

JOHNS HOPKINS ALL CHILDREN'S HOSPITAL

Early Standardized Enteral Nutrition Management of the Preterm Neonate Clinical Pathway



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This pathway is intended as a guide for physicians, physician assistants, nurse practitioners and other healthcare providers. It should be adapted to the care of specific patient based on the patient's individualized circumstances and the practitioner's professional judgment.

Early Standardized Enteral Nutrition Management of the Preterm Neonate Clinical Pathway

Rationale

Optimal nutrition for preterm infants is critical and improves both short and long-term outcomes. The goal of this guideline is to optimize clinical practice, based on the most current available literature to improve patient outcomes, including growth and neurodevelopment, as well as decrease the risk of associated comorbidities of prematurity such as sepsis, bronchopulmonary dysplasia, and possibly retinopathy of prematurity. The focus of this guideline is to assist the clinical staff in optimizing management of enteral nutrition of NICU patients and minimize variation in practice above and beyond what may be necessary due to individual medical situation

Background / Published Data and Levels of Evidence

A. Type of Milk

Freshly expressed mother's own milk (MOM) has many benefits for preterm babies [1, 2]. There is no direct evidence comparing fresh vs. frozen milk, but prioritizing the use of fresh milk when possible has physiologic plausibility due to the depletion of commensals, immune cells, immune factors, and enzyme activity that occurs with freezing. Neonates who receive an exclusively human milk-based diet (MOM or donor breast milk [DBM] with human milk-based fortifier) have significantly lower rates of necrotizing enterocolitis (NEC) compared to those who receive preterm formula or human milk with a bovine-milk-based fortifier (LOE 1b) [2]. In a previous RCT by Schanler, et al, the use of DBM (while on bovine milk-based fortifier) vs. preterm formula did not reduce the rates of NEC (LOE 2b)[3]

AAP recommends any baby regardless of GA needing supplementation of maternal BM should receive DBM if possible. (2022 AAP policy statement, Breastfeeding and the use of human milk).

B. Trophic feeds versus nutritional feeds

Trophic Feeds - defined as minimal volumes of milk feedings for several days before advancing, volumes that have ranged between 10-25 ml/kg/day (LOE 1a) [4]

- a. Timing of initiation and duration of – Early introduction of trophic feeds compared to fasting had a non-significant trend towards reaching full feeds earlier (mean difference – 1.05 days (95% CI – 2.61, 0.51)) and no difference in incidence of NEC (LOE 1a-)[4].

Several studies that were included in the Cochrane review by Morgan, et al included VLBW infants with asphyxia, respiratory distress, sepsis, hypotension,

glucose disturbances, ventilation, and umbilical lines, without any excess adverse effects being reported (LOE 1a-) which suggests few if any contraindications to trophic feeds other than bowel obstruction

Two studies demonstrated that even when preterm formula was used exclusively, the trophic feeding group had less feeding intolerance and reached full feedings faster without increase in incidence of NEC. [6, 7]

A single center randomized trial of early progressive feeding in infants ≤ 28 weeks GA compared trophic feeds x 4 days versus early advancement of 25 ml/kg/d with 30 infants in each group showed no difference in NEC or death but decreased need for parenteral nutrition (PN) (-4 days) and central venous lines (CVL) (-4 days) in the early advancement group. (LOE 1b)[5]

Volume – A 2021 Cochrane review compared slow daily increments (15-20 ml/kg/day) versus fast daily increments of enteral feeding volume (30-35 ml/kg/day) [8]. Fast increment did not increase the risk of NEC (pooled RR 1.06 with 95% CI 0.83, 1.37), mortality (pooled RR 1.13 with 95% CI 0.91, 1.39), or interruption of feedings (pooled RR 1.29 with 95% CI 0.90, 1.85). 14 RCTs (n=4033) were included and each trial individually reported that the fast daily increment group regained birth weight and reached full feeds faster (LOE 1b and 2b). *1/3 of the infants were extremely preterm or EBLW and 1/5 for SGA/IUGR with absent or reversed end diastolic flow.* [8]

Time to reach full feedings – Reaching full enteral feedings faster results in earlier removal of vascular catheters, and less sepsis and other catheter-related complications (LOE 2b) [9-11]. Standardized feeding protocols improve outcomes in VLBW infants [11, 12]. Reaching full feeds within a week is achievable as demonstrated by an RCT on VLBW infants wherein the median time to reach 170ml/kg/day was 7 days after fast advancement of enteral feeding, with no increase in apneas, feed interruptions, and intolerance [13]

Frequency of feedings – In an RCT of 92 neonates weighing <1750 g allocated to either three-hourly or two-hourly feeds, the incidence of feeding intolerance, apnea, hypoglycemia, and NEC did not significantly differ and nursing time spent on feeding was significantly less in the three-hourly group (LOE 2b)[14].

Bolus vs continuous feeds – In a study of 28 VLBW infants, gravity bolus feeds were more effective than continuous feeds to promote feeding tolerance and were associated with shorter duration to full enteral feeds.[15] In a study of 33 healthy preterm infants (<32 weeks), continuous feeds were associated with greater number of apneas (>20 seconds), and mild hypoxia (pulse oximetry 81%-85%, < 10 seconds) compared to bolus feeds.[16] (LOE 2b). Two meta-analyses, a Cochrane Review of seven trials (511 infants) and a meta-analysis by Wang Z et al (707 infants), found no difference between feeding method in terms of time to reach full feeds, growth, or NEC and they concluded that there is insufficient evidence to make a recommendation over which method is best in VLBW infants [17, 42]. (LOE 1a). Study by Bozzeti, et al, of 40 VLBW infants (11 with

IUGR), found that there is improved superior mesenteric artery blood flow velocity with bolus feeds compared to continuous feedings. [18] (LOE 1b).

Transpyloric versus gastric feedings – Little evidence is available for benefit or harm of transpyloric feedings in preterm neonates although sometimes utilized due to clinical concern for GER, reflux associated apneas or aspiration pneumonia. A Cochrane Review (2013) of 9 trials of 359 infants with birth weight < 1500g did not show any difference in feeding intolerance, NEC, spontaneous intestinal perforation, aspiration pneumonia or in-hospital growth but showed increased risk of gastrointestinal disturbance (RR 1.48, CI 1.05-2.09) and all-case mortality (RR 2.46, CI 1.36-4.46), however all these studies were non-blinded with high risk of bias. [43] A subgroup of ELBW may benefit from transpyloric feeds as determined on individual basis.

C. Human Milk Fortification

In a multicenter RCT by Cristofalo, et al, preterm infants exclusively fed human milk (use of human milk-based fortifier) had a lower incidence of NEC (3% vs 21%, $p=0.08$) and surgical NEC ($p=0.04$), compared to infants who received bovine milk-based preterm formula [19] (LOE 1b).

High cost of human milk-based human milk fortifier is often quoted as an obstacle to using an exclusively human milk-based products. Calculated hospital cost savings in a cohort of 207 ELBW infants resulted in shorter duration of hospitalizations (less by an average of 3.9 days in the NICU and savings of \$8167 per extremely premature infant ($p<0.0001$) because of the reduction in NEC[20]

In a previous RCT by Schanler, et al, the use of DBM (while on powdered bovine milk-based fortifier) vs. preterm formula did not reduce the rates of NEC (LOE 2b)[3]

A 2020 Cochrane review showed that infants receiving early fortification (≤ 100 ml/kg/day or ≤ 7 days postnatal age) compared to later fortification had no adverse outcomes (no change in growth, NEC). Also, the earlier fortification and improved nutritional intake allow for earlier discontinuation of central IV access, a risk factor for infection [44].

Multiple bovine based human milk fortifiers are commercially available. Liquid formulations are sterile therefore preferred for use in hospitalized infants. Three formulations have higher protein content designed to meet the target goals for growing VLBW infants. These are Human Milk Fortifier Acidified Liquid (HMF-AL), Liquid Human Milk Fortifier High Protein (HMF-HP) and Hydrolyzed Protein Concentrated Liquid (HPCL). Research studies examining their use are limited. In a multi-center trial of VLBW infants comparing powder HMF to HPCL, laboratory assessments were normal and similar between groups. For HPCL there was less discontinuation of feeds due to feeding intolerance compared to powder (2% vs 10%, $P = 0.048$). There was a low incidence of confirmed NEC (1.5% in the HPCL group and 3.2% in the PI-HMF group). No statistical significant differences for growth although HPCL group reached 1800 g 7 days sooner than powder HMF.[21] (LOE 1b) Studies that report results with HMF-AL do not show favorable out comes for neonates with increased incidence of metabolic acidosis and NEC rates observed when compared to standard HMF[22].(LOE 2b)

Donor milk is lower in DHA than mothers expressed milk. This lower content is due to the lactation phase of DM and is not affected by the pasteurization process.. ESPGHAN recommends preterm infants get 12-30 mg/kg of DHA. It is difficult to assess how much is in breast milk as it varies greatly based on mom's diet. It is recommended mom achieves an intake of 200-300 mg/d (can be prenatal supplements or 1-3 weekly servings of fish) to allow enough to pass through her breast milk to baby. In HPCL fortifier, there is 3 mg DHA per one packet. In order to meet a preterm infant's needs, infant would need to be on at least 120 ml/kg of HMF 24 kcal/oz. However, DHA content in US donor milk varies with bank location and may not meet the recommended provision for preterm infants.

D. Assessment of Feeding Tolerance and Management of Gastric Residuals

Gastric residual volume (GRV) is not an important a predictor of NEC as earlier thought. In a study by Mihatsch et al, multiple regression model showed that the mean residuals and green residuals had no relationship with enteral feeding volume achieved by Day 14 (LOE 2b). In a prospective study on 50 preterm infants, there was no correlation between feeding outcomes and GRV (ml/kg/day) (LOE 2b) [26]. A pilot RCT of 61 infants (24-32 weeks GA) where they were randomly allocated to receive routine evaluation of gastric residuals versus no routine evaluation showed no difference between groups regarding volume of feeds at 3 weeks of age, growth, and days on TPN [27], but infants without routine evaluation of gastric residuals reached full feeds 6 days earlier (LOE 2b).

In a RCT by Parker et al involving 143 infants <32 weeks and < 1250g Birth weight randomized to GRV monitoring versus no GRV monitoring, no GRV monitored infants advanced quicker to full feeds with improved weight gain and earlier discharge by 8 days without any increase in mortality or NEC. (LOE 1b) [27]

E. Feeding Babies with Intrauterine Growth Restriction (IUGR) or Small for Gestational Age (SGA) with/without history of absent/reversed end-diastolic flow (AREDF)

In the study by Mihatsch, et al, 124 VLBW infants were fed with a standardized protocol and 35 infants had intrauterine growth restriction (IUGR)[24]. They did not show statistical difference in the age to reach full feeds in the IUGR and non-IUGR groups ($p = 0.6$) (LOE 2b). In a multiple regression model, increased umbilical artery resistance, brain sparing, Apgar scores, umbilical artery pH, and IUGR did not predict the age to reach full feeds.

In an RCT on SGA preterm babies (27-34 weeks) who had abnormal antenatal umbilical Doppler flows, the incidence of NEC and feeding intolerance was not significantly different ($p = 0.35$ and $p = 0.53$, respectively) between the early feeders ($n=42$; median age 2 days) and delayed feeders ($n=42$; 7 days) (LOE 2b)[28]

In the Abnormal Doppler Enteral Prescription Trial (ADEPT), 402 preterm SGA infants (<35 weeks GA, birth weight < 10th%) with absent or reversed end diastolic

umbilical blood flow and cerebral redistribution were allocated to early or late onset of enteral feeding (Day 2 vs Day 6, respectively) (LOE 1b)[29]. The early feeding group reached full enteral feeds faster ($p = 0.003$), and there was no difference in the incidence of NEC. The early feeding group had a significantly shorter duration of high-dependency care ($p = 0.002$), and a lower incidence of cholestasis ($p = 0.02$). Exclusive human milk feeding was the only protective factor.

Feeding Babies on Non-invasive Ventilation

Retrospective single center cohort study comparing rapid enteral feeding advance in infants on NIV ($n=293$), deduced that rapid advancement of 20-30 ml/kg/d in <1500g , 27-31 week GA infants was safe and had no difference in survival, NEC, SIP or BPD. (LOE 3a) [30]

F. Feeding Babies with Hypotension

There is limited evidence in neonates regarding the safety of enteral feeds while on vasoactive drugs. A 2015 retrospective study of > 1000 VLBW infants evaluated medications, and demonstrated that the use of vasoactive drugs was not associated with the development of NEC in their cohort, and was actually seen as a protective factor. However, this was a retrospective study and did not specifically evaluate the feeding practices while on vasoactive medications.

The only randomized study found included 100 late preterm neonates in each group of NPO versus feeding while on pressor support. The study showed higher mortality rate among NPO infants and longer duration of stay. Authors concluded that enteral feedings was safe up to dopamine infusion of 10 mcg/kg/min [31]. At this time, the committee feels it is reasonable to initiate trophic feeds while on low dose dopamine ≤ 5 mcg/kg/minute

G. Feeding Babies on Indomethacin or Ibuprofen during treatment of a patent ductus arteriosus

In the Ductus Arteriosus Feed or Fast with Indomethacin or Ibuprofen (DAFFII) trial, 177 infants with a mean GA of 26.3 ± 1.9 weeks who were on ≤ 60 ml/kg/day feedings were randomized (at 6.5 ± 3.9 days of life) to receive trophic feeds or no feeds during the drug administration period [32]. Infants who received trophic feeding subsequently required fewer days to reach 120 ml/kg/day (10.3 ± 6.6 days vs 13.1 ± 7.8 days, $p < 0.05$) with no difference in adverse gastrointestinal outcomes (LOE 1b).

A retrospective cohort study comparing a) NPO ($n=229$), b) Feeds ≤ 60 ml/kg/d ($n=142$) and c) Feeds > 60 ml/kg/d ($n=44$) during indomethacin treatment for PDA showed no association between enteral feed volumes during indomethacin treatment and NEC or other GI complication [33]

A study by Pezzati, et al, showed that ibuprofen does not reduce mesenteric blood flow compared to indomethacin [34], and a meta-analysis of 19 studies (956 infants) showed that NEC rates were lower in the ibuprofen group (RR 0.68 (95%CI 0.47, 0.99)) (LOE 1a)[35]

There are no RCTs comparing feeding during indomethacin therapy vs ibuprofen therapy.

H. Feeding Babies receiving a blood transfusion

Feeding preterm infants during red blood cell (RBC) transfusions remain controversial. Some studies have linked RBC transfusions to the development of NEC [36-38] (LOE 3a), although the pathogenesis of transfusion-related NEC is unclear. One hypothesis proposes enteral feeding during RBC transfusion may alter intestinal circulation predisposing tissues to ischemia [39, 40] (LOE 3b). A recent prospective observational study by Marin, et al, demonstrated that mesenteric tissue oxygenation during RBC transfusion was not influenced by feeding status. However, infants fed during RBC transfusion had decreasing postprandial mesenteric tissue oxygenation patterns for the following 15 hours compared with infants not fed during RBC transfusion (LOE 3b).

Schindler et al in a multiarmed randomized controlled trial of 60 patients with mean GA of 27 weeks, compared feeding full volumes, restricted volumes and NPO during transfusion (and for 12 hrs. after) measuring splanchnic-cerebral oxygenation ratio and splanchnic fractional oxygen extraction before, during and after transfusion (0, 12 and 24 hrs. after) and found no difference in either, nor was there any differences in clinical outcomes or any incidences of NEC [41]

I. Feeding with umbilical artery catheter (UAC)

There is no evidence of harm with feeding with umbilical artery catheters. A prospective randomized trial by Davey et al in 1994 showed no difference in gastrointestinal complications between the infant feed with UAC in place versus those who were kept NPO, but less time to full feeding, shorter duration of TPN (13 versus 30 days)[44]. In 2006 at least 75% of NICUs in the US fed infants with UAC and majority start feeds on DOL 1 (2006 Neonatal nutrition survey. Hans et al) [45].

With this in mind the nutrition task force feels it is safe to start feedings with UAC in place

Clinical Management

A. Type of Milk

- The first choice is mother's own milk (MOM). This should preferably be fresh, but if not available, provide previously frozen milk in the same sequence in which it was expressed.
- Second choice is donor breast milk (DBM).
If MOM is unavailable or in insufficient amounts, donor milk should be offered (parental consent/verbal assent is required).

Criteria for providing DBM

- DBM is recommended if MOM is not available or to supplement MOM for all infants < 1500 g at birth or <32 week GA at birth (VLBW infants).
 - If an infant meets the above criteria and the mother's own milk supply runs out prior to reaching 34 weeks postmenstrual age (PMA) and /or 1800 grams, the infant may be given donor breast milk
- Other considerations for its use include:
 - a- Infants with a history of necrotizing Enterocolitis (NEC)
 - b- Growth restricted (IUGR/SGA) infants, <3rd percentile
 - c- All infants of multiple births in which one multiple meets any above criteria
 - d- Gastroschisis, intestinal failure, and any other post-surgical cases with significant feeding intolerance
 - e- Infants with congenital heart disease that puts them at risk of developing ischemic bowel
 - f- Any infant whose mother intends of providing exclusive BM diet – for the first 5-7 days until she can provide adequate supply of MOM. Immediate switch to formula if inadequate supply by 5-7 days or earlier if mom does not pump.
- Premature infants should transition from DBM when MOM supply becomes adequate, or once they have reached both 34 weeks PMA and 1800 grams (based on which criteria is reached later).
- If not already completed, transition from donor breast milk to formula feedings should be initiated at least 1 week prior to expected discharge home.
 - Transition should take place over 4 days, starting with 1 formula feeding/day and advancing to 2 formula feedings/day, then 4 formula feedings/day on day 3. On day 4, infant should be transitioned to all formula.
- In rare circumstances, weighing risk vs benefits, an infant with severe extrauterine growth failure (z-score decline > -1) may transition earlier than 34 weeks or 1800g if the high risk period for NEC for the infants GA has passed.
- Third choice is preterm formula.
 - Special Care 24 High Protein (SCHP) can be used for babies less than 34 weeks if no breast milk is available and donor milk consent was not given by parent.
 - Neosure 22 can be used for infants ≥ 34 weeks GA.
 - Term formula can be used for AGA infants > 35 weeks GA at birth

B. Human Milk Fortification

- a. For any infant with GA of < 35 weeks
 - i. Fortify MOM or DBM to +2 kcal/oz once feedings reach 80ml/kg/day
 - ii. Fortify MOM or DBM to +4kcal/oz once feedings reach 90-100ml/kg/day
 - iii. Discontinue PICC when feedings reach 120 ml/kg/day

C. Assessment of Feeding

- a. Emesis
 - i. If neonate has bilious or blood tinged **emesis**, stop any infusing feeding and notify MD/ARNP to evaluate
 - ii. If neonate has emesis that looks like digested milk, continue to advance feedings per protocol and follow clinically.
- b. Gastric Residuals
 - i. **Do not check residuals**
- c. Abdominal Exam Changes
 - i. If patient is noted to have abdominal distention (>2 cm increase from baseline girth) in the presence of any of the additional following signs: firmness, tenderness, color change, or has absent bowel sounds, stop any running feed and notify MD/ARNP to evaluate
- d. Stool Pattern
 - i. If there is blood in the stool, stop any infusing feeding and notify MD/ARNP to evaluate

D. Feeding Small For Gestational Age (SGA) or Babies With/Without History Of Absent/Reversed End-Diastolic Flow (AREDF)

- a. If IUGR/SGA **with** history of AREDF, consider shifting one column to the left on the feeding algorithm but do not delay starting enteral feedings for that reason.

E. Feeding Babies On Non-Invasive Ventilation, CPAP (including HHFNC $\geq$ 2 LPM)

- a. Start feedings based on birth weight
- b. Use OGT of minimum 8 Fr. for ventilation
- c. Increase feeds as per usual recommendations
- d. Do not rely solely on abdominal distension as a sign of feeding intolerance.

F. Feeding Babies With Hypotension

Based on the available evidence at this time, the committee feels it is reasonable to initiate trophic feeds while stable on low dose dopamine $\leq 5\text{mcg/kg/minute}$.

G. Feeding Babies On Indomethacin Or Ibuprofen

The evidence supports at least trophic feedings during indomethacin therapy and the nutrition taskforce recommends continuing feeds during medical treatment of PDA.

H. Feeding Babies Receiving A Blood Transfusion

At this time, there is no strong evidence that feeding during transfusion of blood products is associated with transfusion-related gut injury.

- a. It is the consensus of the group that infants who require blood transfusion should be NPO during transfusion.
- b. Hold enteral nutrition for one to two feedings, the one that is due during the blood transfusion and the one due after the blood transfusion.
- d. Check glucose every three hours during the time period when enteral nutrition is held. Start IVF only if indicated due to hypoglycemia.

Summary

Adequate nutrition is essential for the optimal growth and health of preterm infants. Enteral nutrition whenever possible is preferred over Parenteral Nutrition (PN), as the former avoids complications related to vascular catheterization, sepsis, adverse effects of PN, and fasting. Although early PN remains critical in VLBW infants, our ultimate goal in feeding sick infants is to reach full enteral feedings in the shortest time possible while maintaining optimal growth and nutrition and avoiding the potential adverse consequences of rapid advancement of feeding. There is good evidence showing that even extremely low birth weight infants benefit from early feedings, and that mother's own milk is the best choice of nutrition. There are very few contraindications to the initiation and advancement of enteral feedings.

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*Shift LEFT 1 column for: IUGR <3% , if infant has 5 min Apgar < 5,						
	Start feeds ASAP on Day of Birth, unless contraindicated or MOM/DBM unavailable (as defined below)*					
	Ultimate goal feeds 150-160 ml/kg/d					
	Indomethacin prophylaxis, Ibuprofen/Tylenol for PDA is not a contraindication for enteral feeds					
Admission	<26 weeks or <750 g	26- 27 ⁶ Weeks (~750-1000 g)	28-29 ⁶ Weeks (~1000-1250 g)	30-32 ⁶ Weeks (~ 1251-1800g)	33-36 ⁶ Weeks (~1800+)	
	Starter PN IL 1 g/kg/d	Starter PN IL 1-2 g/kg/d	Starter PN IL 2 g/kg/d	Starter PN IL 2 g/kg/d	D10W	
Initiation Of Feeds	GAVAGE 20 ml/kg/d Repeat x 5 days (trophic feeds)	GAVAGE 20ml/kg/d Repeat x 2-3 days	GAVAGE 20ml/kg/d	GAVAGE 30ml/kg/d	GAVAGE/PO 30-40 ml/kg/d	
Advance	Advance by 20 ml/kg/d			Advance by 30 ml/kg/d	Advance to 80ml/kg/day on DOL# 2 DC IVFs Then advance daily as indicated	
Fortification	80ml/kg/day +2 HPCL (22kcal) And 100 ml/kg/day +4 HPCL (24kcal)		80ml/kg/day +2 HPCL (22kcal) And 100 ml/kg/day +4 HPCL (24kcal)	60ml/kg/day +2 HPCL (22kcal) And 90 ml/kg/day +4 HPCL (24kcal)	Fortify < 34 weeks. Consider Fortification in >34 as indicated	
Target Feeding Volume	150-160ml/kg/day	150-160ml/kg/day		150-160ml/kg/day	150-160ml/kg/day	

NPO	*CONTRAINDICATIONS TO FEEDS: Bowel obstruction, MAP < age appropriate minimums, need for pressor (unless Dopamine <= 5 mcg/kg/min) IF NPO Oral Care q6h with colostrum/MOM if available	SPECIAL CIRCUMSTANCES: MOM/DBM 20ml/kg/day, can be used for infants with hypoxic ischemic insult, cardiac lesions, hypoxic respiratory failure etc., as indicated if hemodynamically stable	*If desired by parent may delay starting enteral feeds for up to 24 hrs to provide mom's own milk
-----	--	---	--

Stagnant growth	***Once full +4 (24) kcal/oz fortification has been tolerated for >3days, consider increasing caloric density with Similac Neosure powder to + 6 (26) kcal/oz
Gastric Residual	Do NOT check residuals

Feeding the Preterm Infant if not using DBM or MOM			
<34 Weeks – begin feeds of Premature High Protein 24kcal/oz formula			
34 - 34 ⁶ Weeks – begin feeds of 22kcal/oz Transitional formula			
35 weeks and above can use term formula			
Fortification Guidelines	If on SSC High Pro 24kcal w/some MOM available, fortify MOM +4(24cal) HPCL	If on 22kcal Transitional formula w/some MOM available, fortify MOM+2(22kcal) HPCL	Regardless of caloric density, transition to formula powder fortification once infant achieves 80% PO or reaches term PMA
Ad Lib – set minimum of 120ml/kg/day– and goal of 150-160 ml/kg/d If cannot complete minimum of 2 consecutive times, call MD/NNP/PA (if tube must be inserted, order remainder to goal volume)			

Glossary

- DBM – donor breast milk
- ELBW – extremely low birth weight
- GRV – gastric residual volume
- HSPDA – hemodynamically significant patent ductus arteriosus
- IUGR – intrauterine growth restriction
- LOE – level of evidence (based on Centre for Evidence-based Medicine, United Kingdom, 2015)[39]
 - ❖ 1a - Systematic review (with homogeneity) of randomized controlled trials (RCT)
 - ❖ 1b - Individual RCT with narrow confidence interval (CI)
 - ❖ 2a - Systematic review (with homogeneity) of cohort studies
 - ❖ 2b - Individual cohort studies and low-quality RCTs
 - ❖ 3a - Systematic review (with homogeneity) of case-control studies
 - ❖ 3b - Individual case-control studies
 - ❖ 4 - Case series, poor-quality cohort and poor-quality case-control studies
 - ❖ 5 - Expert opinion without explicit critical appraisal

If a minus sign is suffixed (e.g., 1a- or 1b-), it denotes either a single study with wide CI or a systematic review with troublesome heterogeneity.
- MOM – mother's own milk
- NEC – necrotizing enterocolitis
- SGA – small for gestational age
- TPN – total parenteral nutrition
- VLBW – very low birth weight

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Outcome Measures

Days of PN, DOL once achieves full enteral feeds. Growth, NEC rates, compliance to guidelines

Clinical Pathway Team

Early Standardized Enteral Nutrition Management of the Sick Neonate Clinical Pathway

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