



#### Clinical Practice Guideline: Enteral Nutrition

# Points of emphasis/Primary changes in practice:

The overall goal is to continue to promote consistent and evidence-based enteral nutrition practices in the Neonatal Intensive Care Unit (NICU). This guideline applies to all infants (preterm and full term) in the NICU. Major changes in this clinical practice guideline as compared with previous guidelines are:

- The following previous BWH guidelines are combined into a single guideline:
  - Guidelines for the Use of Human Milk/Infant Formula in Preterm Infants
  - Protocol for Gut Priming in Preterm Infants
  - Enteral Protein Supplementation in Human Milk-fed very low birth weight (VLBW, <1500g) Infants Clinical Guideline
- Enteral nutrition should be initiated as soon as possible after birth if there are no absolute contraindications. Absolute contraindications to enteral nutrition specified in this guideline are: (1) hemodynamic instability; (2)impending need for intubation; (3) significant gastrointestinal pathology; (4) tachypnea in an infant ≥35 weeks' gestation that precludes oral feeding and is expected to resolve in <48 hours.</li>
- In the presence of relative contraindications to enteral nutrition, minimal enteral nutrition (also known as "gut priming" or "trophic feedings") may be provided at **10 mL/kg/day** but not advanced; this volume replaces the volume recommended under the "Gut Priming" guideline (0.5 mL Q4 hours).
  - Relative contraindications to enteral nutrition specified in this guideline are: (1) presence of umbilical artery catheter (UAC); (2) moderate to severe respiratory distress with expected worsening, including likely need for intubation; (3) indomethacin prophylaxis or treatment; (4) hypoxic ischemic encephalopathy (HIE) undergoing therapeutic hypothermia; (5) dopamine at stable dose ≤5 mcg/kg/min.
- Guidelines for initiation of enteral nutrition for infants with birth weight ≥1000 have been updated
  with larger initial volumes and larger increments for advancement. Initiation and advancement
  volumes for infants <1000g are unchanged from previous. For infants of all birth weights,
  advancement can be considered 12-24 hours after initiation.</li>
- For human milk-fed preterm infants, existing fortification practices are updated in 3 ways:
  - Fortification is started routinely at **60 mL/kg/day** (updated from 100 mL/kg/day).
  - Feeding volumes may be advanced 6-12 hours (2-3 feedings) after initiating fortification.
  - Donor milk for preterm infants is routinely fortified with additional energy and protein, to be added in increments of 0.3 g/kg/day once the target feeding volume is reached.
- The standard target feeding volume is specified as 150-160 mL/kg/day, with guidance provided for considering higher or lower target volumes.
- New guidelines are provided for electrolyte monitoring and treatment of hyponatremia and hypochloremia in human milk-fed preterm infants.
- New guidelines are provided for the evaluation and management of feeding intolerance with a focus on minimizing the unnecessary interruptions of enteral nutrition.



Clinical Guideline	Enteral Nutrition
Name	
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This is a clinical practice guideline. While the guideline is useful in approaching enteral nutrition management, 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. Background

VLBW infants are at risk for slow weight gain related to cumulative nutrient deficits.<sup>1,2</sup> Because the newborn brain is uniquely sensitive to nutrition,<sup>3</sup> and other organs and tissues are also at critical developmental stages in early infancy, optimizing nutrient intake during the NICU hospitalization has the potential to benefit long-term neurodevelopment and health outcomes. Current parenteral and enteral nutrition recommendations for preterm infants are designed to provide nutrients to approximate the rate of growth and composition of weight gain for a normal fetus of the same post-conceptual age and to maintain normal concentrations of blood and tissue nutrients.<sup>4,5</sup>

Enteral nutrition is the preferred route for infant feeding because it:

- meets nutritional requirements better than parenteral nutrition (PN)
- promotes gastrointestinal maturity and maintains mucosal integrity
- is safer than parenteral nutrition due to reduced exposure to a central venous catheter

The use of a standardized feeding guideline improves growth outcomes and reduces the incidence of necrotizing enterocolitis (NEC)<sup>6</sup> and hospital-acquired infections.<sup>7</sup>

#### II. Initiation of Enteral Nutrition

Earlier initiation of enteral nutrition is associated with decreased gastrointestinal inflammation and other morbidities<sup>8</sup> and does not appear to increase the risk for NEC.<sup>9,10</sup> A growing body of literature supports the initiation of enteral nutrition as early as the first hours of life,<sup>11-13</sup> including for small for gestational age preterm infants.<sup>14</sup> These data support the recommendation in this guideline to initiate enteral nutrition **as soon as possible after birth** if there are no absolute contraindications. *Waiting for daily rounds to make routine feeding decisions can delay progress and compromise nutritional status unnecessarily.* Infants should be assessed by the clinical team upon admission and regularly throughout the day and night; if no absolute or

relative contraindications are present, enteral nutrition may be initiated with approval by the fellow <u>or</u> attending (see **Table 2**). If relative contraindications are present, minimal enteral nutrition (10 mL/kg/day) may be initiated with approval by the fellow <u>or</u> attending.

Note that colostrum should be provided for mouth care as soon as it is available, on the basis of biologically plausible benefits<sup>15</sup> and a demonstrated reduction in clinical sepsis.<sup>16</sup> Colostrum may be provided for mouth care even when absolute contraindications to feeding are present.

- **Absolute contraindications** to any enteral nutrition are listed here. Infants with these conditions are not eligible for initiation or advancement of enteral nutrition (with the **exception** of colostrum for mouth care):
  - Hemodynamic instability, evidenced by hypotension requiring escalating inotropic support and/or multiple fluid boluses
  - Significant gastrointestinal pathology, e.g. NEC, mechanical or functional bowel obstruction
  - Respiratory failure or profound apnea with impending need for intubation (to minimize risk of aspiration around intubation procedure)
  - Infants ≥35 weeks' gestation with respiratory rate >80 and/or increased work of breathing that precludes oral feeding, with the expectation that respiratory distress will resolve in <48 hours, and thus nasogastric tube placement is not indicated (e.g. TTN)
- Non-nutritive feeding volumes as high as 24 mL/kg/day appear to be safe. 11,17 **Minimal** enteral nutrition (also referred to as "gut priming" or "trophic feedings") at 10 mL/kg/day may be provided at the discretion of the medical team even when relative contraindications to enteral nutrition are present. This volume should be provided in addition to PN (e.g. starter PN + IV fluids at 80 mL/kg/day PLUS minimal enteral nutrition at 10 mL/kg/day for total daily fluids of 90 mL/kg/day) and should not be advanced until the relative contraindication(s) is/are resolved:
  - UAC in place
  - Moderate to severe respiratory distress with likely worsening of course over the next several hours including likely intubation; encourage frequent reassessments as respiratory course evolves
  - During indomethacin prophylaxis [link]
  - During treatment with indomethacin for patent ductus arteriosus (PDA) [link to PDA guideline]
  - HIE undergoing therapeutic hypothermia<sup>18</sup> after 24 hours of life [link to HIE guideline]
  - Dopamine ≤5 mcg/kg/min at stable dose



## III. Type of Enteral Feeding

Human milk is recommended by the American Academy of Pediatrics for feeding virtually all infants, including those born preterm.<sup>19</sup> Mother's own milk is preferred, but when not available donor milk should be used to avoid delaying the initiation of enteral nutrition.<sup>20</sup> Donor milk is specifically preferred for VLBW infants because it confers protection against NEC,<sup>21</sup> and is available for all infants while awaiting maternal milk [link to donor milk guideline]. If parents do not provide consent for donor milk, an infant formula appropriate for birth weight and gestational age should be used (Table 1).

- What to give (in order of preference):
  - Colostrum (preferred for minimal enteral nutrition but do not delay initiation if not available)
  - Maternal milk
  - Pasteurized donor human milk, with consent
  - Infant formula appropriate for birth weight and/or gestational age (Table 1)

Table 1
Infant formula selection if human milk not available

Birth weight and/or Gestational Age	Type of Infant Formula		
≤1800 grams	Preterm, High Protein		
1801-2200 grams and/or <35 weeks	Preterm		
2201-2500 grams and/or 35-37 weeks	Post-discharge nutrient enriched		
>2500 grams and/or >37 weeks	Standard term		

#### IV. Advancement of Enteral Nutrition Volume

Faster advancement of enteral nutrition minimizes cumulative nutrient deficits, reduces dependence on PN, and is associated with a lower risk of late onset sepsis and extrauterine growth restriction.<sup>22-24</sup> Advancing by 30-40 mL/kg/day in VLBW infants appears to be safe, <sup>17,23,25,26</sup> although data are relatively sparse regarding infants born <1000 grams.

• Feeding volume may be initiated and advanced according to birth weight-specific guidelines (Table 2) as long as no absolute or relative contraindications are present. The initial feeding volume should be given for at least 12-24 hours prior to advancement.



Table 2
Guidelines for Initiation and Advancement of Enteral Feeding
by Birth Weight

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Birth weight	Initial volume (mL/kg/day)*	Volume increases (mL/kg/day every 12 hours)			
≤1000 grams	10	10			
1001-1500 grams	20	15			
1501-1800 grams	30	15-20			
1801-2500+ grams	30-40	20			

<sup>\*</sup>Give initial volume for 12-24 hours prior to advancement

### • The standard target feeding volume is 150-160 mL/kg/day.

- Consider target volume >160 mL/kg/day if growth is suboptimal. Consider mild fluid restriction on an individual basis in specific clinical situations, with careful attention to overall growth patterns and macro-/ micronutrient distribution.
- Typically, gastric feedings are provided every 3 hours as a bolus over 30 minutes; however, more frequent or longer duration feedings, including continuous feedings, are also acceptable and may help with management of feeding intolerance and/or gastro-esophageal reflux (GER). <sup>27,28</sup>
- If feeding is interrupted temporarily (e.g. for procedure, blood transfusion, or evaluation for feeding intolerance) [link to transfusion guideline], feedings may be resumed and readvanced more quickly than when first initiated. Decisions about reintroduction of enteral feedings should be individualized based on the patient's history and course. If relatively few concerns are present, one option is to start at 1/3 volume and advance by 1/3 every 8 hours with goal to be back to full volume within 24 hours.

### V. Fortification of human milk/increasing caloric density of infant formula

Current recommendations for enteral nutrition are designed to provide nutrients to approximate the rate of growth and composition of weight gain for a normal fetus of the same postconceptual age and to maintain normal concentrations of blood and tissue nutrients.<sup>5</sup> A summary of current recommendations for selected nutrients is shown in Table 3.



Table 3
Recommended Enteral Intake
of Selected Nutrients<sup>4,5,29</sup>

Nutrient	Enteral Intake		
Energy (kcal/kg/day)	110-150		
Protein (g/kg/day)*	3.4-4.5		
Carbohydrate (g/kg/day)	9-20		
Fat (g/kg/day)	4.8-8.4		
Calcium (mg/kg/day)	100-220		
Phosphorus (mg/kg/day)	60-140		

<sup>\*</sup>upper limit of protein intake is generally ~5 g/kg/day

To meet their nutrient requirements, human milk fed to preterm infants must be fortified with a human milk fortifier (HMF), and formula-fed preterm infants require specialized, fortified formulas.<sup>19</sup> Newer liquid HMFs are well-tolerated and promote growth more effectively than older powdered HMFs.<sup>30,31</sup> Earlier fortification minimizes cumulative nutrient deficits, and recent studies<sup>32,33</sup> support the safety of human milk fortification well before reaching 100 mL/kg/day, as well as benefits to bone health.

While both nutritional and non-nutritional factors (e.g. increased metabolic demand, illness severity, inflammation) influence growth, protein intake is often a limiting factor,<sup>34,35</sup> particularly among human milk-fed preterm infants. <sup>3836</sup> Mother's milk is assumed to contain 1 g/dL of protein, but the actual content varies considerably from day to day.<sup>37</sup> Currently available liquid HMFs provide ~4 g/kg/day of protein when fed at 150 mL/kg/day. Additional protein may be added incrementally if growth is faltering (Figure) to provide the assumed daily intake of protein and energy shown in Table 4.

Donor milk often contains less protein and energy than what is assumed to be in mother's own milk,<sup>38,39</sup> resulting in insufficient protein intake despite fortification with HMF. Fortification of donor milk with additional energy and protein can eliminate the growth deficit attributable to donor milk (vs. formula) use.<sup>21</sup>

Guidelines for routine fortification for infants <2000g birth weight or <35 weeks' gestation are:

- Addition of HMF or advancement to 24 kcal/30 mL preterm infant formula should begin
  once the infant reaches approximately 60 mL/kg/day and tolerates this volume for 2-3
  feedings.
- Advancement of feeding volumes can proceed after 2-3 feedings of fortified human milk or formula are well-tolerated.
- PN and lipid support should be adjusted on the day of anticipated fortification [<u>link to PN Guideline</u>].



- For predominantly (>75%) donor milk-fed infants, routine addition of an energy and liquid protein modular is recommended, once tolerating goal volume enteral nutrition (150-160 mL/kg/day), to be added in increments of ~2 kcal/oz and ~0.3 g protein/kg/day.
- Additional protein and energy should be added if growth faltering is present (Section VII, Figure)
- Table 4 shows the energy and protein provided by different feeding types and volumes

Table 4. Assumed Energy and Protein Provision of Fortified Human Milk (FHM)

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	Unfortified HM	FHM 24	FHM 24 HP1	FHM 24 HP2
Energy content (kcal/100 mL)	68	81	82	84
Energy intake (kcal/kg/day)				
Fed at 150 mL/kg/day	102	122	123	126
Fed at 160 mL/kg/day	109	130	131	134
Protein content (g/100 mL)	1	2.7	2.9	3.2

Protein content (g/100 mL)	1	2.7	2.9	3.2
Protein intake (g/kg/day)				
Fed at 150 mL/kg/day	1.5	4.0	4.4	4.8
Fed at 160 mL/kg/day	1.6	4.3	4.6	5.1

HP1 = "High Protein Step 1;" HP2 = "High Protein Step 2"

# VI. Electrolyte Monitoring and Supplementation

Human milk-fed infants are at risk for hyponatremia and hypochloremia due to inadequate sodium and chloride intake, whereas routine sodium chloride supplementation reduces the risk of hyponatremia and improves weight gain without increasing the risk of other complications.<sup>40</sup> Predominantly (>75%) donor milk fed infants are at higher risk for hyponatremia than mother's milk or formula-fed infants.

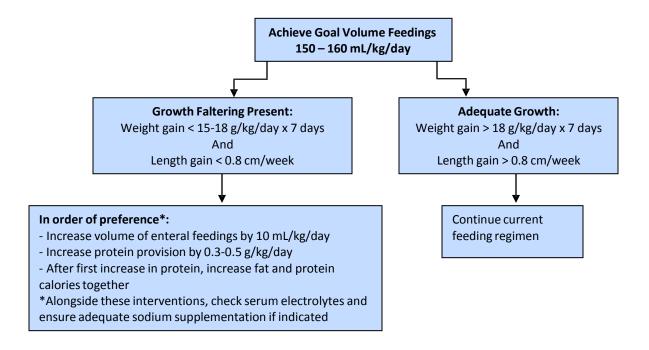
- Routine monitoring of serum electrolytes is recommended within a week of discontinuing IV fluids and reaching goal volume of fortified human milk
- Earlier monitoring and supplementation is recommended for predominantly (>75%) donor milk fed infants
- Subsequent monitoring of electrolytes should be considered if growth faltering is present (see Section VII).
- If indicated, supplementation with sodium chloride or sodium bicarbonate (Bicitra) is typically initiated at 2 mEq/kg/day to meet maintenance requirements, with continued electrolyte monitoring and dose adjustment approximately every 5-7 days.



### VII. Growth monitoring and interventions

- The Olsen intrauterine growth chart<sup>41,42</sup> should be used for longitudinal monitoring of weight, length, and head circumference for preterm infants
- The World Health Organization (WHO) growth chart<sup>43</sup> should be used for full term infants and preterm infants >41 weeks PMA
- Daily targets for weight gain and weekly targets for linear growth are shown in the Figure, with recommendations made for adjustment to enteral nutrition if targets are not met.
- Weight gain is evaluated in g/kg/day until the infant is ~35 weeks' PMA. To calculate weight gain:

• If concerns about disproportionate growth (e.g. rapid weight gain out of proportion to linear growth) are present, the Olsen (preterm and ≤41 weeks PMA) or WHO (full term or preterm and >41 weeks PMA) BMI growth chart<sup>43</sup> should be referenced.





## VIII. Assessment and management of feeding tolerance

Correct gastric tube placement should be verified prior to each feeding. If infant is on CPAP, the orogastric tube should be vented following feeding per policy [link to PPG NICU O.1] Routine assessment of gastric residual volume prior to each feeding is not recommended because neither the size nor the color of the gastric residual is an accurate marker of NEC or other pathology, and this practice delays the time to achieve full feeding volume. Residual volumes may be checked if there are other clinical concerns for feeding intolerance or more serious abdominal pathology. These signs should prompt an evaluation by the responding MD or licensed independent provider (LIP):

- Sudden or substantial (>2cm) increase in abdominal girth
- Bloody stools
- New onset of emesis, particularly bilious emesis
- Abdominal tenderness
- Abdominal erythema or other discoloration
- Diminished or absent bowel sounds
- Large (>50% of feeding volume) gastric residual volume (especially if bilious) in combination with other concerning clinical signs

Assessment by the MD or LIP should always include a physical exam and may also include an abdominal x-ray or laboratory studies. If the assessment (review of history, physical exam,  $\pm$  x-ray) is reassuring, feedings may resume at the discretion of the provider.

Suspicion of mild feeding intolerance without evidence for more severe gastrointestinal pathology may be managed by slowing the administration of the feeding e.g. to 1 hour or more; continuous feedings are also acceptable. <sup>27,28</sup> Note that uncomplicated GER is common in infants (especially preterm infants) and is not itself considered a sign of feeding intolerance. If the infant is receiving nutrition via continuous feeding, elevating the head of the bed is recommended during feeding.



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