Preterm infant feeding and growth monitoring: Implementation of the INTERGROWTH-21st protocol

Module 3
Feeding recommendations for the routine care of preterm infants

On successful completion of this module you should be able to:

- Understand the pathophysiology of breastfeeding and its effects.
- Know the physiological differences between amniotic fluid, premature human milk, and term human milk.
- Know the choices of milk available for preterm feeding.
- Know the benefits of human breast milk and the challenges of providing it to preterm infants.
- Describe the different feeding methods for preterm infants.
- Assess feed intolerance and manage residual feeds in preterm infants.
- Know the diagnosis and treatment of gastro-esophageal reflux in preterm infants.
- Describe gavage feeding.
- Describe the transition from tube feeding to breastfeeding in preterm infants.
- Know the methods by which breastmilk production can be improved in mothers of preterm infants.

Introduction

Breastfeeding is a physiological process that should naturally follow delivery. It has been associated with tremendous benefits for both the mother and infant.

Mothers and infants in lower- and middle-income countries seem to benefit the most, because prevalence of breastfeeding at 12 months is highest in sub-Saharan Africa, south Asia, and parts of Latin America; in most high-income countries, the prevalence is less than 20%,

Victora CG, Bahl R, Barros AJD, França GVA, Horton S, Krasevec J, Murch S, Sankar MJ, Walker N, Rollins NC, Lancet Breastfeeding Series Group. Breastfeeding in the 21st century: epidemiology, mechanisms, and lifelong effect. Lancet. 2016 Jan 30;387(10017):475-90.

Feeding recommendations for the routine care of preterm infants

Exclusive breastfeeding for preterm infants, by the time of hospital discharge and during the first months of life, is the goal of these feeding recommendations.

Although the focus is on moderate and late preterm newborns, who represent close to 90% of all preterms, the recommendations are also relevant to very preterm newborns who are moving to enteral feeding.

They are based on 1) the feeding practices used during the implementation of the Preterm Postnatal Follow-up study (PPFS) of the INTERGROWTH-21st Project (Villar, 2015); 2) a review of evidence-based information up to December 2016, and 3) an extensive consultation with clinicians worldwide and the INTERGROWTH-21st Neonatal Advisory Committee (Victora CG, 2016).

They should be adapted for clinically unstable preterms according to the judgment of the attending clinical teams at the local institutions.

Victora CG, Bahl R, Barros AJD, França GVA, Horton S, Krasevec J, Murch S, Sankar MJ, Walker N, Rollins NC, Lancet Breastfeeding Series Group. Breastfeeding in the 21st century: epidemiology, mechanisms, and lifelong effect. Lancet. 2016 Jan 30;387(10017):475-90.

Villar J, Giuliani F, Bhutta ZA, Bertino E, Ohuma EO, Ismail LC, Barros FC, Altman DG, Victora C, Noble JA, Gravett MG, Purwar M, Pang R, Lambert A, Papageorghiou AT, Ochieng R, Jaffer YA, Kennedy SH, International Fetal and Newborn Growth Consortium for the 21(st) Century (INTERGROWTH-21(st)). Postnatal growth standards for preterm infants: the Preterm Postnatal Follow-up Study of the INTERGROWTH-21(st) Project. Lancet Glob Health. 2015 Nov;3(11):e681-691.

Benefits of human breast milk

Benefits of human breast milk are derived largely from comparisons with infant formula. Comparisons with human donor milk have not been widely studied.

In the early postnatal period and early life, these benefits include decreased rates of late-onset sepsis, necrotizing enterocolitis (NEC) and retinopathy of prematurity, fewer re-hospitalizations in the first year of life, and improved neurodevelopmental outcomes.

Following the immunoprotective nature of human breast milk as seen previously, there seems to be a dose-related decrease in the risk of necrotizing enterocolitis and late-onset sepsis with mother's breast milk.

A dose of mother's own milk of more than 50 mL/kg per day decreases the risk of late-onset sepsis and NEC compared with less than 50 mL/kg per day and for each 10 mL/kg per day increase in human milk in the diet there is a 5% reduction in hospital readmission rate.

Underwood MA. Human milk for the premature infant. Pediatr Clin North Am. 2013 Feb;60(1):189-207.

Benefits of human breast milk

In addition, premature infants who receive human milk have lower rates of metabolic syndrome, lower blood pressure and low-density lipoprotein levels, and less insulin and leptin resistance when they reach adolescence, compared with premature infants receiving formula.

Other potential benefits in which concrete evidence in support is lacking include: decreased parental anxiety, increased skin-to-skin contact and parent–infant bonding. It has also been postulated that human colostrum in the form of oral care for intubated premature infants stimulates the oropharyngeal-associated lymphatic tissue, altering the oral microbiota.

Underwood MA. Human milk for the premature infant. Pediatr Clin North Am. 2013 Feb;60(1):189-207.

Gavage feeding

It is notable that many preterm infants may not be able to suck from the mothers milk at the time of birth.

Subsequently, if breastfeeding is not possible, human milk may be given via an oro-gastric or naso-gastric tube either intermittently or continuously. Given the lack of high quality evidence comparing the two methods, local practice should dictate which method is used (Premji SS, 2011).

Babies should be encouraged to suck at the breast once sucking behavior is observed and the practice of non-nutritive sucking is advised during the transition from gavage to full oral feeding (Foster JP, 2016).

Foster JP, Psaila K, Patterson T. Non-nutritive sucking for increasing physiologic stability and nutrition in preterm infants. In: The Cochrane Collaboration, ed. Cochrane Database of Systematic Reviews. Chichester, UK: John Wiley & Sons, Ltd; 2016 Oct 4.
Premji SS, Chessell L. Continuous nasogastric milk feeding versus intermittent bolus milk feeding for premature infants less than 1500 grams. Cochrane Database Syst Rev. 2011 Nov 9;(11):CD001819.
Wellington A, Perlman JM. Infant-driven feeding in premature infants: a quality improvement project. Arch Dis Child Fetal Neonatal Ed. 2015 Nov;100(6):F495-500. .

First choice of milk- mother's own milk

The first choice is always mother's own freshly expressed breast milk or colostrum. If the mother's own breast milk was frozen and fresh breast milk is unavailable, provide it in the sequence in which it was expressed. However, freezing is associated with depletion of commensals, immune cells, immune factors, and enzyme activity (Dutta S, 2015).

Under certain circumstances, mother's own milk may be withheld from the premature baby. First, there is a risk of a mother transmitting cytomegalovirus (CMV) to a premature infant through breast milk given that approximately 50% of adults are carriers of CMV. Symptomatic postnatal CMV infection is rare in term infants, probably because of maternal antibody transfer in the third trimester (Underwood MA, 2013).

With no consensus, recommendations include a) pasteurizing all human milk until corrected gestational age of 32 weeks; b) screening all mothers who deliver preterm and withholding colostrum and pasteurizing milk of women who are CMV IgG positive, and c) freezing all CMV positive milk for premature infants younger than 32 weeks' gestation (Underwood MA, 2013).

Dutta S, Singh B, Chessell L, Wilson J, Janes M, McDonald K, Shahid S, Gardner VA, Hjartarson A, Purcha M, Watson J, de Boer C, Gaal B, Fusch C. Guidelines for Feeding Very Low Birth Weight Infants. Nutrients. 2015 Jan 8;7(1):423-42.
Underwood MA. Human milk for the premature infant. Pediatr Clin North Am. 2013 Feb;60(1):189-207.

Second choice of milk- donor human milk

Donor human milk is the second choice when mother's own expressed breast milk is unavailable. It is usually fortified with either a human-milk or bovine-milk based fortifier. Donor human milk with a human-milk based fortifier is preferable (Dutta S, 2015).

Neonates who receive an exclusively human milk-based diet (mother's milk or donor human milk with human milk-based fortifier) have significantly lower rates of NEC compared to those who receive preterm formula or human milk with a bovine milk-based fortifier. The rates of NEC in preterm babies who have received donor milk with bovine fortifier are not reduced compared to preterm babies who have received preterm formula (Dutta S, 2015).

While the cost of human milk-based human milk fortifier (HMF) is prohibitive, in general this does not compare with the costs saved from reduced hospitalization and NEC in extremely low birthweight (ELBW) babies (Dutta S, 2015).

Dutta S, Singh B, Chessell L, Wilson J, Janes M, McDonald K, Shahid S, Gardner VA, Hjartarson A, Purcha M, Watson J, de Boer C, Gaal B, Fusch C. Guidelines for Feeding Very Low Birth Weight Infants. Nutrients. 2015 Jan 8;7(1):423-42.
Underwood MA. Human milk for the premature infant. Pediatr Clin North Am. 2013 Feb;60(1):189-207.

Pasteurized donor human milk for premature infants

Pasteurization, together with donor screening and testing, is highly effective at decreasing the risk of transmission of HIV, cytomegalovirus (CMV), Hepatitis B and Hepatitis C.

Holder pasteurization

The current pasteurization method of choice. Milk is pasteurized at 62.5 degrees Celsius over 30 minutes. This process:

- Does not alter oligosaccharides, long-chain polyunsaturated fatty acids, gangliosides, lactose, fat-soluble vitamins, or epidermal growth factor
- Increases some medium chain saturated fatty acids
- Increases cytokine IL8
- Decreases other cytokines (TNFα, IFNγ, IL1β, and IL10)
- Significantly decreases sIgA, lactoferrin, lysozyme, insulin-like growth factors, hepatocyte growth factor, water-soluble vitamins, bile salt-stimulated lipase, lipoprotein lipase, and anti-oxidant activity

Underwood MA. Human milk for the premature infant. Pediatr Clin North Am. 2013 Feb;60(1):189-207.

Pasteurized donor human milk for premature infants

High temperature short-term pasteurization
In this method, milk is pasteurized over 72–75 degrees Celsius for 15–16 seconds. This process eliminates bacteria and many viruses, with less protein loss (including maintenance of bile salt stimulating lipase, lactoferrin, and some IgAs), less severe loss of antioxidant activity, but greater loss of antimicrobial activity.

Flash-heat treatment (temperature above 56 degrees Celsius for 6 min 15 seconds) has been applied in resource-poor settings. It does not alter milk antibacterial activity against E. coli and S. aureus, only minimally decreases lactoferrin antibacterial activity, but significantly diminishes lysozyme antibacterial activity.

Underwood MA. Human milk for the premature infant. Pediatr Clin North Am. 2013 Feb;60(1):189-207.

Challenges of providing human breast milk

While proper nutrition with mother's milk offers the best chances of survival, it is in itself **NOT** without challenges for the preterm and mother.

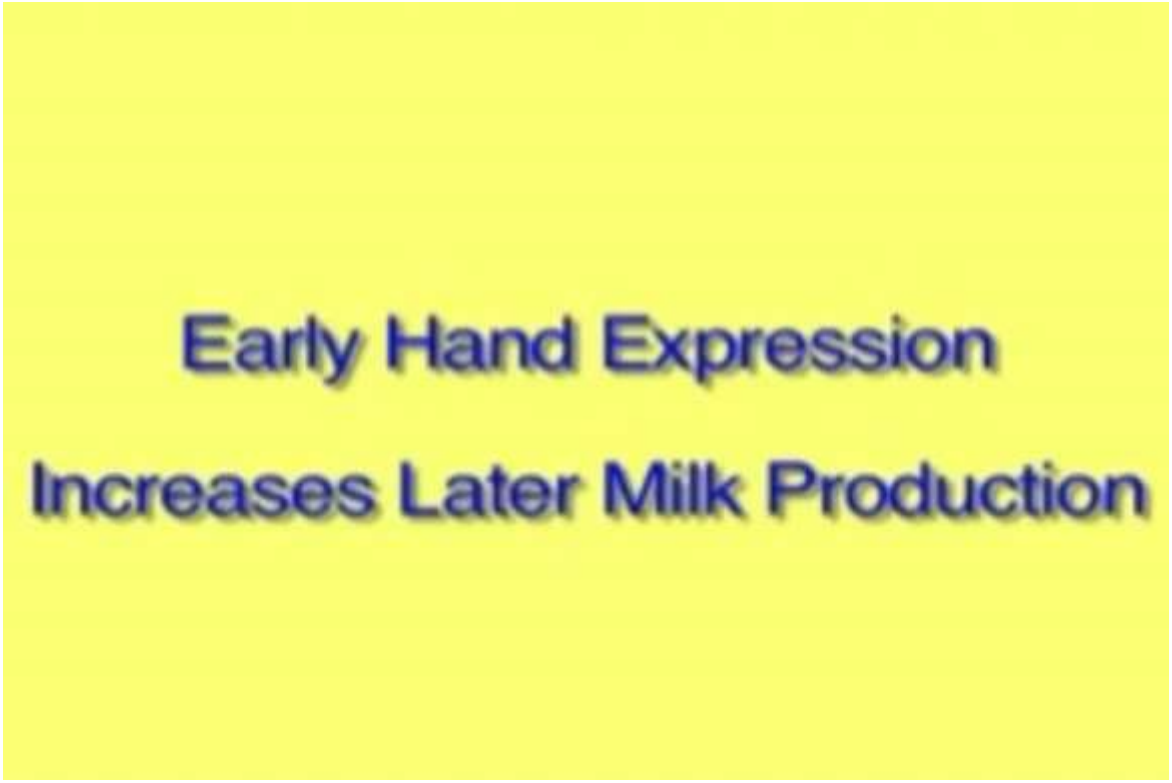
First, milk supply may be inadequate for new mothers. Mothers are therefore encouraged to start pumping breast milk as soon as possible after delivery. Mothers whose babies are in the neonatal intensive care unit (NICU) should be encouraged to begin pumping within 6 to 12 hours of delivery and to pump after every 2 to 3 hours (8 to 12 times per day), ensuring that they empty the breast each time.

Preterm infants miss out on much of the third-trimester rapid growth and therefore have a higher nutritional requirement per kilo basis and would, in principle, need more milk. For example, studies suggest that a higher protein intake is beneficial for premature infants. However, energy and protein content of human milk varies between mothers, over time in a given mother, and between foremilk and hindmilk with a decrease in protein content over time of lactation.

Underwood MA. Human milk for the premature infant. Pediatr Clin North Am. 2013 Feb;60(1):189-207.

Hand Expressing Milk

"Hand expression and spoon feeding after each breastfeeding can provide more stimulation to the breast than breastfeeding alone". Click on the image to play clip for demonstration.



Morton J. Hand Expression of Breast Milk. Breastfeeding. Available from: http://med.stanford.edu/newborns/professional-education/breastfeeding/hand-expressing-milk.html

Human breast milk fortification

It is worth noting that donor human milk is more likely to be from mothers who delivered at term and hence lower in protein content than milk from mothers delivering prematurely (Underwood MA, 2013).

Based on this, and given the differences in composition of preterm and term breast milk, and that preterm infants would need higher volumes to compensate, which they cannot tolerate, fortification of preterm breast milk is necessary especially for birth weight less than 1500gm, to maximize protein, calcium, phosphorus and vitamin D intake per feed (Underwood MA, 2013).

Therefore, in the event that the infant is unable to suck at the breast, expressed breast milk or donor human milk should be fortified in order to reach the recommended nutrient intakes as summarised in Table 1 (Agostoni C, 2010; Edmond K, 2006).

Since a fortifier is considered to be a medication, any fully breastfed infant receiving only “fortification” may be considered to be exclusively breastfed (Nyqvist KH, 2013).

Agostoni C, Buonocore G, Carnielli VP, et al. Enteral nutrient supply for preterm infants: commentary from the European Society of Paediatric Gastroenterology, Hepatology and Nutrition Committee on Nutrition. J Pediatr Gastroenterol Nutr 2010;50: 85–91

Edmond K, Bahl R editors. WHO Technical Review: Optimal Feeding of Low-Birth-Weight Infants. Geneva: World Health Organisation;2006. pp 1–121

Nyqvist KH, Häggkvist AP, Hansen MN, Kylberg E, Frandsen AL, Maastrup R, Ezeonodo A, Hannula L, Haiek LN. Expansion of the Baby-Friendly Hospital Initiative Ten Steps to Successful Breastfeeding into Neonatal Intensive Care: Expert Group Recommendations. Journal of Human Lactation 2013;29(3):300–309.

Underwood MA. Human milk for the premature infant. Pediatr Clin North Am. 2013 Feb;60(1):189-207.

Human breast milk fortification

Table 1. Recommended daily enteral macronutrients for preterm infants >1000 g at birth

Nutrient	Birth to 7 days	Stable - growing up to term	Term to 1 year of age
Energy, kcal/kg	70 - 80	105 - 135	100 - 120
Protein, g/kg	1.0 - 3.0	3.0 - 4.0	2.2
Fat, g/kg	0.5 - 3.6	4.5 - 6.8	4.4 - 7.3
Carbohydrate, g/kg	5.0 - 20.0	7.5 - 15.5	7.5 - 15.5

Agostoni C, Buonocore G, Carnielli VP, et al. Enteral nutrient supply for preterm infants: commentary from the European Society of Paediatric Gastroenterology, Hepatology and Nutrition Committee on Nutrition. J Pediatr Gastroenterol Nutr 2010;50: 85–91

Edmond K, Bahl R editors. WHO Technical Review: Optimal Feeding of Low-Birth-Weight Infants. Geneva: World Health Organisation;2006. pp 1–121

Human breast milk fortification

Documented benefits of fortification of human milk include improved growth in weight, length and head circumference. However, improvements in bone mineralization and neurodevelopmental outcomes are unclear (Underwood MA, 2013).

Standard fortification leads to a lower than assumed protein intake and hence adjusting the amount of added protein based on actual measurements of milk samples or based on metabolic parameters indicative of protein accretion in the neonate (e.g. blood urea nitrogen) on a case by case leads to increased protein intake and improved growth (Underwood MA, 2013).

Individualized fortification is not recommended for preterm infants >32 weeks' gestation or infants with birthweight >1.5 kg. It has been suggested that for very preterm infants the use of individualised human milk fortification may be effective in maintaining adequate growth, with no detrimental effects (Arslanoglu S, 2006; Arslanoglu S, 2015; Morlacchi L, 2016; Underwood MA, 2013).

Arslanoglu S, Moro GE, Ziegler EE. Adjustable fortification of human milk fed to preterm infants: does it make a difference? J Perinatol. 2006 Oct;26(10):614-21.
Arslanoglu S. Individualized Fortification of Human Milk: Adjustable Fortification. J Pediatr Gastroenterol Nutr 2015;61:s4-5
Morlacchi L, Mallardi D, Giannì ML, Roggero P, Amato O, Piemontese P, Consonni D, Mosca F. Is targeted fortification of human breast milk an optimal nutrition strategy for preterm infants? An interventional study. J Transl Med 2016 Jul 1;14(1):195.
Polberger S. Individualized Fortification of Human Milk: Targeted Fortification. J Pediatr Gastroenterol Nutr 2015;61:s3-4.
Underwood MA. Human milk for the premature infant. Pediatr Clin North Am. 2013 Feb;60(1):189-207.

Human breast milk fortification

Current evidence suggests that human milk fortifier (HMF) should be initiated after attaining enteral intake of 100ml/kg/day threshold, at a concentration of 1:50 increasing to 1:25 if tolerated for 48 h (Dutta S, 2015).

Human milk fortifiers containing 0.8 - 1.1 g proteins, 1.1 - 3.6 g carbohydrates, and minerals (e.g. calcium 51 - 117 mg and phosphorus 34 - 67 mg) may be added to expressed human milk until the infant's weight has reached 1800 - 2000 g (Edmond K, 2006)

Challenges of human breast milk fortification

Fortification has been associated with a number of risks as well (Underwood MA, 2013):

- Metabolic acidosis.
- Increased markers of oxidative stress compared to unfortified human milk and to infant formula.
- Bacterial contamination of powdered infant formulas and associated sepsis from neonatal Cronobacter (Enterobacter sakazakii) infections.
- Liquid fortifiers lead to displacement of the volume of mother's own milk, such that the infant receives less total volume of human milk.

Dutta S, Singh B, Chessell L, Wilson J, Janes M, McDonald K, Shahid S, Gardner VA, Hjartarson A, Purcha M, Watson J, de Boer C, Gaal B, Fusch C. Guidelines for Feeding Very Low Birth Weight Infants. Nutrients. 2015 Jan 8;7(1):423-42.
Edmond K, Bahl R editors. WHO Technical Review: Optimal Feeding of Low-Birth-Weight Infants. Geneva: World Health Organisation;2006. pp 1–121
Underwood MA. Human milk for the premature infant. Pediatr Clin North Am. 2013 Feb;60(1):189-207.

Choice of milk- preterm formula

Rare exceptions wherein an infant should receive no or limited volumes of human milk include galactosemia, and some inborn errors of metabolism and human milk protein intolerance respectively (Underwood MA, 2013).

Preterm formula is therefore a third option, where the mother's own breast milk or human donor milk is not available (Dutta S, 2015).

The Milk Trial seeks to determine the effect on neurodevelopmental outcomes at age 22-26 months of donor human milk as compared to preterm infant formula as the in-hospital diet for infants whose mothers choose not to provide breast milk or are able to provide only a minimal amount (Underwood MA, 2013).

Proportional growth (length and weight) should be carefully monitored to avoid overfeeding given the marked heterogeneity of studies examining the effects of formulas. For uncomplicated preterm infants, nutrient enriched formulas are not recommended (Teller IC, 2016).

Dutta S, Singh B, Chessell L, Wilson J, Janes M, McDonald K, Shahid S, Gardner VA, Hjartarson A, Purcha M, Watson J, de Boer C, Gaal B, Fusch C. Guidelines for Feeding Very Low Birth Weight Infants. Nutrients. 2015 Jan 8;7(1):423-42.
Teller IC, Embleton ND, Griffin IJ, van Elburg RM. Post-discharge formula feeding in preterm infants: A systematic review mapping evidence about the role of macronutrient enrichment. Clin Nutr. 2016 Aug;35(4):791-801
Underwood MA. Human milk for the premature infant. Pediatr Clin North Am. 2013 Feb;60(1):189-207.

The role of Probiotics

Probiotic bacteria are live microbial supplements (mostly lactobacillus and Bifidobacterium species) introduced in the gastrointestinal tract to provide certain benefits to the host.

In preterm infants, enteral administration of probiotics reduces the incidence of severe NEC, mortality, and NEC related mortality.

In addition, the administration of probiotic organisms results in a shorter time to achieve full enteral feeding as well as shortened hospitalization days.

In a Cochrane review looking at the effect of probiotics in prevention of necrotizing enterocolitis in preterm infants, none of the included studies noted any adverse effect related to the supplemental organism , including systemic infection by the probiotic bacteria.

AlFaleh K, Anabrees J. Probiotics for prevention of necrotizing enterocolitis in preterm infants. Cochrane Database Syst Rev. 2014(4):CD005496. Epub 2014/04/10. doi: 10.1002/14651858.CD005496.pub4.

Trophic feeds: time of starting, volume, duration

Early trophic feeding is defined as giving small volumes of milk (10-15 ml/kg/day) intragastrically in the early neonatal period, without advancing the feed volumes during the first week postnatally.

This is necessary in order to hasten gastrointestinal physiological, endocrine and metabolic maturity and so allow infants to transition to full enteral feeding independent of parenteral nutrition more quickly.

Trophic feeds should preferably be started within 24 hours of delivery. This should be mother's own milk (colostrum) or donor milk if mother's milk is not available. Formula should only be considered as the last option if within 24-48 hours the other two choices are not an option.

Contraindications to trophic feeds

- Intestinal obstruction or a setting for intestinal obstruction or ileus.

Asphyxia, respiratory distress, sepsis, hypotension, glucose disturbances, ventilation, and umbilical lines **are not** contraindications for trophic feeds.

Dutta S, Singh B, Chessell L, Wilson J, Janes M, McDonald K, Shahid S, Gardner VA, Hjartarson A, Purcha M, Watson J, de Boer C, Gaal B, Fusch C. Guidelines for Feeding Very Low Birth Weight Infants. Nutrients. 2015 Jan 8;7(1):423-42.

Nutritional feeds: day of starting, volume, frequency, increase

For infants fed with expressed human milk, a starting volume of approximately 60 - 80 ml/kg/day is indicated, to a maximum of approximately 160 -180 ml/kg/day by the end of the first week of life.

Daily increases of 10 - 20 ml/kg are indicated but there are suggestions that the increases may be as high as 30 ml/kg/day, which in very low birth weight infants (VLBW) is associated with a reduction in the time needed to establish full enteral feeding without increasing rates of NEC or death in stable very preterm newborns (Agostoni C, 2010; Fallon EM, 2012; Morgan J, 2015).

Agostoni C, Buonocore G, Carnielli VP et al. Enteral nutrient supply for preterm infants: commentary from the European Society of Paediatric Gastroenterology, Hepatology and Nutrition Committee on Nutrition. J Pediatr Gastroenterol Nutr. 2010 Jan;50(1):85-91.
Dutta S, Singh B, Chessell L, Wilson J, Janes M, McDonald K, Shahid S, Gardner VA, Hjartarson A, Purcha M, Watson J, de Boer C, Gaal B, Fusch C. Guidelines for Feeding Very Low Birth Weight Infants. Nutrients. 2015 Jan 8;7(1):423-42.
Fallon EM, Nehra D, Potemkin AK, Gura KM, Simpser E, Compher C, American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.) Board of Directors, Puder M. A.S.P.E.N. clinical guidelines: nutrition support of neonatal patients at risk for necrotizing enterocolitis. JPEN J Parenter Enteral Nutr. 2012 Sep;36(5):506-23.
Morgan J, Young L, McGuire W. Slow advancement of enteral feed volumes to prevent necrotising enterocolitis in very low birth weight infants. In: The Cochrane Collaboration, ed. Cochrane Database of Systematic Reviews. Chichester, UK: John Wiley & Sons, Ltd; 2015 Oct 15.

Full enteral feeding: time of starting, volume, frequency

Mothers and clinical staff should be encouraged to observe and implement cue-based feeding practices that are associated with a reduction in the time needed to establish full feeds and hospital discharge (Wellington A, 2015)

Full enteral feeding is reached when the infant can take in between 150-180 ml. Full enteral feeding if reached faster, minimizes the need for vascular catheters, subsequently reducing sepsis (Dutta S, 2015).

However, it should be emphasized that glycerin enemas should not be used to hasten full enteral feeding or for meconium emptying because preterm babies take longer to pass the first motion, the more premature they are. If a glycerin tip has to be used, it should be on a case-by-case basis, putting into consideration the normal stooling pattern and volume of milk consumed (Dutta S, 2015).

Timelines to full enteral feeding are as follows:

- By about two weeks in babies weighing <1000 g at birth
- By one week in babies weighing 1000–1500 g

Frequency of feeding may affect incidence of feed intolerance, apnea, hypoglycemia, NEC and nursing time spent on feeding (Dutta S 2015).

Dutta S, Singh B, Chessell L, Wilson J, Janes M, McDonald K, Shahid S, Gardner VA, Hjartarson A, Purcha M, Watson J, de Boer C, Gaal B, Fusch C. Guidelines for Feeding Very Low Birth Weight Infants. Nutrients. 2015 Jan 8;7(1):423-42.
Wellington A, Perlman JM. Infant-driven feeding in premature infants: a quality improvement project. Arch Dis Child Fetal Neonatal Ed 2015 Nov;100(6):F495-500

Assessment of feed tolerance

Gastric residuals (GR) have been variously used as a diagnostic window. Though aspiration of gastric residuals has been used to determine proper gastric positioning of nasogastric and orogastric tubes, this has been shown to be unreliable.

GRs have additionally been used in the past as a measure of feed tolerance, hence facilitating the decision to transition to full enteral feeds, as well as an indicator of NEC, as seen in the preceding chapter. However, there is growing doubt over GR in playing the aforementioned roles, and in fact thought to be a practice detrimental to the preterm baby.

First, the negative pressure created through aspiration coupled with contact of the tip of the tube may damage the mucosa. Secondly, it is important to remember that there remains lack of consensus on quantity and quality of GRs. What volume constitutes an acceptable gastric residual volume? What should be considered abnormal GR?

Subsequently, enteral feedings may be inappropriately discontinued or delayed, resulting in the prolongation of parenteral nutrition and delays in the attainment of full enteral feedings. Delays in reaching full enteral feeds in turn negatively impacts the preterm baby's neurodevelopment and gastric maturation.

Li YF, Lin HC, Torrazza RM, Parker L, Talaga E, Neu J. Gastric residual evaluation in preterm neonates: a useful monitoring technique or a hindrance? Pediatr Neonatol. 2014;55(5):335-40. Epub 2014/08/14. doi: 10.1016/j.pedneo.2014.02.008.

Assessment of feed tolerance

It is therefore not recommended to check gastric residual volume (GRV) routinely, and when done, pre-feed gastric residual volume after attainment of minimum intake per feed is a better measure. The following prefeed gastric volume thresholds are guides:

Weight	Gastric residual volume threshold
<500 g	2 mL
500–749 g	3 mL
750–1000 g	4 mL
>1000 g	5 mL

Dutta S, Singh B, Chessell L, Wilson J, Janes M, McDonald K, Shahid S, Gardner VA, Hjartarson A, Purcha M, Watson J, de Boer C, Gaal B, Fusch C. Guidelines for Feeding Very Low Birth Weight Infants. Nutrients. 2015 Jan 8;7(1):423-42.

Assessment of feed tolerance

Abdominal girth should not be checked routinely. Abdominal distension with bileous vomitus however denotes intestinal obstruction and feeds should not be given. Hemorrhagic residuals suggest NEC and therefore justify stoppage of feeds. Isolated green or yellow residual is insignificant.

Management of residual feeds

With lack of consensus as noted in the preceding slide, some studies suggest ≤5 mL/kg as an acceptable GRV. Therefore, push back GRV of up to 5 mL/kg or 50% (whichever is higher) of the previous feed volume. If it recurs, subtract the residual volume from the current feed.

If GRV >5 mL/kg and >50% of the previous feed volume, push back 50% of the feeds and consider slow bolus with recurrence or withhold feeds completely depending on the clinical picture.

When checking for GRV, use smallest volume syringes for aspiration because they are better as they exert less negative pressure. Nursing the baby in the prone position for half an hour after a feed ensures maximum decrease in GRV.

Adjust feeds to the last well-tolerated feed volume if recurrence of GRV persists.

Dutta S, Singh B, Chessell L, Wilson J, Janes M, McDonald K, Shahid S, Gardner VA, Hjartarson A, Purcha M, Watson J, de Boer C, Gaal B, Fusch C. Guidelines for Feeding Very Low Birth Weight Infants. Nutrients. 2015 Jan 8;7(1):423-42.

Clinical diagnosis of gastro-esophageal reflux (GER)

In establishing acid- and nonacid reflux, combined multi-channel intraluminal impedance (MII) and pH monitoring is the modality of choice.

Apnea, desaturation, bradycardia, gagging, irritability, coughing or arching are not good indicators of GER in preterms.

Treatment of GER

So far, positioning seems to offer the best results. Positioning the baby in the left lateral position immediately after a feed ensures the lowest esophageal acid exposure. However, ensure to reposition the baby in prone position after 30 minutes postprandial.

If repositioning does not help, one may increase the feed duration to 30–90 min. Make all attempts to shorten the duration as soon as possible but taking care to avoid continuous feeding. Continuous or transpyloric feeding should be a last resort for the management of GER. Continuous feeding is associated with nutrient loss due to attachment on the tubing and if inevitable, a shorter tubing is recommended.

Dutta S, Singh B, Chessell L, Wilson J, Janes M, McDonald K, Shahid S, Gardner VA, Hjartarson A, Purcha M, Watson J, de Boer C, Gaal B, Fusch C. Guidelines for Feeding Very Low Birth Weight Infants. Nutrients. 2015 Jan 8;7(1):423-42.

Treatment of GER

Transpyloric feeding does not improve feed tolerance or growth and has been associated with an increased risk for cessation of feeds and mortality in a Cochrane review.

Regarding drugs, domperidone and metoclopramide have been associated with increased frequency of GER episodes and in addition, domperidone causes prolongation of QTc interval in neonates above 32 weeks' gestation.

Ranitidine is associated with late onset sepsis and NEC in preterms. In studies, omeprazole and esomeprazole have been shown not to reduce the frequency of GER episodes although omeprazole reduces intragastric acidity.

Observational studies however suggest an association between gastric acid suppression and adverse events, making pharmacologic management of GER unjustified.

Even though data is still limited, thickeners have been associated with NEC and should therefore be avoided.

Dutta S, Singh B, Chessell L, Wilson J, Janes M, McDonald K, Shahid S, Gardner VA, Hjartarson A, Purcha M, Watson J, de Boer C, Gaal B, Fusch C. Guidelines for Feeding Very Low Birth Weight Infants. Nutrients. 2015 Jan 8;7(1):423-42.

Transition from gavage feeding to breastfeeding

Non-nutritive sucking (mother pumps first and then places the baby to the breast) can be attempted as soon as the baby is extubated and stable with success noted as early as 28 weeks corrected gestational age. Most premature infants can begin nutritive sucking at about 32 weeks gestation (Underwood MA, 2013).

Positioning that supports the mother's breast and the baby's head and neck are essential, with the cross-cradle and football holds being most effective. Early use of nipple shields increases milk intake and duration of breastfeeding (Underwood MA, 2013).

The indicated duration of exclusive breastfeeding is 6 months supplemented with 1 mg vitamin K given intramuscularly at birth, 400 IU vitamin D per day started in the first days of life, and 2 - 3 mg/kg iron per day starting between 2 and 8 weeks after birth (Abrams SA, 2013; Barros FC, 2010; Edmond K, 2006).

It is recognised, however, that in some specific clinical situations it may be necessary to introduce complementary feeding at 4 months for promoting optimal growth according to the new Preterm Postnatal Growth Standards (EFSA, 2009).

Abrams SA, Committee on Nutrition. Calcium and vitamin d requirements of enterally fed preterm infants. Pediatrics. 2013 May;131(5):e1676-1683.
Barros FC, Bhutta ZA, Batra M, Hansen TN, Victora CG, Rubens CE. Global report on preterm birth and stillbirth (3 of 7): evidence for effectiveness of interventions. BMC Pregnancy and Childbirth. 2010;10(1):S3.
Edmond K, Bahl R. Optimal feeding of low-birth-weight infants: technical review. World Health Organisation, 2006. pp 1–121.
EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA). Scientific Opinion on the appropriate age for introduction of complementary feeding of infants: Opinion on complementary feeding of infants. EFSA Journal. 2009 Dec;7(12):1423.
Underwood MA. Human milk for the premature infant. Pediatr Clin North Am. 2013 Feb;60(1):189-207.

Breastfeeding for the preterm infant

Breastfeeding is synchronized by the central nervous system characterized by oscillation of the infant's mandible, rhythmic motility of the tongue, and the breast milk ejection reflex that drives maternal milk toward the nipple outlet that needs to be coordinated with breathing (Elad D, 2014).

Sucking is accomplished by subatmospheric pressures created and not by mouthing the nipple–areola complex, to induce a peristaltic-like extraction mechanism as previously thought (Elad D, 2014).

Evidence of early components of sucking have been demonstrated from about seven to eight weeks' postconceptual age. Oral and gag reflexes appear at about 12 to 16 weeks and sucking at 15 to 18 weeks' gestation (Foster JP, 2016).

A suck-swallow-breathe cycle may be present at 28 weeks, but it needs to be accompanied by the physiological stability to maintain this cycle so as to prevent variable oxygenation, irregular breathing sequence and poor digestion. The smooth integration of sucking, swallowing and breathing during nutritive feeding may not be fully developed until 32 to 34 weeks' gestation (Foster JP, 2016).

Elad D, Kozlovsky P, Blum O, Laine AF, Po MJ, Botzer E, Dollberg S, Zelicovich M, Sira LB. Biomechanics of milk extraction during breast-feeding. PNAS. 2014 Aug 4;111(14):5230-5.

Foster JP, Psaila K, Patterson T. Non-nutritive sucking for increasing physiologic stability and nutrition in preterm infants. In: The Cochrane Collaboration, ed. Cochrane Database of Systematic Reviews. Chichester, UK: John Wiley & Sons, Ltd; 2016 Oct 4.

Breastfeeding effects

Click on the image to watch the video.

Bonventure MA, Neema L. Breastfeeding effects: mother and baby. In: Solomon K, Mark O, Dorcas K, Winnie L, editors. Breastfeeding. Nairobi: The Health Channel; 2017. p. 02:26. Available from: https://www.youtube.com/watch?v=qJpmOEyVZcc

Special considerations

Small for gestational age (SGA) babies

Once it is confirmed that the abdominal examination is normal, start feeding within 24 hours of life. Feeds should by all means be human milk and volumes should be started at the lowest end of the range and increased slowly in the first 10 days among preterm SGA babies with gestation <29 weeks and Absent/Reversed End Diastolic Umbilical Flow (AREDF).

Babies on non-invasive ventilation

Non-invasive ventilation can cause gaseous abdominal distension making reliance on abdominal distension an unreliable indicator of feed intolerance. On the other hand, nasal continuous positive airway pressure (nCPAP) decreases pre-and post-prandial intestinal blood flow in preterm infants. Based on these two facts, it is recommended to increase feeds cautiously.

Dutta S, Singh B, Chessell L, Wilson J, Janes M, McDonald K, Shahid S, Gardner VA, Hjartarson A, Purcha M, Watson J, de Boer C, Gaal B, Fusch C. Guidelines for Feeding Very Low Birth Weight Infants. Nutrients. 2015 Jan 8;7(1):423-42.

Special considerations (cont'd)

Babies on indomethacin or ibuprofen

Indomethacin and Ibuprofen have been used in facilitating closure of patent ductus arteriosus. Ibuprofen is safer than indomethacin as it does not reduce mesenteric blood flow. In a meta-analysis of 19 studies, NEC rates were lower in the Ibuprofen group.

Findings from the Ductus Arteriosus Feed or Fast with Indomethacin or Ibuprofen (DAFFII) trial suggest that trophic feeding promises fewer days in reaching maximum volumes.

Therefore, if the neonate is already on minimal feeds, continue to give trophic feeds until the indomethacin course finishes. If the neonate is fasting, introduce trophic feeds with human milk.

Dutta S, Singh B, Chessell L, Wilson J, Janes M, McDonald K, Shahid S, Gardner VA, Hjartarson A, Purcha M, Watson J, de Boer C, Gaal B, Fusch C. Guidelines for Feeding Very Low Birth Weight Infants. Nutrients. 2015 Jan 8;7(1):423-42.

HIV infection

Maternal HIV infection is a risk factor for preterm birth and risks associated with prematurity such as NEC. Human breast milk is generally protective against NEC compared to formula, believed to be due to presence of human milk oligosaccharides (HMOs), absent in formula (Van Niekerk E, 2014).

Whereas many structurally-distinct HMOs exist, their concentration in breast milk varies from one lactating mother to another, within the course of lactation, between HIV-infected and HIV-uninfected mothers, and with gestation.

While Bode and colleagues (2012) demonstrated that higher proportions of 3′-sialyllactose (3′-SL) were significantly associated with a lower CD4 cell count and a higher plasma viral load in the mother (theoretically increasing chances of mother-to-child transmission of HIV), a higher total HMO concentration in general (and especially non 3'-SL HMOs) above median was significantly associated with a reduced risk of postpartum transmission after adjustment for the maternal CD4 cell count and breast-milk HIV RNA viral load.

On the other hand, higher concentrations of disialyllacto-N-tetraose (DSLNT) are thought to be protective against NEC (Van Niekerk E, 2014).

Bode L, Kuhn L, Kim HY, Hsiao L, Nissan C, Sinkala M, et al. Human milk oligosaccharide concentration and risk of postnatal transmission of HIV through breastfeeding. Am J Clin Nutr. 2012;96(4):831-9. Epub 2012/08/15. doi: 10.3945/ajcn.112.039503.
Van Niekerk E, Autran CA, Nel DG, Kirsten GF, Blaauw R, Bode L. Human milk oligosaccharides differ between HIV-infected and HIV-uninfected mothers and are related to necrotizing enterocolitis incidence in their preterm very-low-birth-weight infants. J Nutr. 2014;144(8):1227-33. Epub 2014/06/11. doi: 10.3945/jn.113.187799.

Medication and substance abuse

Medication Use

Maternal antidepressant use has been associated with preterm labor, neonatal seizures, and neonatal primary pulmonary hypertension. Lactating mothers should avoid fluoxetine, doxepine and nefazodone (Underwood MA, 2013).

Substance abuse

Substance abuse by the mother other than opiates may be associated with untoward consequences to the rapidly developing central nervous system of the premature infant and mothers should refrain from providing milk for their infants (or donating) until they are free of the abused drugs (Underwood MA, 2013).

Underwood MA. Human milk for the premature infant. Pediatr Clin North Am. 2013 Feb;60(1):189-207.

Improving breastfeeding amongst preterm babies

Premature delivery is stressful to the mother and any form of stress impedes milk production. Therefore, counselling and education on importance of breastfeeding should be started during pregnancy.

Frequency of pumping increases milk production and this should be started soon after delivery, within 6-12 hours. Skin-to-skin contact between mother and baby also improves breastfeeding. Skin-to-skin care begun as soon as the baby is stable improves hemodynamic stability without increasing energy expenditure (see kangaroo mother care).

Given the benefits of hindmilk as seen above, which has higher viscosity and may be therefore more difficult to express with an electric pump, the combination of hand expression and electric pumping has been shown to increase milk production and fat content of expressed milk.

Proper nutritional and dietary support to the mother, adequate sleep and rest are also important remedies in improving milk production.

Underwood MA. Human milk for the premature infant. Pediatr Clin North Am. 2013 Feb;60(1):189-207.

Improving breastfeeding amongst preterm babies

“Nothing makes milk better than a baby..”

Click on the image to watch the video.

Morton J. Maximizing milk production with hands-on pumping. Breastfeeding. Available from: http://med.stanford.edu/newborns/professional-education/breastfeeding/maximizing-milk-production.html

Improving breastfeeding amongst preterm babies

Galactagogues

There have been few controlled trials examining the effect of medications on milk production amongst mothers of preterm infants who experience a decrease in expressed breast milk (EBM).

In a Cochrane review domperidone (10mg three times a day for 7 or 14 days) was shown to improve EBM volume in the short term. It should be noted that included studies examined domperidone use after 14 days post-delivery (Donovan TJ, 2012).

Metoclopramide use is not recommended because of its association with tardive dyskinesia (Underwood MA, 2013).

Donovan TJ, Buchanan K. Medications for increasing milk supply in mothers expressing breastmilk for their preterm hospitalised infants. In: The Cochrane Collaboration, ed. Cochrane Database of Systematic Reviews. Chichester, UK: John Wiley & Sons, Ltd; 2012 Mar 14.
Underwood MA. Human milk for the premature infant. Pediatr Clin North Am. 2013 Feb;60(1):189-207.

Improving breastfeeding amongst preterm babies

Herbal galactagogues

Fenugreek is reported to increase milk supply within 24 to 72 hours in most women with two small, randomized, blinded, placebo-controlled trials giving conflicting results. The first showed no difference in milk supply in women receiving capsules of fenugreek compared with the reference group while in the second milk supply almost doubled in women receiving tea containing fenugreek, fennel, raspberry leaf, and goat's rue compared with a placebo tea.

Maternal side effects of fenugreek include nausea, diarrhea, and exacerbation of asthma. It also imparts a maple syrup odor to sweat and urine and should not be used by mothers allergic to chickpeas, soybeans, or peanuts

Milk thistle has been demonstrated in a placebo-controlled trial to almost double milk production with no change in nutrient content of the milk or detectable levels of the active ingredient. Side effects seem to be rare and include nausea, diarrhea, and anaphylaxis.

Shatavari: Two randomized, placebo-controlled, blinded studies have yielded mixed results, with one study demonstrating increased maternal prolactin levels and increased infant weight gain and the other showing no benefit. Side effects include runny nose, conjunctivitis, and contact dermatitis.

Underwood MA. Human milk for the premature infant. Pediatr Clin North Am. 2013 Feb;60(1):189-207.

You have completed the module Feeding recommendations for the routine care of preterm infants and you should now be able to:

- Understand the pathophysiology of breastfeeding and its effects.
- Know the physiological differences between amniotic fluid, premature human milk, and term human milk.
- Know the choices of milk available for preterm feeding.
- Know the benefits of human breast milk and the challenges of providing it to preterm infants.
- Describe the different feeding methods for preterm infants.
- Assess feed intolerance and manage residual feeds in preterm infants.
- Know the diagnosis and treatment of gastro-esophageal reflux in preterm infants.
- Describe gavage feeding.
- Describe the transition from tube feeding to breastfeeding in preterm infants.
- Know the methods by which breastmilk production can be improved in mothers of preterm infants.

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