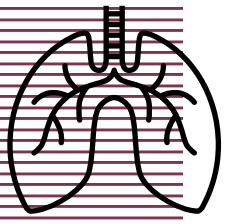

DISCHARGE GUIDELINES FOR INFANTS WITH BRONCHOPULMONARY DYSPLASIA (BPD)

JOINT RECOMMENDATIONS FROM NEONATAL-PERINATAL MEDICINE & PEDIATRIC PULMONOLOGY

These discharge guidelines should apply to infants with moderate to severe bronchopulmonary dysplasia, specifically those who require supplemental oxygen via nasal cannula following discharge. Infants with other types of chronic lung disease may also require respiratory support following discharge. Though they may benefit from similar discharge recommendations, we recommend that they are discussed individually with consultation.

PULMONOLOGY CONSULTATION

- ☐ Consider pulmonology consult at 36-38 weeks and follow-up consult 1-2 weeks prior to discharge
- ☐ If no previous consult, please consult pulmonology at least 1 week prior to discharge

CARDIOLOGY CONSULTATION

- ☐ Consider cardiology consult at 36-38 weeks for infants with echocardiograms showing pulmonary hypertension OR at any gestation for infants requiring treatment with Sildenafil

OXYGENATION

- ☐ Recommend no oxygen weaning or changes in respiratory medications < 1 week before discharge
- ☐ Goal effective $FiO_2 \leq 30\%$ prior to discharge
  - Low flow effective oxygen estimation: http://lhp.leedsth.nhs.uk/other_versions/3925FiO2Table.pdf
- ☐ Goal oxygen saturations 92-96%
  - If suspected or confirmed pulmonary hypertension, consider higher end of this range
  - Once discharged, parents should use goal > 92%; Parents should not wean oxygen at home
- ☐ Family should be discharged with pulse oximetry and receive adequate training for use at home
  - Recommend intermittent pulse oximetry while awake & continuous while sleeping

VENTILATION

- ☐ Obtain basic metabolic panel and blood gas < 1 week prior to discharge
  - Goal serum bicarbonate: < 32
  - Goal pCO_2: < 60
- ☐ Trend serum bicarbonate with electrolytes every 2 weeks to monitor chronic respiratory status

SCREENING FOR PULMONARY HYPERTENSION

- ☐ Echocardiograms
  - Obtain routinely at 36-38 weeks corrected gestational age
  - If prolonged mechanical ventilation or positive pressure, consider repeat ECHO monthly until off positive pressure
  - If suspected or confirmed pulmonary hypertension, repeat ECHO monthly and < 1 week prior to discharge
  - Goal for discharge: Pulmonary hypertension should be resolved OR mild and stable for several ECHOs before consideration of discharge

Rev: Nov 2021

Growth

- ☐ Ensure consistent proportional growth
  - Obtain length weekly (consider length board measurement if available)
- ☐ As infant nears the last 2-3 weeks of hospital stay, recommend evaluation by NCCU dietician for growth, discharge readiness, home nutrition plan, and goals for nutritional rehabilitation
- ☐ Consider repeat evaluation of bone health (calcium, phosphorus, & vitamin D level) prior to discharge, especially for infants previously on elemental formula

Diuretics

- ☐ Avoid chronic diuretics when possible
- ☐ If history of diuretic use, attempt to wean or reduce to single diuretic prior to discharge
- ☐ If unable to wean diuretics prior to discharge, consider thiazide diuretic instead of furosemide
- ☐ Wean electrolyte supplements prior to discharge, if tolerated
  - Patient should have stable electrolytes before discharge

Bronchodilators

- ☐ For infants with BPD requiring positive pressure at term OR infants with frequent use during admission, consider albuterol as needed for signs of bronchospasm

Inhaled Corticosteroids

- ☐ Consider for infants with recurrent bronchospasm needing bronchodilators OR infants with severe ventilator-dependent BPD if benefit was demonstrated during admission
- ☐ Attempt to wean prior to discharge. If unable to wean, transition to Flovent MDI with spacer

Social Determinants & Preventive Care

- ☐ Parents should receive training on BPD care prior to discharge per NCCC protocol
- ☐ Assess for adequate understanding, transportation, and parental engagement to safely care for infant
- ☐ Recommend immunoprophylaxis with palivizumab (Synagis) prior to & following discharge

Follow Up After Discharge

- ☐ Follow up with Pediatric Pulmonology or Pulmonology/Special Infant Care Clinic for in-person visit within 4 weeks of discharge, depending on the complexity of the patient
- ☐ If questions or concerns after discharge:
  - For all respiratory concerns, parents should contact on-call pulmonology team:
    - During business hours: 919-966-1055
    - After 5PM or weekends: 984-974-1000 and ask for on-call pulmonology team
  - On-call pulmonology team should forward information to pulmonologist & SICC team
  - For non-respiratory concerns, families should contact patient's PCP

Readmission

- ☐ Patients should be admitted to Pediatric Pulmonology service if admission for respiratory concerns
- ☐ NCCC and cardiology teams are available for consult as needed

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DISCHARGE GUIDELINES FOR INFANTS WITH BRONCHOPULMONARY DYSPLASIA (BPD)

IN-DEPTH DISCUSSION OF TRANSITION TO OUTPATIENT MANAGEMENT FOR INFANTS WITH BRONCHOPULMONARY DYSPLASIA (BPD)

JOINT RECOMMENDATIONS FROM NEONATAL-PERINATAL MEDICINE & PEDIATRIC PULMONOLOGY
UNIVERSITY OF NORTH CAROLINA AT CHAPEL HILL, NORTH CAROLINA

INTRODUCTION

Bronchopulmonary dysplasia (BPD) is a chronic lung condition associated with prematurity that is caused by lung injury and impaired lung development in infants. In the United States, BPD is the most common chronic lung disease in infancy, and impacts 10,000–15,000 infants annually, including 40-50% of the infants born < 28 weeks.[1] Importantly, BPD is the most common complication and morbidity of prematurity.[2] Despite advances in neonatal care, including antenatal steroids, surfactant therapy, and new ventilator strategies, the incidence of BPD has increased due to increased survival rates of very premature infants.[2] For infants who survive, BPD is associated with longer hospitalization lengths, increased risk of respiratory and cardiovascular problems, neurodevelopmental delays, and impaired growth. Infants with BPD remain at increased risk for continued medical issues following discharge. These infants require comprehensive discharge planning to ensure a smooth transition from the Neonatal Critical Care Center (NCCC) and reduce morbidity and mortality after discharge.

The National Institutes of Health (NIH) defines bronchopulmonary dysplasia as the need for supplemental oxygen for at least 28 days and/or at 36 weeks postmenstrual age (PMA). For infants born > 32 weeks gestation, diagnosis is based on clinical status at 56 days chronological age. Additionally, bronchopulmonary dysplasia can be further stratified by severity, including:

- Mild – weaned to room air by 36 weeks PMA or discharge, whichever comes first
- Moderate – need for < 30% FiO2 at 36 weeks PMA or discharge
- Severe – need for ≥ 30% FiO2 and/or positive pressure at 36 weeks PMA or discharge

However, infants with severe BPD span a variety of phenotypes, including infants who require supplemental oxygen via nasal cannula, those who require noninvasive positive pressure, those who require intubation or tracheostomy with mechanical ventilation. The NIH diagnostic criteria for BPD relies heavily on duration and level of oxygen therapy, but since it was developed in 2000, it does not consider modern neonatal practices and does not distinguish between need for noninvasive positive pressure and invasive mechanical ventilation. Alternatively, the National Institute of Child Health and Human Development Neonatal Research Network (NICHD NRN) published revised criteria for BPD based on severity and mode of respiratory support, using subtypes to stratify risk for significant respiratory sequalae or death.[41] For preterm infants born < 32 weeks gestation, criteria for diagnosis of BPD includes:

- Grade 0 or no BPD – no support required at 36 weeks PMA
- Grade 1 – need for nasal cannula ≤ 2 L/min at 36 weeks PMA
- Grade 2 – need for nasal cannula > 2 L/min or noninvasive positive airway pressure
- Grade 3 – need for invasive mechanical ventilation at 36 weeks PMA

Studies suggest this new grading approach better predicts risk for serious respiratory outcomes and mortality, with Grade 0 demonstrating a 10% risk and Grade 3 demonstrating a 70% risk. This new diagnostic criterion distinguishes between degree of positive pressure support at 36 weeks and demonstrates a relationship between degree of support and outcomes. However, this approach is still limited as it does not consider additional comorbidities (such as pulmonary hypertension) or use of other supportive medications (such as diuretics and steroids).

BPD is commonly divided into early, evolving, and established BPD. Early BPD refers to the period from birth through the first few weeks of life. Evolving BPD refers to the period after the first month of life.[2] Established BPD is estimated to occur after 36 weeks PMA. Once diagnosed, the management of BPD is directed at reducing ongoing lung injury, optimizing oxygenation and ventilation with use of respiratory support and pharmacologic therapies, screening for comorbidities, and ensuring adequate nutrition to promote growth and development. Due to medical complexity, discharge planning for infants with BPD should include an interdisciplinary team approach involving neonatologists, pulmonologists, cardiologists, nutritionists, nurses, respiratory therapists, and developmental specialists.[4]

Infants with other types of chronic lung disease apart from BPD may also require respiratory support following discharge. Though these children may also benefit from similar discharge recommendations, we recommend that they are discussed individually with pulmonology and/or cardiology consultation.

OXYGENATION

BPD is characterized by heterogeneous hyperinflation, inflammation, atelectasis, decreased alveolarization, and increased airway resistance - all resulting in impaired oxygenation and ventilation.[5] The treatment for infants with BPD focuses on minimizing damage to the lungs and providing respiratory support to allow the infant's lungs to heal and grow. Supplemental oxygen improves impaired oxygenation, enhances growth, and improves sleep duration. Additionally, oxygen therapy promotes pulmonary vasodilation which prevents pulmonary vasoconstriction associated with chronic hypoxia. Of importance, the risk of retinopathy of prematurity and need to avoid excessive oxygenation decreases significantly as the infant approaches term (corrected gestational age).[6]

The current guidelines on home oxygen therapy for children recommends home oxygen therapy for patients with BPD complicated by chronic hypoxemia. Many clinical studies have examined use of home supplemental oxygen and show that oxygen therapy for infants with BPD can lead to increased growth rate, decreased mean pulmonary artery pressure, and improved sleep duration and quality at night.[2] Though there are no studies that concretely offer definitive

target oxygen saturations for oxygen therapy in children born preterm, current recommendations suggest that saturation levels <90% should be avoided, and that levels >92–94% may be protective against adverse effects.[7,8] Therefore, we recommend a minimum threshold oxygen saturation measured by pulse oximetry (S_{pO2}) of 92% for infants with BPD and goal of 95% for infants with confirmed pulmonary hypertension.[8] In order to assess infant's chronic respiratory status and to ensure adequate ventilation, serum electrolytes and blood gas analysis should be performed at least one week prior to discharge. Recommended goal values include a serum bicarbonate of less than 32 and serum pCO2 of less than 60. Electrolyte studies can also help to rule out renal disease and other etiologies for metabolic acidosis.

Non-invasive respiratory support can be administered in several ways: CPAP, NIPPV, HFNC, or low-flow nasal cannula. To safely discharge home, an infant must be stable on low-flow nasal cannula with goal effective FiO2 <30%, based on definition of BPD. An estimation of effective FiO2 can be calculated using infant's weight and oxygen flow rate. Examples include:

- 3 kg infant on 300 ml or 0.3 LPM of LFNC is receiving approximately 30% oxygen
- 4 kg infant on 500 ml or 0.5 LPM LFNC is receiving approximately 30% oxygen
- 6 kg infant on 700 ml or 0.7 LPM LFNC is receiving approximately 30% oxygen

Ideally, the infant must also have sufficient pulmonary reserve to theoretically remain stable during a brief, accidental disconnection from oxygen support. Alternatively, patients who require positive pressure or mechanical ventilation may be discharged home with a tracheostomy. All BPD infants who are discharged home with respiratory support require cardiorespiratory monitoring. The caregivers of these infants will need additional support and education for use of home respiratory equipment and to ensure understanding of goal oxygen saturations. To ensure adequate stability on anticipated home respiratory support, we recommend no further changes or weaning of supplemental oxygen at least one week prior to discharge. Once discharged, parents should use goal of > 92% for oxygen saturations.

PULMONARY HYPERTENSION

Preterm birth is associated with interrupted alveolar and vascular development, resulting in alveolar simplification. This increases the risk for vascular simplification, remodeling of the pulmonary arterial circulation and increased vasoreactivity, including hypoxic vasoconstriction. This leads to increased pulmonary vascular resistance and contributes to pulmonary hypertension as a complication of bronchopulmonary dysplasia.[9] Infants with pulmonary hypertension associated with BPD have prolonged lengths of stay, increased morbidity, and increased risk of mortality.[10]

Definitions of pulmonary hypertension associated with BPD vary widely.[11] Many sources agree that pulmonary hypertension is a common complication in infants with moderate and severe BPD. We also know that it is more common in infants with the most severe forms of BPD and has been associated with inadequate or rapid weaning of respiratory support, leading to

atelectasis, hypercarbia, and hypoxemia.[9] As attempts are made to wean anti-inflammatory medications, sedation medications, supplemental oxygen, and ventilator or CPAP support, the infant's stability and ongoing tolerance must be carefully and effectively monitored regularly. Echocardiography is reasonably sensitive to detection of pulmonary hypertension. However, it can be variable in determination of degree of disease and dependent on availability of the various markers. If there are any questions regarding the findings of an echocardiograms, pediatric cardiology consultation is recommended.

In addition, infants born small for gestational age appear particularly susceptible to this complication, as well as infants with extrauterine growth retardation. This link between pulmonary hypertension and intrauterine growth is secondary to pro-inflammatory states and the infant reaches term and beyond, based on a balance of these growth factors.[12,13] For infants born SGA, pulmonary hypertension may present early in the course, improve, and then re-emerge later in the course, usually near or at term gestation. For infants with severe BPD (especially if unstable) the period of 36 weeks to 3 months (corrected age) appears to be a period of particular risk for the emergence of symptomatic pulmonary hypertension.[14] This may possibly be related to increased metabolic demands and weaning of support during that period.

Consensus recommendations from the Pediatric Pulmonary Hypertension Network and the BPD Collaborative include the need for multi-disciplinary teams, surveillance for pulmonary hypertension by echocardiogram in infants with ongoing support needs, addressing adequacy of lung support to decrease V/Q mismatch and periods of hypoxemia, and outcome management with multidisciplinary teams.[5,15] For children with BPD and complex cardiac disease we recommend individual consultation with pediatric cardiology.

USE OF DIURETICS

Patients with BPD have been shown to have chronic interstitial pulmonary edema, primarily from iatrogenic causes that result in increased capillary permeability, which can decrease lung compliance.[2] Diuretics may decrease the amount of interstitial pulmonary edema, improving the mechanics of respiration and reducing the amount of respiratory support needed. However, evidence that long-term diuretic use in these patients improves outcomes is lacking, and there is wide variation in the use of diuretics between centers.[3] The one randomized control trial of the use of chronic diuretic therapy in infants with BPD did not find significant differences between rehospitalizations, pulmonary function tests, or duration needing supplemental oxygen.[16] Retrospective studies have shown that the use of diuretics may be associated with some improvement in respiratory status, but also associated with electrolyte abnormalities and decreased growth.[17]

Given the lack of evidence that chronic diuretic therapy improves long-term outcomes for patients with BPD, we recommend using sparingly, such as for patients who are unable to wean off positive pressure therapy without diuretics, or have clinical evidence of fluid overload.[7,18] Diuretics may be more useful for acute respiratory worsening or exacerbations. Patients should

be monitored for potential adverse effects of diuretics include electrolyte abnormalities and decreased growth, as well as nephrocalcinosis/ nephrolithiasis for loop diuretics.

USE OF INHALED CORTICOSTEROIDS

Inflammation is believed to play a key role in the pathogenesis of BPD. Though systemic steroids have been shown to improve pulmonary outcomes for patients with severe lung disease, adverse effects of systemic steroids have led to interest in the use of inhaled corticosteroids (ICS) for patients with BPD. However, there is inconclusive evidence on the utility of ICS. The largest trial of ICS in mechanically ventilated preterm infants showed some reduced risk of BPD in the ICS group, but significantly higher long-term mortality for the ICS group.[19, 20] A small RCT comparing the use of ICS to placebo in patients with BPD did not find any differences in outcomes.[21]

We therefore do not recommend the routine use of ICS for prevention of BPD. However, patients with established BPD may develop significant airway reactivity. Treatment of chronic airway inflammation with ICS may help reduce the degree of airway reactivity in these patients, though recurrent wheezing in patients with BPD is less responsive to ICS in patients with classic asthma. For unstable patients with severe BPD, ICS may allow these patients to achieve stability without continued use of systemic steroids. We therefore only recommend using ICS only for patients with frequent bronchospasm, ventilator dependent BPD patients unable to wean off systemic steroids or whom are unstable, or those whom had a clear benefit from ICS during admission. For infants who require discharge with inhaled corticosteroids, we recommend transition to inhaled corticosteroids via metered-dose inhalers (MDI) with infant spacer prior to discharge due to ease of administration and portability.

USE OF BRONCHODILATORS

Small airway dysfunction and obstruction are common in patients with BPD, and there are higher rates of airway reactivity in patients with BPD.[22] These findings are likely related to both chronic airway inflammation as well as structural abnormalities such as reduced small airway size and reduced elastic recoil. Though studies have shown temporary improvement in pulmonary mechanics with bronchodilators in patients with BPD, clinical trials have not shown improved clinical outcomes from routine use of bronchodilators.[23,24] The effect of bronchodilators can vary between patients depending on their specific lung pathophysiology. A large percentage of patients with severe BPD have been shown to be bronchodilator responsive, and therefore regular (scheduled) use of bronchodilators may help reduce respiratory support required, reduce further iatrogenic trauma, and improve stability with fewer adverse effects than other therapies such as systemic steroids.

We therefore recommend bronchodilators be used routinely only for episodes of bronchospasm that has been shown to be albuterol-responsive, or for unstable patients with severe BPD.[25]

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DISCHARGE GUIDELINES FOR INFANTS WITH BRONCHOPULMONARY DYSPLASIA (BPD)

GROWTH AND NUTRITION

Proportional growth, linear growth, and growth trajectory are important variables to monitor in infants with severe BPD and are associated with improved survival and improved developmental outcomes in preterm infants. Infants with BPD nearing discharge should display consistent proportional growth, defined by adequate (but not excessive) weight gain and consistent linear growth. These parameters are most accurately followed by examination of Z-scores and should use corrected age on a standardized growth chart (Fenton Growth Chart for infants < 50 weeks postnatal age and transition to WHO Growth Chart > 42 weeks corrected age). The WHO Growth Chart additionally allows tracking of growth using weight-for-length parameter. Poor growth has been associated with worse developmental outcomes and may also reflect instability.[26] Infants with BPD appear to have complex nutritional needs and demonstrate consistent proportional growth when they are receiving adequate respiratory support, have respiratory reserve adequate to avoid stress and inflammation, and have established adequate neuro-regulation. This ideal state is called the "pro-growth" state. Infants with proportional growth have been shown to have decreased morbidity and mortality in established BPD.[27, 28, 29, 30]

Therefore, prior to discharge, we recommend evaluation of nutrition and growth as a measure of stability and adequate support, with the goal of reducing morbidity and mortality following initial discharge. This nutritional review should occur 2-3 weeks before discharge. This entails reviewing trends in anthropometrics and measurement of linear growth (using a length board if available. Along with growth parameters, nutritional assessment regarding caloric and protein intake should be reviewed to determine if nutrition plan is appropriate and adequate for discharge.[43] Although infants with BPD may have increased caloric needs, protein needs are not as clearly defined. A thorough review of the nutrition plan, including feeding schedule, formula choice, and consideration for g-tube feeds will be necessary before discharge. If infant is primarily fed with maternal breastmilk, a review of caloric density of feeds and should occur with consideration for formula supplementation if needed.[44] Since growth is a dynamic process, it is difficult to define specific growth patterns. Instead, the evaluation of growth parameters should be performed on an individualized basis.[46]

Regardless of the etiology for nutritional deficits, nutritional repletion should be attempted to regain these deficits prior to discharge home. In the NCCC, it is now standard practice to avoid or reduce diuretic and steroid use in order to limit negative impact on bone health and growth. For infants who are exposed to these interventions, evaluation of bone health (including monitoring of calcium, phosphorus, magnesium, alkaline phosphate, vitamin D, and possibly parathyroid hormone level) should be performed.[43,45] Continued evaluation and monitoring for nutritional supplementation should also occur at time of discharge. BPD patients can also have gastroesophageal reflux, which can impact oral intake and tolerance to enteral nutrition. At times, reflux medications or specialized formulas (elemental or hydrolyzed protein) should be considered for alternate treatments. However, such formulas have decreased mineral availability and absorption and therefore, may also contribute to other challenges for infants with

BPD. Further changes in medications and formula may occur following discharge. These strategies for optimizing bone health may also contribute to improve linear growth.

OUTPATIENT MANAGEMENT

No established guidelines for post-discharge management and frequency of visits for patients with BPD exist. However, patients with BPD, particularly severe BPD, are at risk for ongoing morbidity and long-term sequelae of BPD and should be followed closely by neonatology, pediatric pulmonology, and other pertinent specialists. For patients discharged home on supplemental oxygen or diuretics, or with other significant respiratory symptoms, we recommend follow up with pediatric pulmonology with or without the neonatology Special Infant Care Clinic (SICC) within 4 weeks of discharge to ensure medical and family needs are being met, as well as to ensure timely weaning of therapies if appropriate. It is essential that this initial pulmonology visit be in-person, as respiratory stability is difficult to assess virtually.

There also is little evidence on best practices regarding weaning of oxygen therapy or diuretics for these patients, and weaning practices vary widely between centers.[31] Patients on oxygen or diuretic therapy should be seen by Pulmonology every 1-2 months to ensure adequate monitoring and appropriate weaning. Appropriate growth should be achieved prior to weaning oxygen. Pulse oximetry, while useful for patients receiving supplemental oxygen, may lead to many false alarms and increase parental stress. Therefore, pulse oximetry can be used intermittently with "spot-checks" while awake during the day. However, due to concern for hypoxemia during deep sleep and occasional dislodgement of nasal cannula, pulse oximetry should be used continuously while sleeping at night and with daytime naps. Once the pulmonologist feels the patient is ready to wean as an outpatient, oxygen should be weaned during daytime first prior to weaning nighttime oxygen, in-line with saturation goals described above. We generally recommend weaning oxygen at increments of 0.1lpm – 0.25lpm depending on the starting flow rate.[32,33]

For patients with BPD that are on chronic diuretics, weaning practices also vary widely, and little evidence is available to guide best practices, including whether diuretics or oxygen should be weaned first for patients receiving both therapies.[2,34] Given that furosemide is associated with increased adverse effects than thiazide diuretics, providers may want to wean furosemide first prior oxygen for patients on furosemide, while weaning oxygen first for patients receiving thiazides. Individual circumstances and family preferences should also be considered when determining a weaning strategy.

INTERDISCLIPINARY CARE

Infants with established BPD have increased length of NCCC stay compared to preterm infants without BPD.[10] They may also have other factors affecting their medical care, such as public insurance, feeding challenges, mechanical ventilation needs, pulmonary hypertension or

ongoing oxygen needs that contribute further to prolonged length of stay.[35] Interdisciplinary care, team approach, and clinical guidelines have been associated with improved survival overall, improved neurodevelopmental outcomes, and decreased readmission rates.[36, 37, 38] Standardized discharge processes have been associated with decreases in length of stay, decreased variability in care, improved nutrition at discharge and less failure to thrive post discharge.[39,40] Interdisciplinary care is highly recommended for optimal outcomes for infants with BPD.[15]

Due to all the above factors, we have created a discharge guideline and checklist to improve outcomes as discussed above, in infants with moderate or severe BPD at term or beyond.

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