JOHNS HOPKINS ALL CHILDREN'S HOSPITAL
Maternal, Fetal, and Neonatal Institute

Fluid, Electrolyte, and Nutrition Management in Bronchopulmonary Dysplasia Clinical Pathway

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Rationale:

This clinical pathway was developed by a consensus group of Johns Hopkins All Children's Hospital (JHACH) physicians, dieticians, and pharmacists to standardize the management of infants hospitalized with bronchopulmonary dysplasia (BPD) in the Neonatal Intensive Care Unit (NICU). It addresses the following clinical questions or problems:

1. Evaluation of any oxygen (O_2) requirement at 28 days of life, with or without invasive or non-invasive ventilation
2. Support of optimal lung growth and repair
3. Prevention of postnatal growth failure
4. Improve long-term pulmonary and neurodevelopmental outcomes
5. Balance the unique challenges of fluid restriction and increased energy needs

Background:

Suboptimal intrauterine and extrauterine growth is associated with increased risk for developing BPD. Severity of illness is often related to inadequate nutritional delivery to the highest-risk infants in the NICU. It is essential to prevent growth failure early and correct nutrient deficiencies to support lung growth and tissue repair. Increased energy expenditure is associated with chronic disease, and it is challenging to provide adequate nutrition while restricting fluids and using diuretics (Miller, 2014; Poindexter, 2015).

Inadequate postnatal nutrition can lead to delayed somatic growth, delayed alveolar development, and abnormal lung healing. Nutritional status has been shown to influence the development of BPD. Adequate nutrition is crucial because it affects the preterm infant's ability to resist hyperoxic injury, repair barotrauma-induced cell injury, fight infection, tolerate prolonged stress, and promote lung growth (Jobe, 2001; Shaik, 2014).

Infants with BPD are sensitive to rapid changes and frequent weaning of respiratory support that may lead to increased levels of stress, work of breathing, and energy expenditure.

Published data and levels of evidence:

- Definitions (Jobe, 2021):
    - BPD is defined based on treatment with the following support at 36 weeks' post-menstrual age (PMA) or discharge to home, if earlier:
        - Grade 0 or no disease: No O_2 or respiratory support requirement

        - Grade 1: Nasal cannula (NC) 2 liters/minute (L/min) or “low” flow NC
        - Grade 2: NC > 2 L/min, “high” flow or nasal continuous positive airway pressure (nCPAP), or non-invasive positive pressure ventilation (NIPPV)
        - Grade 3: Invasive positive pressure ventilation (PPV) (e.g., mechanical ventilation)
        - At risk for development of BPD: Refer to the 2022 National Institutes of Health (NIH) calculator

BPD prevention:

- Poor intrauterine nutrition with fetal growth restriction and small for gestation age (SGA) infants are at higher risk for developing BPD compared with appropriate for gestation age (AGA) preterm infants (Poindexter, 2015).
- Excessive fluid intake and failure to lose weight in the first week of life increase the risk of BPD.
- Inadequate nutritional intake in the first 14 days of life is associated with increased risk for BPD.
- Suboptimal nutrient intake expends nutritional reserves and leads to decreased surfactant production, reduced respiratory muscle function, impaired lung tissue repair, growth, and maturation.
- Breast milk is ideal and may decrease the risk of developing BPD (Spiegler, 2016).
- Vitamin A deficiency can predispose an infant to the development of BPD, as it is an essential regulator of normal lung growth and is involved in maintaining the integrity of epithelial cells of the respiratory tract.
    - There is currently no available formulation for intramuscular (IM) vitamin A. Should a formulation become available, IM vitamin A supplementation may be considered for extremely low birth weight (ELBW) infants who require ventilator support within 24 hours after birth, as evidence suggests a reduction in the incidence of BPD (Darlow, 2016).
- Polyunsaturated fatty acids (PUFA) have anti-inflammatory properties and implications in decreasing BPD incidence.
- Vitamin D has anti-inflammatory properties and is essential for lung growth and repair.
    - Early vitamin D supplementation (during the first month of life) has been shown to reduce the incidence of BPD (Ge, 2022).
        - For recommendations on vitamin D dosing, refer to the NICU - Vitamin D Deficiency and Metabolic Bone Disease in NICU Clinical Pathway.
- Vitamin E, known to neutralize free radicals and reduce oxidative stress, has been studied in the pathophysiology of BPD, with vitamin E deficiency increasing BPD risk.

Growth monitoring:

- Growth failure is almost always due to inadequate nutritional intake.
- Growth failure is common in preterm infants with BPD.
- The goal is proportional growth (weight, length, and head circumference).
- Excessive weight gain is undesirable and may contribute to metabolic syndrome in adulthood (Poindexter, 2015).

- Linear growth is a better marker of nutrition status than weight gain alone.
    - Obtain reliable length measurements using a recumbent length board.
- Monitoring the weight-for-length ratio is essential to identify abnormal growth patterns.
    - Increasing weight gain velocity out of proportion to linear growth velocity may indicate edema or a significant decrease in energy expenditure.
- Mid-upper arm circumference (MUAC) measurements may help differentiate edema from "true" weight gain, as the upper arm is less affected by fluid status (Jobe, 2001; Shaik, 2014).
    - It is also essential to consider that optimal weight and linear growth ranges change as the patient ages.
    - Reference values for MUAC are available for infants at 2 months corrected gestational age (CGA).

Table 1 – Growth Goals (adapted from Miller, 2024)

Weight Gain Goals		**Length Goals** (cm/week)		**Head Circumference Goals** (cm/week)	
Preemie < 1 kg	10 – 15 g/kg/day	**Preemie < 40 weeks CGA**	0.8 – 1.1	**Preemie < 40 weeks CGA**	0.8 – 1
Preemie 1 – 2 kg	15 – 20 g/kg/day				
0 – 3 months or preemie > 2 kg	25 – 35 g/day	**0 – 4 months CGA**	0.8 – 0.93	**0 – 4 months CGA**	0.38 – 0.48
> 3 – 6 months CGA	15 – 21 g/day	**> 4 – 8 months CGA**	0.37 – 0.47	**> 4 – 8 months CGA**	0.16 – 0.2
> 6 – 12 months CGA	10 – 13 g/day	**> 8 – 12 months CGA**	0.28 – 0.37	**> 8 – 12 months CGA**	0.08 – 0.11

Abbreviations: cm, centimeter; g, gram; kg, kilogram

Enteral nutrition:

- Enteral energy and protein needs:
    - Human milk is recommended as the ideal source of nutrition for all infants.
        - If maternal milk is not available, preterm infant formulas are recommended due to high protein, mineral, and vitamin provision.
    - Medium-chain triglycerides (MCT) or liquid protein can be added to meet caloric needs and/or provide additional calories with close monitoring of energy/protein ratio and osmolality.
    - Infants with BPD require 15 – 25% more kilocalories (kcal) compared to other preterm infants.
    - Energy needs may reach 140 – 150 kcal/kg/day (Dani, 2012; Poindexter, 2015).
        - Energy needs vary based on the infant's age, clinical severity, and activity level.
        - Infants with BPD have exceptionally high energy expenditures secondary to increased work of breathing and oxygen requirements.

    - Refer to *NICU – Early Standardized Enteral Nutrition Management of the Sick Neonate Clinical Pathway* and *Neonatal Nutrition Reference Guide* for further details.
- Enteral protein requirements:
    - Preterm infants with BPD require 3.5 – 4 g protein/kg daily (Dani, 2012).
    - Preterm infants whose birth weight is < 1,000 g may require 4 – 4.5 g protein/kg
    - Infants with BPD who are fed formula with added protein have improved linear growth, lean mass accretion, and greater bone mass.
    - Refer to *NICU – Early Standardized Enteral Nutrition Management of the Sick Neonate Clinical Pathway* and *Neonatal Nutrition Reference Guide* for further details.
- Fluid restriction:
    - Therapeutic fluid restriction can contribute to calorie and protein deficits.
    - Breast milk fortification, high-calorie formulas, and modular additives may be warranted to ensure not only adequate calories and protein for growth but also proper allocation of macronutrients.
    - Be mindful of the potential renal solute load from concentrated formulas and the patient's urine-concentrating ability.
    - Consider liberalizing total fluids once the patient's condition allows and is on enteral nutrition.
- Vitamins, minerals, and electrolytes:
    - Refer to *NICU – Enteral Vitamin and Mineral Supplementation Clinical Pathway*
    - Closely monitor serum electrolytes and zinc for patients starting on diuretics, as urinary electrolyte losses may be increased.
        - Once stable, labs can be obtained less frequently
    - MCT or liquid protein can be added to meet caloric needs and/or provide additional calories with close monitoring of energy/protein ratio and osmolality.
- Medications:
    - Corticosteroids affect body composition (e.g., increase fat, decrease protein accretion) and reduce bone mineral accretion, increasing the risk of osteopenia (Dani, 2012).
        - Corticosteroids may cause hyperglycemia
            - Monitor serum glucose levels if the patient is on total parenteral nutrition (TPN) and adjust the glucose infusion rate (GIR) accordingly
            - Dexamethasone interferes with bone metabolism and hinders growth
            - Higher protein intake may help with development (Groh-Wargo, 2016)

Clinical Management:

Nutrition strategies for patients diagnosed with BPD:

- Growth and monitoring goals:

- Once the patient is 36 weeks' PMA and is diagnosed with moderate to severe BPD, it is recommended:
  - Anthropometric measurements should be plotted on an intrauterine growth chart (2013 Fenton Growth Curve) until 50 weeks' PMA and on the World Health Organization (WHO) growth chart, thereafter, correcting for prematurity.
  - Monitoring standardized scores (z-scores) for weight, length, and head circumference can assist in better assessing growth.
    - Serial z-scores can illustrate if a patient is falling further off the growth chart, approximating intrauterine growth, or demonstrating "catch-up" growth, whereas percentiles may solely show that the patient is below the 3rd percentile for gestational age (GA).
  - Consult Speech Therapy for evaluation for oral feeding readiness, signs of feeding aversion, micro-aspiration, aspiration risk, risk of aspiration pneumonia, altered gag reflex, and respiratory status during feeds.
  - Refer to *NICU – Gastroesophageal Reflux Disease (GERD) Management in the NICU for Preterm Infants Clinical Pathway*

BPD-specific fluid, calorie, and protein needs:

- Fluid, caloric need, and macronutrient quantity and quality goals:
  - Advance fluids to the maximum goal tolerated to minimize pulmonary edema:
    - 120 – 130 milliliters (mL)/kg/day = moderate fluid restriction when on TPN, but can be liberalized to 140 mL/kg/day once full enteral nutrition is achieved
    - 110 – 120 mL/kg/day = severe fluid restriction on TPN, but can be liberalized to 130 mL/kg/day once full enteral nutrition is achieved
  - Provide enteral intake of > 130 kcal/kg with a goal of 140 – 150 kcal/kg/day as needed to match growth goals.
  - Use high protein fortifier to achieve > 3.5 g protein/kg.
  - Liquid protein fortifier: Commercially sterile, extensively hydrolyzed liquid protein fortifier for infants who may require additional protein
    - Made from casein hydrolysate
    - 6 mL liquid protein fortifier = 1 g protein, 4 calories
  - Discuss with a Dietitian to optimize protein intake as needed
  - Oil boluses, such as MCT oil, can provide additional fat calories in small volumes and produce less carbon dioxide (CO_2) than carbohydrate additives.
    - MCT oil provides approximately 8 kcal/mL
    - Walnut oil provides 8 kcal/mL (Biniwale, 2006)
    - Warning: Providing additional fat may delay gastric emptying and exacerbate gastroesophageal reflux (GER)

Figure 1 – Nutritional needs of infants with BPD (adapted from Miller, 2024)

Phase 1: Acute	Phase 2: Transitional	Phase 3: Pro-growth
Characteristics: ○High O_2 need ○Respiratory instability ○High-dose steroids ○Intravenous (IV) sedation/paralysis ○Pulmonary hypertension Growth: ○Variable weight trend ○Poor linear growth	Characteristics: ○Weaning O_2 ○Improving work of breathing ○Weaning steroids/sedation ○Emerging developmental state ○Improving pulmonary hypertension Growth: ○Improving weight trend ○Slow linear growth	Characteristics: ○Stable O_2 ○Comfortable breathing ○Low or off steroids/sedation ○Developmental progress ○Resolving pulmonary hypertension Growth: ○Improving weight-for-length trend ○Consistent linear growth

Micronutrient supplementation:

- Please reference the *NICU – Enteral Vitamin and Mineral Supplementation Clinical Pathway*
  - Zinc:
    - Enteral zinc supplementation is recommended in infants with BPD on full feeds who fail to meet weight gain goals despite providing energy and protein intake at goal, especially in infants on diuretics and with alkaline phosphatase levels lower than expected.
    - Provide zinc sulfate, see dosing below in Table 2.

Electrolytes:

- Diuretics increase the risk for hyponatremia and hypokalemia and increase urinary loss of calcium and phosphorus.
- Monitor serum calcium, phosphorus, and alkaline phosphatase levels every 2 weeks minimally (Dani, 2012; Theile, 2012).
  - Proper fortification of breastmilk and vitamin/mineral supplementation are paramount, as osteopenia of prematurity is more common in infants with BPD (refer to NICU- Early Standardized Enteral Nutrition Management of the Sick Neonate for < 1,500 g).
- Consider sodium and chloride supplements when serum sodium < 130 mEq/L and/or serum chloride < 90 mEq/L (Dani, 2012).
- Potassium supplementation may irritate the gastrointestinal (GI) tract (Groh-Wargo, 2016).
- Consider nephrocalcinosis risk when supplementing calcium while on diuretics.
  - Consider renal ultrasound when on diuretics for greater than 1
  - month and adjusting formula/breast milk fortification (Groh-Wargo, 2016).

Table 2 - Micronutrient and electrolyte supplementation (adapted from Miller, 2024)

Micronutrient/ Electrolyte	Preterm Infants	Term Infants up to 6 months of age and Preterm Infants Once Corrected to Term
Iron	1 – 3 mg elemental iron/kg/day	0.27 mg/day (11 mg/day for 7 – 12 months of age)
Zinc	2 – 3 mg/kg/day	2 mg/day
Calcium	120 – 220 mg/kg/day	200 mg/day
Phosphorous	70 – 120 mg/kg/day	100 mg/day
Fluoride	1.5 – 60 mcg/kg/day	0.01 mg/day (0.5 mg/day 7 – 12 months)
Vitamin D	400 – 1,000 units/day	400 units/day
Sodium	~3 – 5 mEq/kg/day (69 – 115 mg/kg/day)	4.8 mEq/day

Summary:

Nutrition strategies for patients diagnosed with BPD:

1. Once weekly 'Nutrition Rounds' with discussion of growth and monitoring goals
2. Fluid/caloric/macronutrient quantity and quality goal, refer to Table 3
3. Micronutrient supplementation, refer to Table 3

Table 3 – Macro- and Micronutrient Recommendations (adapted from Miller, 2024)

Recommendation	Acute Phase	Transitional Phase	Pro-growth Phase
Fluid (mL/kg/day)	130 – 150	120 – 140	110 – 130
Energy (kcal/kg/day)	120 – 150	110 – 120	70 – 120
Protein (g/kg/day)	4	2.5 – 4	2.5 – 3
Zinc	2 – 3 mg/kg/day	2 – 3 mg/day	2 mg/day
Sodium	Maintain sodium > 130 mEq/L		
Vitamin D	400 – 1,000 units/day		
Calcium	120 – 220 mg/kg/day	200 mg/day	
Phosphorus	70 – 120 mg/kg/day	100 mg/day	
Iron	1 – 3 mg elemental iron/kg/day		

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Is the patient admitted to NICU, and has BPD?

YES | NO

What phase is the patient in?

Off Pathway

Phase 1: Acute Phase

Characteristics:
- High O_2 need
- Respiratory instability
- High-dose steroids
- IV sedation/paralysis
- Pulmonary hypertension

Growth:
- Variable weight trend
- Poor linear growth

Recommendations

Fluids/macronutrients:
- Fluid: 130 – 150 mL/kg/day
- Energy: 120 – 150 kcal/kg/day
- Protein: 4 g/kg/day

Electrolytes/micronutrients:
- Zinc: 2 – 3 mg/kg/day
- Sodium: maintain > 130 mEq/L
- Vitamin D: 400 – 1,000 units/day
- Calcium: 120 – 220 mg/kg/day
- Phosphorus: 70 – 120 mg/kg/day
- Iron: 1 – 3 mg elemental iron/kg/day

Phase 2: Transitional Phase

Characteristics:
- Weaning O_2
- Improving work of breathing
- Weaning steroids/sedation
- Emerging developmental state
- Improving pulmonary hypertension

Growth:
- Improving weight trend
- Slow linear growth

Recommendations

Fluids/macronutrients:
- Fluid: 120 – 140 mL/kg/day
- Energy: 110 – 120 kcal/kg/day
- Protein: 2.5 – 4 g/kg/day

Electrolytes/micronutrients:
- Zinc: 2 – 3 mg/day
- Sodium: maintain > 130 mEq/L
- Vitamin D: 400 – 1,000 units/day
- Calcium: 120 – 220 mg/kg/day
- Phosphorus: 70 – 120 mg/kg/day
- Iron: 1 – 3 mg elemental iron/kg/day

Phase 3: Pro-growth Phase

Characteristics:
- Stable O_2
- Comfortable breathing
- Low dose, or off steroids/sedation
- Developmental progress
- Resolving pulmonary hypertension

Growth:
- Improving weight-for-length trend
- Consistent linear growth

Recommendations

Fluids/macronutrients:
- Fluid: 110 – 130 mL/kg/day
- Energy: 70 – 120 kcal/kg/day
- Protein: 2.5 – 3 g/kg/day

Electrolytes/micronutrients:
- Zinc: 2 mg/day
- Sodium: maintain > 130 mEq/L
- Vitamin D: 400 – 1,000 units/day
- Calcium: 200 mg/day
- Phosphorus: 100 mg/day
- Iron: 1 – 3 mg elemental iron/kg/day

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Outcome Measures:

- Length of stay in NICU
- Growth parameters, including weight, length, and head circumference < 10% at discharge from NICU
- Patients discharged home on respiratory support or oxygen
- Patients requiring tracheostomy for severe chronic lung disease/BPD

Clinical Pathway Team

Fluid, Electrolyte, and Nutrition Management in BPD Clinical Pathway

Johns Hopkins All Children's Hospital

Maternal, Fetal, and Neonatal Institute

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Disclaimer:

Clinical Pathways are intended to assist physicians, physician assistants, nurse practitioners, and other healthcare providers in clinical decision-making by describing a range of generally accepted approaches for the diagnosis, management, or prevention of specific diseases or conditions. The physician must make the ultimate judgment regarding care of a particular patient in light of the individual circumstances presented by the patient.

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