have no impact on the duration of oxygen supplementation [4, 5]. Individual trials of bronchodilators (albuterol with or without ipratropium) may be considered in preterm infant with wheezing or worsening compliance for symptomatic relief. Administration should be followed by meticulous assessments of clinical response by examination and measured changes in pulmonary mechanics. Careful monitoring for tachycardia and arrhythmias is also required (Appendix 3). Levalbuterol has no efficacy or toxicity advantages compared to albuterol and, therefore, has no place in therapy [6].

**Methylxanthines:** Methylxanthines, specifically caffeine, have an established role for the prevention of BPD in premature infants at risk for BPD [7]. Methylxanthines also have bronchodilatory and diuretic properties that may be desirable in the palliation of established BPD. However, standard doses of caffeine have diminishing clinical impact with advancing PMA; in fact, a tangible impact on oxygenation disappears at 36 weeks PMA [8]. Therefore, caffeine therapy should generally be discontinued at this age. If compelling indications exist to continue therapy (i.e., persistent central apnea), dose adjustment is indicated. We recommend continuation of caffeine in the NICU until after discontinuation of respiratory support.

**Corticosteroids:** Postnatal systemic corticosteroid therapy improves pulmonary outcomes of infants with established BPD. However, corticosteroids, primarily, dexamethasone, is associated with increased risk of cerebral palsy [9]. Current literature support the notion that the potential benefit of postnatal corticosteroid therapy in treatment of established BPD may not outweigh its known adverse effects and therefore should be used only in select cases after careful discussions with the parents.

- **Low dose dexamethasone treatment:** Although the investigators targeted neonates in the second week of life, “the Dexamethasone: A Randomized Trial (DART)” enrolled patients at a median age of 23 and 22 days in the treatment and placebo groups, respectively [10]. This trial of low-dose dexamethasone did not reduce the incidence of BPD, however, there was a significant reduction in failure to extubate on day 3, day 7, and day 10 of therapy. Therefore, this regimen (0.89 mg/kg total dexamethasone over 10 days) may be considered for infants with severe BPD, who remain on invasive mechanical ventilation beyond 36 weeks PMA (Appendix 4). However, it should be noted that the 2010 revised AAP policy statement indicate that data are insufficient to make a recommendation in the use of low-dose dexamethasone (< 0.2 mg/kg/d) in the management of BPD [11].
- Prednisolone treatment: After 40 weeks PMA, preterm infants with BPD, who have not responded to a trial of diuretics and/or bronchodilators and continue to require invasive or non-invasive ventilation, may benefit from a short-course prednisolone therapy. Cessation of supplemental oxygen was possible in a high percentage of infants with a pulmonary acuity score \( < 0.5 \) or baseline capillary \( P_{\text{CO2}} < 49 \) mm Hg treated with prednisolone (16 mg/kg total over 14 days) [12]. Notably, infants with a higher pulmonary acuity score or baseline \( P_{\text{CO2}} \) also responded to this therapy 40-50% of the time. Although prospective data and long-term follow-up studies are lacking, this may be a reasonable approach for patients in which protracted respiratory support is delaying discharge or other milestones, although the potential harm of systemic corticosteroids must still be considered (Appendix 5).

V. Respiratory Management

The primary goal of treatment for infants who require invasive mechanical ventilation is extubation to a non-invasive form of ventilation. Extubation should be considered when MAP < 10 and FIO\(_2\) < 0.4. A short course of diuretics, caffeine bolus, and optimization of O2 carrying capacity by a PRBC transfusion to achieve a hct of 30-35 should be considered prior to the extubation attempt (see flowchart).

Post-extubation support is initiated with CPAP or NIPPV as this mode of non-invasive ventilation has been shown to reduce the incidence of extubation failure [13]. Suggested initial NIPPV settings and reintubation criteria are indicated on the Flowchart. Weaning from NIPPV to CPAP and CPAP to RA will be gradually accomplished according to the guidelines shown on the Flowchart.

VI. Nutritional Management

Growth in the NICU is an important determinant of neurodevelopmental outcomes for very low birth weight infants [14]. However, infants with established BPD commonly demonstrate poor postnatal growth during their hospitalization. Established BPD is commonly assumed to increase resting energy expenditure compared to healthy neonates [15], and therapeutic interventions for BPD, such as diuretics, systemic steroids, and fluid restriction, may place these infants at higher risk of energy and protein deficits [16]. Although evidence exists supporting early fluid restriction in relation to BPD prevention [17], there is a paucity of data regarding fluid management in the neonate with relation to BPD beyond the first 7-14 days of life. Fluid restriction beyond the initial transitional phase, particularly in the human milk-fed preterm infant, is typically coupled with the use of macronutrient modular supplementation to meet target and/or increased energy and protein goals in order to achieve optimal growth patterns. However, fluid restriction and the use of modulars can alter macronutrient ratios and impact available volume of multi-nutrient human milk fortifiers. Energy needs for an infant with BPD have been estimated to be up to 25% greater than for an infant without BPD, thus in the range of 120 to 150 kcal/kg/day [18]. To ensure adequate energy and nutrient intakes, optimizing enteral volumes of 150-160 mL/kg/day using preterm infant feedings (ie, fortified human milk or preterm infant formula) may allow for appropriate intake and substrate to support optimal growth. Target growth trends for most preterm infants, including those with established BPD, include weight gain of 15-20 g/kg/day, and ideally 18-22 g/kg/day if a history of poor growth or known nutrient deficits from early NICU course exist, along with \( > 0.9 \) cm/week for both length and OFC growth. These trends should guide optimization of nutritional management of infants with established BPD during their NICU stay.
VII. Developmental and Feeding Therapy:

The Developmental Therapy Program at Brigham and Women’s Hospital consists of a team of pediatric therapists with training in the fields of Physical Therapy (PT) and Speech Language Pathology (SLP). These practitioners have specialized knowledge of the neurodevelopment of both preterm and full-term infants, as well as neonatal and childhood developmental milestones. The Developmental Therapy Team works alongside medical, nursing, and allied health professionals to provide developmentally supportive care of infants in the unit, including those with BPD.

The role of the Developmental Therapy Team in treating infants with BPD include the following:

- Perform standardized assessments and evaluate developmental progress of each infant
- Assess caregiver/family goals for each infant, provide caregiver/family education, guide caregiver/family participation during routine handling
- Provide an individualized therapeutic program to help facilitate the acquisition of age appropriate developmental milestones
- Incorporate therapeutic activities into routine care and age appropriate play

**Developmental Therapy:**

Infants with established BPD are at risk of developmental delays and disorders as a result of prematurity, underlying respiratory disease, necessary medical management (e.g. intubation, CPAP), and time spent in hospital.

All infants who meet the following criteria will automatically receive developmental therapy input from BWH NICU therapy staff (PT and SLP):

- GA at birth <32 weeks
- Respiratory support at ≥34 weeks GA

Other infants can be referred for developmental therapy on a case-by-case basis, as needed.

**Neurodevelopmental Goals for Infants with BPD:**

- Facilitate maintenance of physiological and behavioral stability during routine handling and while performing age appropriate developmental skills, including:
  - Physical/motor, cognitive, emotional, social, neurobehavioral, and neurosensory (i.e. visual/auditory) skills
- Modulate sensory inputs and facilitate age appropriate external environment
- Promote guided movement, muscle strengthening, and proper positioning for musculoskeletal alignment, postural control, and breathing mechanics
- Encourage family participation, caregiver-infant bonding, and family involvement in monitoring infant’s progress
**Feeding Therapy:**

Please refer to the existing CPG: Feeding in the Weeks Leading up to Discharge

Of note, infants with established BPD are at risk of feeding delays and disorders as a result of prematurity, underlying respiratory disease, necessary medical management (e.g. intubation, CPAP), and time spent in hospital.

While receiving positive pressure support (ventilation, CPAP, or HFNC), infants shall not be fed by mouth (per os, PO) due to risk of aspiration. Infants who are on LFNC or RA, may be fed PO when they are physiologically stable (e.g. not tachypneic). Given the high risk of silent aspiration in the BPD population, infants should start PO feeds with full precautions in place:

- Encourage breastfeeding, where possible
- Start any bottle feeds with an ultra slow flow bottle nipple (i.e. Dr Brown’s ULTRA Preemie)
- Position the infants in side-lying with horizontal milk flow
- Provide external pacing as required (i.e. tip the bottle down to slow milk flow and/or impose a break in sucking)

If the infant shows any signs (e.g. cough, increased congestion, SpO2 desaturation, apnea, bradycardia) and/or any symptoms (e.g. failure to wean from respiratory support, failure to progress with PO feeds) suggestive of aspiration and/or airway compromise during PO feeds, consider placing the infant NPO for a period of 48-72hrs before reevaluating. Where suspicions of aspiration continue, a modified barium swallow (MBS) study may be required to objectively evaluate swallow function and determine aspiration risk. Thickened feeds should not be considered as a treatment for swallowing dysfunction without objective information from MBS that thin fluids feeds cannot be tolerated and that thickened feeds are effective in remediating aspiration risk.

**VIII. Discharge Planning and Follow-up Care**

It is important to obtain tests to document the baseline status on discharge and to screen for late complications of BPD. Therefore, a capillary or venous blood gas as well as a CXR should be obtained within a month prior to discharge to assess for baseline CO₂ retention and radiographic features characteristic of this disease. Infants with BPD who are being discharged home on any kind of ventilator support, O₂ or medications, such as diuretics, should also be screened for pulmonary hypertension (PAH) with an echocardiogram within a month prior to discharge.

Discharge planning must be organized by a multidisciplinary team including the neonatologist, primary nursing team, discharge care coordinator, dietitian, occupational/physical and feeding therapists. Discharge preparation should start within a month of the anticipated discharge date with a multidisciplinary team meeting followed by a team meeting with the parents for planning and discussion of the following:

a) an assessment of the home environment and social support
b) identifying supplies and equipment that will be needed at home
c) teaching parents use of home equipment and all other aspects of care
d) referrals to early intervention, infant follow-up, pulmonology, and feeding clinics
e) contacting primary care physician
Preterm Infant (> 28 d) with Evolving/Established BPD on Invasive Mechanical Ventilation

MAP < 10, FiO2 < 0.4

Consider the following 24 h prior to extubation:
- Caffeine bolus
- PRBC tx if hct < 30-35
- Furosemide 1-2 doses if any evidence of fluid overload, pulmonary edema, or with PRBC tx

First extubation attempt to CPAP\(^a\) or NIPPV\(^b\)

Successful

- Continue NIPPV or CPAP for 2-3 d
- Transition to bubble CPAP (BCPAP) (7-8 cm H\(_2\)O) if FiO2 < 0.3 and RR < 70-80
- Wean BCPAP by 1 cm H\(_2\)O every 3-5 d if FiO2 < 0.3\(^d\)
- Trial of RA/LFNC O2 when BCPAP 5 and RA for 3-5 d and PMA > 32 wks\(^d, e\)
- Transition from BCPAP to HFNC (3-4 lpm) if unable to wean to RA/ LFNC > 36 wks PMA and/or nasal trauma
- Wean HFNC by 1 Lpm every 2-3 d until 2 Lpm, then trial of RA/LFNCO\(^d\)

Unsuccessful\(^c\) or MAP > 10 and FiO2 > 0.4

- Consider low dose dexamethasone or prednisolone Rx if PMA > 36 wks
- Wean ventilator settings as tolerated and reattempt extubation within 3-4 d

\(^a\) Suggested initial CPAP settings, 8-9 cm H\(_2\)O; if trial of CPAP fails\(^d\), trial of NIPPV before reintubation

\(^b\) Suggested initial NIPPV settings [17]:
- Rate: initial 10, max 40;
- PIP: initial 10 above PEEP, max 18;
- PEEP: initial same as when intubated, max 8

\(^c\) Extubation failure criteria:
- one episode of apnea requiring bag mask ventilation (BMV) or
- more than six episodes of apnea requiring stimulation in a 6-h period or
- more than 100% increase in baseline FiO2 for more than 4-6 h (for example from 30% to 60%) or
- significantly increased work of breathing and/or RR >80 consistently

\(^d\) Criteria for failure to wean or discontinue CPAP/HFNC:
- more than 20% increase in baseline respiratory rate for more than 4-6 h or
- more than 30% increase in baseline FiO2 requirement for more than 4-6 h (for example from 30% to 40%) or
- LFNC O2 requirement > 200 ml for more than 4-6 h

\(^e\) Return to previous settings if unable to wean based on criteria defined in \(^d\)
References