Quality Improvement Toolkit: Improving Neonatal Nutrition

Adapted for IL-PQC from Vermont Oxford NICQ 2009

OVERVIEW

This Quality Improvement Kit is designed to provide your IL-PQC quality improvement team with readymade material that you can use to initiate improvement efforts.

This Quality Improvement Kit is based on a set of clinical practices that have the potential to improve the outcomes of neonatal care, known as Potentially Better Practices (PBP’s).

They are labeled ‘potentially better’ rather than ‘better’ or ‘best’ because until the practices are evaluated, customized, and tested in your own NICU, you will not know whether are truly ‘better’ or ‘best’ (or ‘worse’). Depending on the particular circumstances in your unit, you may have to implement other practices or modify existing ones in order to successfully improve neonatal outcomes in your unit.

The PBP’s in this collection are not necessarily the only ones required to achieve the improved outcomes you are targeting. Thus this list of PBP’s is not exhaustive, exclusive, or all-inclusive. Changes in practice, guided by these PBPs, will require testing and adaptation to your particular circumstances and context in order to achieve measured improvements in outcomes.

As you test and implement these PBP’s you should monitor the results closely to ensure that you are obtaining the desired results, that no harm is being done, and that no unanticipated results are seen. In addition to the suggested measures, you should track some balancing measures.
Your team can implement as many of the PBP’s in this Kit as you wish, based on an assessment of your unit’s priorities, and based on availability of resources, time, and individuals with quality improvement skills.
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PBP #1: Consistent, comprehensive, multidisciplinary monitoring of
nutritional status, outcomes and practice is an integral component of improving nutrition outcomes in the neonatal population.

Rationale: Nutritional management of the VLBW is marked by a lack of uniformity. This heterogeneity of practice applies to every aspect of nutritional management and persists from the first few hours of life all the way to the time of hospital discharge and beyond. Although the diversity of practice is greatest between nurseries, for instance see reports from Boston, (Olson 2002) and North Carolina (Porcelli 2004), it often exists between individual neonatologists within the same institution (Ziegler 2002). “Diversity of practice thrives where there is uncertainty” (Ziegler 2002). Although there is general agreement regarding the concept that nutrition should support "postnatal growth that approximates the in utero growth of a normal fetus" (AAP 1985, AAP Committee on Nutrition 1998), and estimates of amounts of nutrients needed to achieve that model of growth, there is far less agreement, and much more uncertainty, about the details of how to provide those nutrients.

We urge a decrease in practice diversity for three reasons, not withstanding the current state of uncertainty surrounding so many current practices. First, consistent practice makes for perfectible practice. This notion is at the heart of the randomized control trial (RCT) technique, an exercise in which trialists attempt to control as many practice process variables as possible. Indeed there is even evidence that control groups do better than those not enrolled in RCTs (Schmidt 1999, Braunholtz 2001). Second, more intense process control, such as experienced by patients being treated with “algorithms” or “guidelines,” is consistently associated with significant improvements in adherence to care guidelines and often with better disease control (Ofman 2004). Third, the quality improvement (QI) literature demonstrates the effectiveness of continuing cycles of planning a process, implementing it consistently, studying its use and effectiveness and then acting on ones' conclusions (Horbar 2003). The efficacy of the QI approach is illustrated by reports on improving neonatal nutritional practices in particular (Kuzma-O'Reilly 2003, Bloom 2003) and practices in general (Galvin 2003). The “measure to improve" paradigm is buttressed by both data and theory and leads to pragmatic steps that improve performance (Galvin 2003)

Implementation Strategies:
- Infant weight should be monitored at least daily while on parenteral nutrition or advancing enteral feedings. After full enteral feedings have been established and the infant is otherwise stable, weight can be monitored less frequently, but plotted at least weekly, and plotted against standard preterm growth curves (Anderson 2002, Kuzma-O'Reilly 2003, Schanler, 2003). Standard growth curves are Ehrenkranz, and the website version of it (http://neonatal.rti.org/) (Ehrenkranz 1999, Pauls 1998, Wright 1993)
- Infant length and head circumference should be measured weekly (Anderson 2002, Kuzma-O'Reilly 2003, Schanler 2003, Ehrenkranz 1999)
- Infant biochemical parameters should be monitored frequently in infants on parenteral nutrition Expert opinion suggests that once full enteral feeding is
achieved, biochemical monitoring should be done weekly for 2 weeks, then every other week

- Mothers’ milk production should be monitored. Mothers should be assisted in maintaining a full milk supply, even though the infant may be consuming only a small amount of the milk produced. Adequacy of milk supply is a key factor in transitioning to breastfeeding. RN and LC to check with mom periodically and assist her to keep a breastmilk log (Furman 2002, Wooldridge 2003, Meier 2003)

- Every NICU that cares for VLBW infants should have a Neonatal Nutritionist as part of the team to monitor infant growth and outcomes, calculate and relate parenteral nutrition and enteral intakes to current growth and medical conditions, suggest improvements in nutritional management, manage the formulary of premature infant feedings and supplements, and make nutritional plans with goals and resource referral information at discharge (Kuzma-O’Reilly 2003, Valentine1993, Elsaesser 1988, Rubin 1997, Anderson 2002, Olsen 2004).

**Barriers:**
- Large current variation in practice
- Cost associated with registered dietician and lactation consultation
- Systems to support daily calculation and trending

**Measurement:**
- Growth charts on every VLBW infant chart
- Documented assessments by registered dieticians
- Health care provider variation
- Use of established monitoring protocols with nutritional goals
- Consistent appraisal of mother’s milk supply (pumping log, discussion on rounds)
- Rate of conversion of AGA infants at birth to SGA infants at discharge (i.e. B Wt/EGA vs Discharge Wt/CGA)
II. PARENTERAL NUTRITION

OVERVIEW

The development of sophisticated techniques for providing short- and long-term parenteral nutrition to critically ill infants has been one of the major advances in neonatology of the last several decades. However, there is still a wide variation in practice between nurseries, and even within nurseries, in how and when parenteral nutrition is started in VLBW infants. This document will review the current literature on initiation of parenteral nutrition in VLBW infants, recommend evidence-based best practices in this area, and discuss some of the barriers (as well as ways to overcome them) to implementing these best practices. There are several recent excellent reviews of neonatal nutrition, including information on early parenteral nutrition (Perreira 1995, Hay 1999, Thureen 2000, Thureen 2001, Pinchasik 2001, Ziegler 2002, Yeung 2003, ASPEN 2002). In addition, the latest version of Polin and Fox’s Fetal and Neonatal Physiology contains several very detailed chapters on protein requirements for the fetus and preterm newborn (Matthews 2004, Hay 2004, Heird 2004).

At birth, a VLBW infant is abruptly disconnected from the ideal source of parenteral nutrition - the placenta. If the goal of postnatal nutrition in the VLBW infant is to mimic in utero nutrition, as recommended by the AAP, then the VLBW infant should be immediately placed on balanced parenteral nutrition, including sugar, protein, lipids, trace elements, and vitamins. It is clear that current parenteral nutrition does not entirely mimic in utero nutrition and is not without some undesired side effects. It is also clear that the preterm infant is in many ways a fundamentally different organism than an infant of the same gestation who is still in utero. Thus, decisions about how and when to implement parenteral nutrition in the VLBW infant are really best estimates, based on incomplete information and utilizing a still-evolving technology. Despite these limitations, there is no reason to believe there are advantages to under-nourishing the VLBW infant.

Parenteral nutrition used to be delayed for several days, however, by the late 1980s it was clear that earlier institution of parenteral nutrition was associated with improved growth and outcome (Georgieff 1989). Since the late 1980s, there has been a gradual shift in most US nurseries toward beginning total parenteral nutrition within the first day or two.

There is considerable evidence that nutritional status early in gestation and in post-natal life affects health status throughout life. The fact that infants who are small at birth appear to be more at risk for subsequent diabetes and cardiovascular disease suggests that the fetal adaptation to limited nutrition has long term end-organ consequences (Barker 1993). Presumably, post-natal under-nutrition (or over-nutrition) could cause similar significant long-lasting effects.

PBP #1: Begin amino acids as part of balanced parenteral nutrition, within the first 24 hours of life. The amount of amino acids administered can be as high as 3.5 g/kg/d on the first day of life. Adequate non-protein calories (80-100 kcal/kg/d) and amino acids (3.0-4.0 g/kg/d) should be administered as soon as possible, preferably no later than 5-7 days of age.

Rationale: Despite what most clinicians consider “aggressive” nutritional support, postnatal growth of VLBW infants is usually significantly less than in-utero growth rates.
While 60-80 kcal/kg/d is probably adequate to support the basal metabolic needs of the VLBW infant, a minimum of 90 non-protein kcal/kg/d is a more realistic estimate of what is required to achieve growth (Dusick 2003). Similarly, approximately 3.0-4.0 g/kg/d of protein is required to achieve adequate growth in the VLBW infant. Other reviewers have concluded that even higher caloric intake (125-130 kcal/kg/d and 3.5-4 g/kg/d of protein) is required to achieve normal growth (Denne 2001).

In a recent review of the growth pattern of all surviving infants with birth weight less than 1300 g, Carlson showed that despite an average of 75 kcal/kg/d and 1.9 g/kg/d protein in the first two weeks of life, with subsequent increases in both total calories and protein, growth was less than the in utero rate (Carlson 1998). In a similar study from the UK, 105 infants less than 1750 g at birth developed a significant calorie and protein deficit, despite aggressive attempts to meet recommended nutritional intake (Embleton 2001). It appears that most VLBW infants in ICNs are not achieving desired growth (Olsen 2002). Unfortunately, for many VLBW infants the initial calorie and protein deficit is never entirely corrected, and infants remain below their ideal growth curves long after hospital discharge (Ernst 2003). Data from the NICHD Neonatal Research Network suggests that by 36 weeks corrected age, nearly 90% of VLBW infants have growth failure, and that this growth failure persists into early childhood in a significant proportion of these infants (Dusick 2003).

Berry analyzed the course of 109 AGA infants who weighed less than 1000 g at birth to determine the factors that influenced their growth. Not surprisingly, better caloric and protein intake early in their course were associated with better growth (Berry 1997). Pauls recently published growth curves for infants born at less than 1000 g who were started on combined enteral and parenteral nutrition on day one, and rapidly advanced to 92 kcal/kg/d within the first week of life, and suggested that these are more appropriate growth curves to use for VLBW infants than the older published growth curves (Pauls 1998). Increasing the early nutritional status of infants can improve their growth curves without any adverse effects on their clinical course (Wilson 1997).

It is clear that early and “aggressive” use of parenteral nutrition containing amino acids is well tolerated and improves growth. Fifteen years ago, Saini showed that sick infants who were started on parenteral amino acids in the first day of life had better protein intake, energy intake, and nitrogen retention than infants who were not started on amino acids until 72 hours of age (Saini 1989). In a recent study, Thureen randomized 28 infants with a mean birth weight 946 g to either 1 or 3 g/kg/d of amino acids, starting at approximately 48 hrs of age. She was able to show a difference in protein balance after only 12 hours of amino acid administration, with more protein synthesis occurring in the 3 g/kg/d group. There was no evidence of toxicity in the high amino acid group (Thureen 2003). Ibrahim recently published a randomized trial in which ventilator dependent preterm infants were randomized to begin early total parenteral nutrition, including 3.5 g/kg/d of amino acids and 3 g/kg/d of 20% Intralipid® within one hour of birth, vs later parenteral nutrition. Infants in the early parenteral nutrition group had better energy and nitrogen balance with no adverse clinical or laboratory effects (Ibrahim 2004). Looking at even higher amino acid doses, Porcelli randomized VLBW infants to receive a maximum of 3 vs 4 g/kg/d amino acids. The high amino acid group reached a mean of 3.3 g/kg/d by the end of week one, and a mean of 3.8 g/kg/d by the end of week two. They tolerated the high dose amino acids well, with no evidence of
acidosis and only a minimal increase in BUN. The high dose amino acid group had better growth from week one (Porcelli 2002). Amino acid intake is not correlated with BUN concentration in the first days of life (Ridout 2005). Ideally, the total non-protein calories and the amount of amino acid infused will be matched, so that the amino acids can be used for protein deposition, rather than as an energy source. The ideal ratio has been estimated as 24-32 non-protein calories per g of protein infused (Kerner 2003). However, there is evidence that the fetus can effectively utilize amino acids as an energy source, so there is probably little downside in administering maximum amino acid amounts, even to the infant who is receiving slightly sub-optimal calories (Ziegler 2002). The concept of total nutritional deficit is a useful one which has not yet made its way into most US nurseries, but is a simple and powerful tool for evaluating how far behind nutritional goals an infant has fallen. To calculate nutritional debt for calories or protein, total the amount of calories or protein the infant has received, and subtract that from the amount of calories or protein the infant would have received under ideal circumstances. (Embleton 2001, Dusick 2003). However, the “gold standard” of adequate protein and calorie nutrition is appropriate growth, rather than arbitrary amounts of protein and/or calorie amounts delivered. A simple way to think of this is that VLBW infants, once growing, increase their body weight by 2% a day (Ziegler 2002).

Implementation Strategies:
- Standardized policies and admission order sets which include balanced parenteral nutrition as the “maintenance” fluid
- Availability of “pre-mixed” amino-acid (Beecroft 1999) containing parenteral nutrition solutions in hospital pharmacy

Barriers:
- Perception that early amino acid administration is of no benefit
- Perception that early amino acid administration is potentially toxic
- Perception that early amino acid administration is more expensive than glucose and electrolyte-containing fluids
- Lack of pharmacy resources
- Pharmacy policies regarding limited timeframe of ordering parenteral nutrition

Measurement:
- Measure provider consistency in implementation
- % of VLBW infants started on amino acids at admission
- % of VLBW infants on amino acids by 24 hours of age
- % of VLBW infants receiving 3-4 g/kg/d parenteral protein by 72 hours of age
- % of VLBW infants receiving 80-100 non-protein kcal/kg/d by 5 days of age
PBP #2: Start Intralipid® at 0.5 –1.0 g/kg/day within the first 24 hours of life (adequate to avoid fatty acid deficiency) and advance over the first week. Achievement of optimal Intralipid® administration, 3.0 - 3.5 g/kg/day, may be limited by hyperglycemia and hypertriglyceridemia.

Rationale: The role of lipids in early nutrition is particularly complex, largely because of the complex interactions of lipids and disease states. However, there is fairly convincing evidence that early lipids are well tolerated, and that delaying the introduction of lipids has adverse consequences. Specifically, the Aspen study showed that administering .0.5 gms/kg/day Intralipid® is necessary to prevent essential fatty acid deficiency (ASPEN 2002, Lee 1993). Lipid administration should advance to 3.0 - 3.5 gm/kg/day (ASPEN 2002, Kerner 2003, Putet 2000, AAP 2004).

Lipids and brain development: Both arachadonic acid and docosahexaenoic acid are essential components of brain structure, and animal studies have shown that early essential fatty acid deficiency has long term adverse effects on brain development (Crawford 1993). The ability to synthesize arachadonic acid and docosahexaenoic acid from linoleic acid is decreased in preterm infants (Decsi 1994). Given the high rate of long-term CNS abnormalities in the smallest of preterm infants, one wonders about the advisability of delaying the introduction of lipids in these infants.

Lipids and glucose: Infants receiving lipids in addition to parenteral glucose, with or without amino acids, have higher serum glucose levels than infants who are not receiving lipids (Savich 1988). This suggests there may be advantages to delaying the introduction of lipids in infants where hyperglycemia is a significant problem. In contrast, there are data that suggest parenteral lipids play an important role in supporting neonatal gluconeogenesis (Sunehag 2003).

Lipids and bilirubin displacement: A recent Cochrane database review failed to find any relationship between early parenteral nutrition and jaundice (Farber 2003).

Lipids and free-radical issues: The lipids which make up Intralipid® can easily undergo peroxidation to form hydroperoxides, potentially damaging substances which might alter arachidonic acid metabolism and/or form free radicals (Helbock 1993). However, whether these hypdroperoxides are of any clinical consequence is unknown. In contrast, Tomsits’ data suggests that VLBW infants who are not given lipids during the first week of life develop essential fatty acid deficiency, a condition which when combined with Vitamin E deficiency, leads to increased free radical formation (Tomsits 2000). Multivitamins given together with Intralipid® (3-in-1) prevent lipid peroxidation and vitamin loss in the infusate (Silvers 2001). Light exposure has been associated with the formation of malondialdehyde (MDA) in light exposed lipids (Picaud 2004), but there is insufficient evidence to recommend for or against light shielding for parenteral nutrition or lipid during preparation or delivery to the patient.

Lipids and Nosocomial Infection: Of particular concern for protracted use of parenteral nutrition are the data which link Intralipid® administration to a significantly increased risk of coagulase negative Staphylococcus sepsis (Freeman 1990, Avila-Figueroa 1998).
Lipids and Chronic Lung Disease (CLD): Although there is some concern that early administration of lipids might increase the risk of CLD, clinical trials have not supported this. In a trial, which randomized 129 infants who weighed less than 1750 g to early vs late parenteral nutrition with lipids, there was no difference in the incidence of BPD (Brownlee 1993). Another small trial randomized VLBW infants to initiation of Intralipid® at 5 vs 14 days of age and failed to show any difference in the risk of CLD (Alwaidh 1996).

The most concerning data about the potential adverse side effects of early lipids comes from a study designed to determine whether early administration of Intralipid® decreased the incidence of CLD. In this study, 133 infants weighing between 600 and 1000 g at birth were randomized to receive lipids starting within the first 12 hours of life vs no lipids for the first 7 days. Overall, there was no difference in the mortality rate or incidence of BPD between the two groups. However, sub-group analysis showed that for infants with birth weight 600-800 g, infants receiving early lipids were more likely to have pulmonary hemorrhage and had a higher mortality rate than the control infants. Whether this was related to lipid administration, or was a statistical anomaly in this group is unclear. Somewhat reassuring is the fact that there were no differences in the 800-1000 g sub-group (Sosenko 1993).

In contrast to the theoretical concerns about the possibility of lipids contributing to CLD, there is good evidence that under-nutrition can worsen the condition of the infant with CLD (Frank 1988). There is also intriguing animal evidence that maternal undernutrition decreases lung surfactant lipid content in the early neonatal period. Whether this indicates that early post-natal lipid deprivation could interfere with surfactant lipid formation is unknown (Chen 2004).

Lipids and pulmonary hypertension: When intravenous lipids were first introduced into adult critical care units, there were a number of publications showing an association between lipid administration and hypoxia. Similar results were also reported in neonates (Pereira 1980). Based primarily on animal data, it appears that the rapid administration of a large dose of lipid led to a significant increase in pulmonary vascular resistance. Presumably, the prostinoid precursors in the Intralipid® led to a thromboxane-mediated constriction of the pulmonary vascular bed. However, this effect has been seen only with rapid administration of large doses of lipid (Hammerman 1988). It is probably not a clinically significant problem in neonates who are given the usual dose of Intralipid® over 24 hours. In a clinical trial in which critically ill VLBW infants were randomized to receive 1 g/kg/d of Intralipid® on day one and increasing to 3 g/kg/d by day four, or to receive no lipid until day eight, there were no differences in oxygenation or in any other marker of lipid toxicity (Gilbertson 1991).

Recent clinical trials: In their recent study of very early parenteral nutrition (3.5 g/kg/d amino acids and 3 g/kg/d of Intralipid® starting in the first hour of life) Ibrahim found no evidence of hyperlipidemia or other adverse effect of the early aggressive lipid administration (Ibrahim 2004). Similarly, in Thureen’s study of early aggressive amino acid administration, infants were started on Intralipid® at 1 g/kg/d within 48 hrs of life and appeared to tolerate this dose well (Thureen 2003).
Implementation Strategies:
- Standardized policies and admission order sets which include Intralipid® administration starting within the first 24 hours of life
- Consideration of a combined amino acid and lipid solution, also known as “3-in-1” or “Total Nutrition Admixture (TNA) solutions to simplify administration issues

Barriers:
- Perception that early lipid administration is of no benefit
- Perception that early lipid administration is potentially toxic

Measurement:
- Measure provider consistency in implementation
- % of VLBW infants receiving lipids by 24 hours of age

PBP #3: Nutritional assessment of all VLBW infants should include daily calculations of energy and nutrient intake. In addition, weight should be followed frequently enough to monitor growth.

Rationale: Multiple studies have shown that, in most centers, VLBW infants receive significantly less protein and fewer calories than ideal. Monitoring of intake should be structured so that day-by-day evaluation of nutritional adequacy is possible. Given the high risk of post-natal growth failure among VLBW infants, maintaining adequate growth should take precedence over merely reaching some theoretical target of protein or energy intake.

Implementation:
- Readily accessible growth curves, including both weight and head circumference
- Readily accessible flow charts which display fluid intake, glucose intake (g/kg/d), protein intake (g/kg/d), fat intake (g/kg/d), and caloric intake (kcal/kg/d)
- Encourage parents to become involved in charting growth parameters

Barriers:
- Perception that nutritional status can be adequately managed on a day-by-day basis without looking at trending data
- Lack of standardized flow-sheets or charting tools
- Lack of personnel for doing accurate daily calculations

Measurement:
- % of charts that contain routine nutritional assessment
PBP #4: VLBW infants on parenteral nutrition should have routine monitoring of serum chemistries. This includes sodium, potassium, chloride, calcium, phosphorus, magnesium, direct bilirubin, BUN, creatinine, alkaline phosphatase, and triglycerides, at least weekly but more frequently with parenteral nutrition changes. Measurement of albumin and/or pre-albumin may also be useful.

Rationale: Infants on parenteral nutrition are usually premature and/or moderately ill, and are at risk of abnormalities in electrolyte and mineral balance. Prolonged parenteral nutrition predisposes infants to both cholestasis and osteopenia. While there are little data to support choices of the most cost efficient way to monitor the VLBW infant receiving parenteral nutrition, it seems prudent to follow electrolytes, hepatic function, renal function, triglyceride levels, bone metabolism, and a marker of protein synthesis on a regular basis (Kerner 2003, Schanler 2003, Valentine 2003). Serum albumin has a half-life of 18-20 days and can reflect the severity of malnutrition. Prealbumin has a shorter half-life (2 days) and is often used to monitor acute nutritional changes (Benjamin 1989).

Implementation Strategies:
- Standing orders for monitoring of patients on parenteral

Barriers:
- Perception that “ad hoc” monitoring is adequate

Measurement:
- % of infants receiving routine monitoring
- % of infants with “unacceptable” values
III.ESTABLISHING ENTERAL NUTRITION

PBP #1: Human milk should be used whenever possible as the enteral feeding of choice for VLBW infants.

Rationale: There are notable benefits of human milk for the VLBW infant and the corresponding risks of not using human milk. The objective of feeding during the early days of life is to stimulate gut hormone maturation, stimulate gut hormone release, and to induce gut motility. The preferred feeding is breast milk, preferably started on day 1 (Ziegler 2002, AAP 2005, Schanler 2003). A frequently encountered practical limitation is that lactogenesis II (milk “coming in”) does not occur for 2-5 days after birth. During that time, only small quantities of colostrum are available but are especially useful for the infant (“liquid gold”) and should be fed. Colostrum (the first milk) contains high concentrations of antimicrobial, anti-inflammatory and immunomodulating factors, and prepares the gut for the mature milk. (Goldman AS 1993; Akers 2002). In general, as milk protein decreases over time, human milk should be used in the order pumped for the first 2-3 weeks, then fresh milk as available (Ziegler 2002). Feedings should be started with full strength milks (Berseth 1992a, Koenig 1995). Routine culturing or heat treatment of mothers’ own milk has not been demonstrated to be necessary or cost-effective (AAP 2003). If mother’s own milk is not immediately available, the clinician should consider the use of pasteurized donor human milk (PDHM), which has most of the properties of fresh human milk (immunoglobulins, growth and developmental hormones, enzymes, anti-inflammatory factors, etc.), is sterile, and reduces NEC while improving feeding tolerance (Lucas 1990, Arnold 2004, Ziegler 2002).

When infant formulas must be used, premature formulas should be used instead of elemental formulas designed for full term infants, unless there is a compelling contraindication. A hydrolyzed protein preterm formula might be preferred, but this is only currently available in Europe (Mihatsch 2002).

Implementation Strategies:

- Create a supportive environment to maximize milk production in the early postpartum period
- Teach every mother hand expression and collection techniques to maximize colostrum availability
- Establish a relationship with the nearest milk bank and procedures for obtaining the milk quickly or maintaining a reserve supply

Barriers:

- Maternal disappointment over small expressed volumes
- Because other issues are perceived as higher priority, there may be a lack of appreciation of the importance of small volumes of colostrum,
• The desire to initiate trophic feeds regardless of breastmilk availability
• Difficulty with collection and labeling of small expressed volumes
• Mother’s own milk not always available
• Lack of knowledge regarding use of pasteurized donor human milk (PDHM):
• Lack of knowledge regarding use of premature formulas.
• Resistance to changing current practices.
• Lack of recognition of the role of pumping in the mothers’ recovery process

Measurement:
• Documentation of utilization of colostrum or breastmilk for the initial feeding
• Maternal education on manual expression, breast massage and colostrum collection
• Documentation of post-partum provider’s competency in helping mothers collect colostrum
• If colostrum or breastmilk is not available in the NICU, are there documented efforts to contact the mother before providing alternatives?
• Survey of NICU staff attitudes and knowledge regarding human milk and breastfeeding

PBP #2: Enteral feeds, in the form of trophic or minimal enteral feeds (also called GI priming), should be initiated within 1-2 days after birth, except when there are clear contraindications such as a congenital anomaly precluding feeding (e.g. omphalocele or gastroschisis), or evidence of GI dysfunction associated with hypoxic-ischemic compromise.

Rationale: The objective of feeding during the early days of life is to stimulate gut maturation, hormone release, and motility. Although it was never shown that prolonged withholding of feedings actually prevented necrotizing enterocolitis (NEC), some form of this strategy was widely adopted in the 1970s and 1980s. Starvation leads to atrophy of the gut (La Gamma 1994), so withholding feedings may actually render subsequently introduced feedings less safe (Ziegler 2002). Withholding of feedings was eventually reevaluated with a number of trials of early introduction of feedings (Heicher 1976, La Gamma 1985, Lucas 1986, Ostertag 1986, Dunn 1988, Slagle 1988, Berseth 1992b, Meetz 1992, Thureen 1999, Schanler 2003). A systematic review of the results of published trials (Tyson 1997) concluded that early introduction of feedings shortens the time to full feeds and to discharge and does not increase the incidence of NEC. A controlled study involving 100 LBW infants (McClure 2000) confirmed these findings and found, in addition, a significant reduction in serious infections with “early” introduction of feedings.

Another practice, implemented with the idea of detecting NEC earlier, was focusing particular attention on gastric residuals as a presumed manifestation of early NEC. However, in the first few days following birth, gastric residuals are extremely common and are rarely associated with NEC (Ziegler 1999, Mihatsch 2002, Moody 2000). The paradoxical motility, which is responsible for most of the residuals, transitions more
rapidly to a normal progressive pattern if feedings are started early and are persistently offered, than when feedings are withheld (Berseth 1993). A recent retrospective case control study of 51 VLBW infants and 102 matched controls found that the maximum residual in the previous 6 days, maximum residual as a percentage of a feed, and the total residuals as a percentage of feeds were all higher in the NEC group. Although these differences were statistically significant, there was much overlap of these variables with those of control infants, limiting the clinical utility of these observations (Cobb 2004).

Yet another strategy aimed at preventing NEC has been to slow the rate of feeding advancement. A retrospective analysis of 19 cases of NEC (Anderson 1991) found that infants who went on to develop NEC had feedings advanced more rapidly than in control infants; they advocated feedings not be advanced by more than 20 mL/kg/day. Rayyis, in a randomized controlled trial that compared increments of 15 mL/kg/d with 35 mL/kg/d, found that the infants who advanced faster achieved full feedings and weight gain sooner, and there was no difference in the incidence of NEC (Rayyis 1999). On the other hand, a recent study of prolonging minimal enteral feedings (20 mL/kg/d for 10 days) before advancement was closed early because of significantly increased NEC in the group who were started on 20 mL/kg/day and advanced to 140 mL/kg/d over the same 10 days (Berseth 2003). The prolonged use of small enteral feeds resulted, as expected, in greater need for central venous line placement and prolonged use of parenteral nutrition. The incidence of death was the same in both groups. Although the prolonged use of small enteral feeds reduced the risk for NEC, it did so by delaying the establishment of full feedings by 10 days and prolonged the hospital stay (Berseth 2003). The most recent randomized, controlled single center trial of intermediate rates of feeding advancement (20 mL/kg/d vs. 30 mL/kg/day) done in 1000-2000 gm, δ 35-week infants (Caple 2004) found no difference in NEC. The infants in the faster advancement group achieved full volume feedings sooner, regained birth weight faster and had fewer days of intravenous fluids. Approximately 30% of infants in both the intervention and control groups in this study received breastmilk. The day of life feedings were initiated was determined by the attending physician and was not specified in the paper, although < 1000 gm infants were excluded “because their feedings are often started many days after birth”. (Caple 2004) Whether protective against NEC or not, limiting feeding increments to 20 mL/kg/d still permits achievement of full feedings in a reasonable period of about 8 days (Ziegler 2002, Kennedy 2004).

Additional controversial areas are feeding infants who have umbilical artery catheters in place and/or who exhibit cardiovascular instability. Most infants in the GI priming studies were fed with umbilical artery catheters in place and the studies still noted a decreased incidence of NEC (Dunn 1988, Schanler 1999, Davey 1994). Although feeding an infant with a PDA is thought to be risky, a recent study of feedings during indomethacin therapy for a persistent ductus arteriosus found otherwise (Bellander 2003). Further research is needed to ascertain just how “unstable” an infant needs to be before feedings are withheld.

Use of diluted feeds has been suggested for premature infants. However, intestinal motility responses to feeds were elicited earlier and persisted longer following the use of
full-strength formula in comparison to 1/3 and 2/3 dilutions (Koenig 1995). Enteral water, although possibly useful in hypernatremic/hyperglycemic infants, does not affect intestinal motility when compared to milk (Berseth 1992a). In light of the current variations in feeding practice, paying close attention to feeding parameters with a standardized feeding regimen appears to significantly decrease NEC and improve nutrition (Kamitsuka 2000, Patole 2003). We recognize that studies of feeding rates and NEC may be difficult to compare due to the variation of populations studied, feeding used and baseline or control NEC rates.

**Implementation Strategies:**
- Enteral feeding policies should be available in each NICU specifying:
  - Early (day 1-2) initiation of feedings for most infants
  - Initiation of feedings with full strength human milk (preferred) or formula
  - Consider extending minimal enteral feedings in the presence of cardiorespiratory instability
  - Progressive advancement of feeding is dependent on clinical status and should be standardized as much as possible within each NICU
  - Definition of feeding intolerance
- Reasons for withholding feedings should be documented in the hospital chart/progress notes and discussed on rounds.

**Barriers:**
- Lack of staff information about the hazards of delayed feedings in VLBW infants
- Current practices/beliefs regarding contraindications of umbilical artery catheters and PDA
- Lack of consensus about physiology and definition of feeding intolerance
  - Lack of consistency across studies about content and advancement of feeds and relationship to outcomes

**Measurement:**
- Hour or day of life when trophic feeds initiated
- Day of life when feeding advancement begun
- Day of life when full enteral feeds achieved
- Day of life when birthweight regained
- Days of parenteral nutrition

**PBP #3: NICU’s should standardize their definition of feeding intolerance, with specific reference to acceptable residual volumes, changes in abdominal girth and the presence of heme-positive stools.**

**Rationale:** Enteral feedings of VLBW infants are frequently stopped, or feeding advances held, based on “feeding intolerance.” The definition of intolerance may include the presence and quality (normal, yellow, green, blood-tinged) of gastric residuals (See PBP #2, above), emesis, an increase in abdominal girth or...
abdominal tenderness, the presence of heme-positive or abnormal-appearing stools, the presence, absence or quality of bowel sounds, or any combination thereof. (Jadcherla 2002, Mihatsch 2002). As all of these phenomena may occur in a healthy premature infant tolerating feedings (Moody 2000) it is important to put these findings into a clinical context that is understood by nursing and physician staff. Failure to do so may lead to unnecessary limitation of enteral feeds and reliance on parental nutrition. In one study, when feeding intolerance was more clearly defined, nutritional outcomes were dramatically improved (Patole 2003).

Cobb demonstrated that maximum residuals in premature who get NEC were 40% of the feeding volume vs. 14% for those who didn’t, and residuals were noted to increase most dramatically in the 3 days preceding the onset of NEC (Cobb 2004). Given the variability of residuals upon initiation of feedings, it may be more appropriate to use significant increases in residual only as one part of the decision to limit feeding advancement. One should be cautious about using residuals as the sole reason to completely stop enteral feedings.

Kamitsuka, et al. showed that implementation of a consistent feeding schedule and standardized feeding evaluation alone reduced NEC and improved weight gain (Kamitsuka 2000).

**Implementation Strategies:**

- Key NICU team members should discuss and come to a conclusion on the definition of feeding intolerance
- Education for staff regarding the new definition, clinical context and potential practice changes

**Barriers:**

- Difficulty in coming to a consensus on definition
- Difficulty in understanding clinical context of phenomena in healthy vs sick infants

**Measurement:**

- Chart review of VLBW infants at risk for feeding intolerance:
  - Feeding stops and starts
  - Documentation of protein and caloric deficits associated with feeding interruption

**Best Practice # 4.** Enteral feeds should usually be given by intermittent bolus, rather than continuously, and by gastric, rather than transpyloric administration.

**Rationale:** VLBW infants are usually started on feedings before they are able to suck and swallow. Tube feeding is an essential tool in enteral nutrition. There are various methods of tube feeding including continuous, semi-continuous or intermittent bolus, and a number of approaches such as orogastric, nasogastric, transpyloric or gastrostomy.

Milk feedings given by intermittent bolus gavage method are thought to be more
physiologic because they promote the cyclical surges of gut hormones seen in normal term infants and adults (Aynsley 1982). Premature infants had more feeding intolerance (Scanler 1999, Dollberg 2000) and a slower rate of weight gain with continuous infusion when compared to the bolus technique (Schanler 1999). The Cochrane analysis, last updated June 2003, concluded that infants fed by the continuous tube method took longer to reach full feeds, but there was no significant difference in somatic growth, days to discharge, or the incidence of NEC (Premji 2004).

Occasionally, intolerance is seen in the bolus-fed preterm infant, with duodenal motility decreasing following the bolus feeding (DeVille 1993). A bolus feeding given over a longer time interval, such as 30-120 minutes, results in a return of motility and improved tolerance (Schanler 2003, Schanler 1999). In infants with gastrointestinal disease, continuous infusion has been associated with better nutrient absorption (Parker 1981).

Delivery of tube feedings into the stomach elicits the associated physiologic stimulation and digestive processes. Transpyloric feedings have the potential benefit of delivering feeds past the pylorus and gastroesophageal junction. Transpyloric (e.g. NJ) feeds must be continuous, which may account for decreased gastroesophageal reflux symptomatology. Transpyloric feedings are not recommended for routine use in preterm infants, as no benefit was found in a meta-analysis, and they are associated with a greater incidence of gastrointestinal disturbance and possibly death (McGuire 2004).

Implementation Strategies:
- NICU feeding policy specifying bolus, intra-gastric feeds
- Documentation of reason for variance in medical record and discussed on rounds

Barriers:
- Staff resistance to change current practice

Measurement:
- Chart audit of enteral feeding practices on 10 VLBW infants

PBP #5: Pumps delivering breastmilk should be oriented so that the syringe is vertically upright, and the tubing (smallest caliber and shortest possible length) should be positioned and cleared to prevent sequestration of fat. Rationale: Fats in breastmilk are of lower density than other components, and will therefore rise and separate. If a syringe is horizontal, fat may float to the top and therefore will be the last fluid emptied into the tubing, resulting in variable fat administration rates and causing some of the highest caloric feed to never reach the baby (Spencer 1981, Greer 1984, Narayanan 1984, Stocks 1985, Mehta 1988). As fortifiers may fall to the bottom of the feeding, the feeding syringe may need to be gently manipulated several times during a continuous or prolonged “bolus” feed to ensure all nutrients are received.
Implementation strategies:
- Education for MDs and RNs regarding the rationale and importance of the pump's position during breastmilk administration
- Policy and procedure regarding pump positioning

Barriers:
- Lack of equipment for pumps and syringes to be positioned on
- Resistance to change in practice

Measurement:
- Survey pump positioning after education/implementation

Best Practice #6: Enteral feeds should be advanced until they are providing adequate nutrition to sustain optimal growth (2% of body weight/day). For infants fed human milk this could mean as much as 170 - 200+ mL/kg/day.

Rationale: The goal of enteral feedings is to provide optimal nutrition and growth and eliminate the need for parenteral nutrition. The historic target for premature infants of 150 mL/kg/day of enteral feedings may be inadequate to overcome prior nitrogen deficits and establish optimal growth. A randomized trial of enteral feeding volumes (150 and 200 mL/kg/d) of infants born less than 30 weeks gestation, once they reached full enteral feeds, found that individual milk volume requirements for adequate weight gain without significant adverse effects varied between 150-200 mL/kg/d (Kusechel 2000). Increased milk intakes were associated with increased daily weight gains and a greater weight at 35 weeks, but no difference in any growth parameter at 1 year or difference in morbidity (Kuschel 2000). Ziegler suggests that feeding volume should be increased until the infant shows signs that GI capacity has been reached, then kept at that volume through daily adjustment of the feeding volume (Ziegler 2002). Restricting feeding volume until a weight plateau has been identified is the most common cause of growth delay (Hay 1999). It has been suggested that fortified human milk must be fed at approximately 180 mL/kg/d if ELBW infants are to achieve adequate growth, nutrient retention, and biochemical indices of nutritional status (Hay 1999). Multifactor supplementation may be required to meet nutritional goals, especially if feeding volume must be restricted for some reason (e.g. pulmonary disease)

Implementation Strategies:
- Daily monitoring of feeding volumes
- Automate calculations of feeding volumes and calories

Barriers:
- Reluctance to go above previous recommendations of 150 mL/kg/d
- Effort to calculate feeding volumes
- Reliance on feedings by the clock rather than relying on early infant clues (i.e., fussiness or excessive pacifier use)
**IV. SUSTAINING ENTERAL NUTRITION AND BREASTFEEDING THROUGH DISCHARGE AND BEYOND**

**PBP #1: Mothers’ milk supply should be maintained and the milk handled safely and appropriately.**

**Rationale:** The single most important factor determining the exclusivity and duration of breastfeeding for the mother-infant dyad is the volume of milk produced which typically plateaus by 1-2 weeks postpartum (Neville 2001). The average baseline milk production on days 6-7 postpartum is highly predictive of adequacy of milk volume (defined as ≥ 500 mL/d) at 6 weeks post-partum (Hill 2005). Mothers of preterm infants were 2.8 times more at risk of not producing adequate milk than term mothers who were fully breastfeeding. Although a better comparison group would have been mothers of fullterm infants who were exclusively pumping and not breastfeeding, it is not clear to what extent, if any, preterm birth contributes to limitation of milk supply in mothers of VLBW infants. Lactogenesis I (the hormonal preparation and growth of breast tissue) starts during pregnancy (Neville 2001). Some experts suggest that the mother of an extremely preterm infant may be at a disadvantage regarding milk production as she has not had the full time for breast growth and development. Also, Lactogenesis II may be delayed in mothers of very preterm infants (Cregan 2002, Henderson 2004). Early, frequent, and effective breastfeeding or pumping appears to be the most important factor in establishing normal lactation (Furman 2002, Smith 2003, Wooldridge 2003). Prolactin bursts associated with the infant suckling or the mother breast pumping support the continued growth of secretory tissue in the maternal breast for several weeks or months after birth (Cox 1999). Initiating early pumping (within the first day) is associated with higher levels of milk production (Wooldridge 2003, Hill 1999, Flacking 2003, Smith 2003, Furman 2002, Bier 2002).

Mothers of VLBW infants typically must express milk for several weeks before the infant can be put to breast, and for several weeks after discharge, before full exclusive breastfeeding is achieved, if ever (Wooldridge 2003, Furman 2002). The initiation (See...
CPQCC Toolkit Part 1 – The First 100 Hours) and maintenance of lactation for mothers of VLBW infants is best accomplished with a hospital grade, automatic-cycling electric “double” pump (Hill 1996, Slusher 2004). It is very common for a mother of a VLBW infant to have her milk supply decrease after 4-6 weeks of pumping, as she resumes her normal daily routine or returns to work (Hill 1999, Ehrenkrantz 1986). Even if a full milk supply was never established, every effort should be made to help mothers of VLBW infants to maintain the supply they have. Returning to an increased pumping schedule (including night-time expression) and galactogogues may be useful after evaluation of the mother’s situation (ABM 2004a). Fenugreek is often used as a first line galactogogue (ABM 2004a, Wight 2001). The use of metoclopramide 10mg tid for 14 days, followed by a tapering dose for mothers who respond favorably, has been demonstrated to be effective way to increase milk production in some women (Budd 1993, Emery 1996)

“What you should know about metoclopramide”) Ongoing monitoring of a mother’s milk supply via a pumping log and lactation vital signs (See Toolkit Part I – “Keeping Score”) can provide opportunity for intervention before the milk supply is irretrievably low.

Although human milk has remarkable antibacterial properties, it is not sterile and should be handled and stored properly to maintain its nutritional, developmental and immunological potential, and prevent transmission of infection (AAP 2003, HMBANA 1999, Tully 2000). Appropriate steps should be taken to ensure an individual mother’s milk is given only to her own child, unless the milk has been heat-treated under standardized conditions (AAP 2003). Mastitis is a complication for pump-dependent mammals and has been associated with irreversible compromise of milk production. In addition to increasing the frequency of emptying, prompt antibiotic treatment may protect milk production. Mothers need to exercise vigilance in examining themselves for areas in the breast which have not been well drained (Thomsen 1984).

Implementation Strategies:

- Each mother’s milk supply should be monitored continuously
  - Use a pumping log (See Appendix H - English and Spanish)
  - Participation of the lactation consultant on work and discharge planning rounds
  - Milk supply as a “vital sign” to be monitored by the RN
- Every NICU should have a policy regarding safe storage, handling and administration of human milk. (HMBANA 1999, Tully 2000)
- Every NICU should have a policy regarding misadministration of human milk i.e. a mother’s milk given to the wrong infant (Warner 2004) NICU staff members should be familiar with galactogogues which may be used or requested by NICU mothers, and have information sheets for mothers’ information
- Mothers should be appropriately treated for mastitis should it occur. Discarding the milk from the affected breast is not recommended, except in unusual
circumstances (AAP Red Book 2003)

- Establishment of communication and education with the mother’s Obstetrician or primary care provider around issues of lactation and galactogogues.
- Lack of appreciation that mothers’ milk supply is a priority in the normal care of a VLBW infant
  - No mention of milk supply on rounds
  - Not encouraging the use of a pumping log
- Lack of policies regarding
  - Misadministration of human milk
  - Safe storage, handling and administration of human milk
- Lack of knowledge regarding treatment of mothers mastitis
  - Reluctance of NICU staff to get involved in maternal medical issues
  - Lack of ready referral sources for maternal treatment

**Measurement:**

- Review all policies regarding human milk in the NICU – what is missing?
- Monitor misadministration cases for appropriate handling of the case
- Periodic assessment of number (%) of mothers with inadequate milk supply after day 14 (< 350 mL/24 hrs)
- One person on rounds designated to monitor discussion of milk supply
- Monitor cases of maternal mastitis and staff’s awareness of treatment of mastitis

**PBP #2:** VLBW infants fed human milk should be supplemented with protein, calcium, phosphorus and micronutrients. Multinutrient fortifiers may be the most efficient way to do this when feeding human milk. Formula fed infants may also require specific caloric and micronutrient supplementation.

**Rationale:** Studies have repeatedly demonstrated that protein and multinutrient fortification of human milk is associated with short-term growth advantages (weight, length and head circumference) for infants < 34 weeks gestation or birthweight <1800g when fortified human milk is given both during and after the infant’s initial hospitalization (Kuschel 2004, Schanler 1998, Schanler 2003). In addition, VLBW infants grow faster and have higher bone mineral content up to 1 year of age if provided with additional nutrients, especially protein, calcium and phosphorus (Lucas 1992, Wheeler 1996; Friel 1993, Worrell 2002). However, exclusively breastfed former preterm infants tend to “catch-up” if given sufficient time (2-8 yrs) (Schanler 1992; Morley 2000; Backstrom 1999). The optimal growth rate (reference target) has not yet been established for post-discharge preterm infants. It is unclear whether the rapid catch-up growth seen with aggressive supplementation is of benefit or harm for long term overall health, growth and neurodevelopment (Hall 2001, Griffin 2002).

Fortification of breastmilk should be initiated well before a full feeding volume is reached.
Studies of feeding types and their advancement have usually started fortifiers at enteral feeds of 100 mL/kg/d, but there is no research to suggest that starting earlier (50-75 mL/kg/day) is harmful. Also, many studies do not specify whether “full” fortification (1 packet powder per 25 mL EBM) or “half” fortification is used to start. There is no research as to how fast to “advance” fortification, but multiple studies demonstrate no increase in feeding intolerance or NEC with multinutrient fortifiers (Lucas 1996, Schanler 1999, Moody 2000, Kuschel 2004). Care must be taken that large doses of multiple additives do not raise the osmolality of breastmilk (or formula) to unacceptable levels (Srinivasan 2004). As no formula powders made today are “commercially sterile”, the CDC has recently provided recommendations on the use of powdered infant formulas in the NICU (CDC 2002, ADA 2004).

VLBW infants fed human milk can benefit from vitamin supplementation, most specifically vitamins A, C and D. Most NICU’s provide such supplementation in the form of a multivitamin solution, 1 mL/day, which may be divided into twice daily dosing for extremely premature infants and for those who do not tolerate full doses. Patients with or recovering from cholestasis may also required additional fat-soluble vitamins (A,D,E,K). Vitamin E supplementation may increase hemoglobin production and decrease the incidence of IVH, but aggressive intravenous administration has been associated with increased sepsis (Brion 2002). True Vitamin E deficiency has been associated with hemolytic anemia in prematures, however such a severe deficiency is exceedingly rare. Vitamin E supplementation (50 IU/day) did not reduce anemia or transfusion requirements for VLBW receiving erythropoietin (Pathak 2003). The AAP currently recommends that preterm infants (<1000 gm birthweight) receive 6 –12 IU/kg/day enterally, which maybe supplied either by preterm formula or by supplementation of human milk (AAP 2004). It is also possible to measure vitamin A and E levels to use as a guide for supplementation of these vitamins. However, as clinical presentations do not consistently correlate with such levels, and the laboratory tests themselves vary in clinical relevance, we can find no evidence-supported basis for following such levels.

Iron supplementation should be given to VLBW infants fed human milk at a dose of 2 mg/kg/d starting at 1 month until 12 months of age. Multivitamins with iron contain 10 mg/mL, which is adequate for supplementation. VLBW infants receiving most or all of their feedings from infant formulas should not require additional iron supplementation when intake is 180 mL/kg/day. Preterm and term infants receiving recombinant erythropoietin require supplemental iron, up to an additional 4-6 mg/kg/day. Folate supplementation, usually dosed at 50 mcg p.o. daily, may increase serum folate levels in prematures, however the clinical relevance of this remains unproven.

VLBW infants are at significant risk for chemical and clinical osteopenia due to inadequate calcium and phosphorous intake, dysfunctional vitamin D metabolism and/or excessive renal losses of these minerals (which may be exacerbated by diuretics, especially furosemide). In one series, over half of infants with a birthweight < 1000 g and nearly 25% of those with a birthweight < 1500 gm. had radiographic evidence of rickets (Backstrom 1996). Nutritional screening usually includes testing for these minerals.

VLBW infants receiving breastmilk that is fortified with commercially available products receive additional calcium and phosphorus, in a quantity associated with improved
growth (Wauben 1998a, Kuschel 2004). Babies considered to be osteopenic may need to be supplemented with calcium and phosphorus, although the effect of such supplementation on bone density remains unproven (Faerk 2000). Similarly, supplementation of a premature’s diet with vitamin D beyond 200-400 IU/day has not been found to increase later bone density (Backstrom 1999).

Implementation Strategies:
- Fortification should be used for all VLBW infants on breastmilk and may be started when enteral feeds reach 50-100 mL/kg/day.
- Every NICU should have a set of guidelines for supplementation of human milk.
- Supplemental iron should be provided to premature infants receiving breastmilk as well as all VLBW infants on erythropoietin
- Regular assessment of mineralization should be done for VLBW infants, with provision of appropriate supplementation when indicated

Barriers:
- Lack of research specific to various types of fortification and timing of their start and advancement
- Fear of NEC due to alteration of human milk with fortifiers or other supplements
- Lack of inpatient neonatal/pediatrics nutritional services and expertise
- Lack of consistent unit-based nutritional practices

Measurement Strategies:
- Documentation of guidelines in use for fortification
- Documentation of compliance with guidelines
- Documentation of a nutritional monitoring schema for stable preterm growing infants

PBP #3: Infants should be transitioned from gavage to oral feedings when physiologically capable, not based on arbitrary weight or gestational age criteria.

Rationale: Kangaroo care (skin-to-skin care), non-nutritive breastfeeding (practicing breastfeeding on an “emptied” breast) and early introduction of the breast have been associated with increased breastmilk production and longer breastfeeding post discharge (Furman 2002, Kirsten 2001, Hurst 1997, Blaymore-Bier 1996, See CPQCC Toolkit Part I, Section 3).
Infants can be introduced to oral feeds as soon as the infant is deemed stable. There are no minimum gestational age or weight requirements. Infants have been shown capable of breast or bottle-feeding much sooner than previously believed, with some breastfeeding as early as 28 weeks, and achievement of full nutritive breastfeeding at 36 weeks (Simpson 2002, McCain 2001, Nyqvist 2001, Nyqvist 1999). An infant is deemed stable for the introduction of the breast or bottle when the infant does not have a persistent physiologic decompensation such as bradycardia or desaturation when
handled, the infant is handling his/her own secretions, and shows sucking behavior on a finger, pacifier or the emptied breast. Introducing the infant to breastfeeding before introducing a bottle may facilitate breastfeeding (Auer 2004). There is no reason to “test” a preterm infant on a bottle before offering the breast. Test weighing, done by standard protocol, is a valid measure of intake at the breast and can be used to determine need for supplementation. (Scanlon 2002, Meier 1994). Mothers can test weigh accurately (Meier 1994, Meier 1990) and without stress, (Hurst 2004) although there were no significant differences in infant weight gain over the first 4 weeks post-discharge between the infants who were test-weighed, and those who were not (Hurst 2004).

Transitioning directly from gavage to breastfeeding is possible, and seems to prolong both exclusive and any breastfeeding (Kliethermes 1999), but requires the mother to be continuously present, which may not be possible because of physical limitations of many NICUs and the mothers’ own outside commitments. Mothers of preterm infants in the USA, in contrast to other countries (e.g. Sweden) are not expected or facilitated to remain with their infants to encourage earlier development of breastfeeding competence, or enable use of at-the-breast supplementation methods such as a supplemental nursing system. Transported infants’ mothers may not be available for frequent feeding practice. The increasing use of individual room NICU care, enabling parents to remain with their ill infants, may well facilitate earlier and increased direct breastfeeding.

Although research as to efficacy is limited, cup-feeding appears safe for preterm infants (Marinelli 2001, Howard 1999, Malhotra 1999, Howard 2003, Kramer 2001, Schubiger 1997, Lang 1994) and may facilitate longer breastfeeding post-discharge (Collins 2003) although may necessitate a somewhat longer hospital stay (Collins 2004). Clinical experience suggests other methods of feeding may be appropriate for specific infants, e.g. finger-feeding for neurologically impaired, or supplemental nursing systems at the breast for mothers with insufficient milk supply (Oddy 2003, Wolfe 1992). Nipple shields can be used, when appropriate, to maximize milk transfer at the breast (Meier 2000). In the absence of good research, every effort should be made to accommodate mothers’ preferences as long as appropriate weight gain is maintained.

**Implementation Strategies:**

- Kangaroo care and non-nutritive breastfeeding policies and procedures should be available
- Policies containing corrected age or weight criteria for initiation of breast- (or bottle-) feedings should be revised based on the information above and a current review of the literature
- Have at least 1 electronic scale (accurate to 1-2 g) and a protocol available for pre-post breastfeeding test weighing
- Nipple shields in various sizes should be available for use in the NICU as appropriate
- Policies and procedures, education, and competency verification, should be available for all feeding methods
• Routine assessment by skilled providers of oral readiness

**Barriers:**
- Outdated recommendations that infants must prove they can feed by bottle, before being allowed to go to breast
- Over-reliance on a single feeding method for all infants
- Lack of maternal availability
- The pressure and desire to get preterm infants discharged home at the earliest possible date
- Varying expertise and comfort level of NICU nursing staff with alternate feeding methods
- Lack of substantive research on optimal feeding methods for preterm infants

**Measurement Strategies:**
- Survey of postnatal and corrected age at first kangaroo care, first non-nutritive breastfeeding, first nutritive breastfeeding
- Protocol availability for test weighing, non-nutritive breastfeeding and kangaroo care

**PBP #4: Nutritional discharge planning should be comprehensive, coordinated and initiated early in the hospital course. Planning should include appropriate nutrient fortification and nutritional follow-up.**

**Rationale:** Discharge planning should be initiated upon admission to the NICU with an assessment of mother’s breastfeeding goals and preferences (Morton 2003, Wight 2004). Prenatal intention to breastfeed is one of the strongest predictors of initiation and duration of breastfeeding (Coreil 1988, Donath 2003, Dennis 2001, de Oliveira 2001). Due to the physiology of breastfeeding, milk expression should begin soon after the infant’s birth (See CPQCC Toolkit Part I: The First 100hrs). A full milk supply at discharge is one of the best predictors of successful breastfeeding post-discharge (Wooldridge 2003, Furman 2002).

Many parents of VLBW infants perceive incorrectly that feeding problems are resolved pre-discharge, and that the infant will be able to breastfeed exclusively at discharge and thrive. If a rooming-in suite is available and parents are amenable, a 1 to 2 night stay before discharge can point out problems and maximize learning (Morton 2003, Wight 2004). At present, however, there are no randomized controlled trials that address whether rooming-in prior to discharge is associated with higher exclusive or any breastfeeding rates, or better long term outcomes for VLBW infants.

In the week prior to discharge an individualized nutritional plan should be prepared in coordination with the neonatologist, lactation consultant, dietitian, and family. If possible, the plan should be reviewed with the post-discharge primary physician at the time of discharge. Post-discharge nutrition is a newly understood concern and many physicians may not be aware of the need for special diets and frequent visits to monitor growth and biochemical status (ABM 2004b). The plan should be based on the skills of the infant, the mother’s milk production, and the infant’s nutritional needs, and parenting.
skills and support, and should include provisions for making the transition to full breastfeeding (Morton 2003, Morton 2002). Included in this plan should be the “type” of feeding, (unfortified human milk, fortified human milk, formula, combination, etc.), frequency of feeding, “amount” of feeding (measurement, test weights if necessary), “method” of feeding (breast, bottle, cup, feeding device at breast, gastrostomy tube, etc.), “adequacy of growth” based on in hospital growth and expected growth and plotted on growth chart (see table below), “adequacy of nutrition” based on in-hospital biochemical nutritional status, when feasible (ABM 2004b).

All infants < 34 wks or < 1800 g at birth, and other larger infants with nutritional risk factors (CLD, short gut, neurologic impairment, etc.), should have a complete nutritional assessment prior to discharge. Experts have suggested this assessment should include both growth parameters (weight, length, head circumference) and biochemical measurements (phosphorus, alkaline phosphatase, urea nitrogen, transthyretin (prealbumin), retinol binding protein) (Hall 2001, Griffin 2002, ABM 2004b). Additional specific laboratory studies may be necessary for the larger, high-risk infant. If the infant is taking ≥160-180 cc/kg/day and growth parameters have been normal or improving on human milk alone for a week or more prior to discharge, human milk alone should provide adequate nutrition post-discharge.

If supplementation is necessary, the mother can directly breastfeed, but substitute postdischarge transitional formula for 1 to 4 feedings per 24 hours as needed, to reach growth and biochemical goals. Alternately, powdered transitional formula (e.g. NeoSure or Enfacare) can be added as a fortifier to expressed breastmilk given in substitute for feedings at the breast. This should be tailored to the specific preparation and calculations must be done carefully by the nutritionist. Human milk fortifier and powdered preterm formula are not usually recommended post-discharge because the nutrient content is far too great for the infant at the time of discharge, is expensive, and is difficult to prepare correctly (ABM 2004b). Hindmilk (the fat-rich milk at the end of a breastfeed) may supply extra calories, but provides no extra protein or minerals (Valentine 1994).

Multivitamins, dosed to deliver at least 1500 IU/day of Vitamin A, 20-70 mg/day of Vitamin C, and 400 IU/day of Vitamin D should be added at discharge. B vitamins are also necessary for the former premie receiving unfortified human milk. A multivitamin preparation dosed at 1 mL/day will usually supply all of the above. If formula constitutes >50% of an infant’s daily intake, the dose should be 0.5 mL per day. Multivitamin administration should be continued for at least 3 to 6 months, although the optimum length of use has yet to be determined (Hall 2001, Griffin 2002, Wight 2004).

At discharge, elemental iron should be continued/added at 2 mg/kg/day. If formula constitutes ≥50% of the diet, the dose should be reduced to 1 mg/kg/day (Hall 2001). When the multivitamin with iron preparation is stopped, the infant should be started on oral vitamin D drops or ACD vitamins to provide at least 200 IU per day until such time as the child is drinking sufficient milk to provide that amount of vitamin D (AAP 2003).

Implementation Strategies:

- Standing order for lactation consultation and discharge planner to consult with mother upon admission to NICU
• Provide for rooming-in for a few nights prior to discharge if appropriate
• Develop a discharge plan with the parents and follow-up physician and provide a copy to both
• A repeat biochemical assessment done at 1 month post-discharge may be helpful
• Follow-up may be arranged with the dietician 2-4 weeks post discharge, then as needed to adjust caloric, protein, and other nutrient intake

**Barriers:**
• Early discharge of the VLBW infant, before breastfeeding is completely established
• Assumption that breastfeeding needs to be addressed only immediately before discharge
• Lack of communication with the follow-up physician
• Lack of research to establish optimal growth patterns and feeding regimens for the post-discharge VLBW infant
• Inadequate diffusion of the emerging recommendations for nutritional surveillance post discharge
• Fear of non-payment for outpatient nutritional services

**Measurement:**
• Presence of a discharge nutritional plan as developed in concert with the parents and private physician
  ❖ As part of the dictated or computerized discharge summary
  ❖ As part of nursing discharge papers
  ❖ As a separate document prepared by the nutritionist
  ❖ Documentation that nutritional assessments are completed prior to discharge on infants with nutritional risk factors
V. CONTROVERSIES/UNRESOLVED ISSUES

A. Calculation of daily intakes. It is controversial as to whether to use the birthweight or actual weight or all calculations during the first week or until the infant regains birthweight. Similarly, there is no clear standard about whether to use actual weight or “estimated dry weight” for infants who are significantly edematous.

B. Cytomegalovirus (CMV). The AAP Committee on Infectious Diseases recommendation is as follows:
“Cytomegalovirus (CMV) may be shed intermittently in human milk. Although transmission of CMV through human milk has occurred, disease in the neonate is uncommon, presumably because of passively transferred maternal antibody. Preterm infants, however, are at greater potential risk of symptomatic disease and sequelae than are term infants. Infants born to CMV-seronegative women who seroconvert during lactation and premature infants with low concentrations of transplacentally acquired maternal antibodies to CMV can develop symptomatic disease with sequelae from acquiring CMV through breastfeeding. Decisions about breastfeeding of premature infants by mothers known to be CMV-seropositive should consider the potential benefits of human milk and the risk of CMV transmission. Pasteurization of milk seems to inactivate CMV; freezing milk at −20°C (−4°F) will decrease viral titers but does not reliably eliminate CMV” (AAP 2003 Red Book, pgs 118-9).

To maintain the advantages of human milk and reduce the risk of symptomatic CMV disease in VLBW infants, a protocol of pre-screening mothers of preterm infants born < 32 weeks for CMV, and freezing their milk if the mother is positive, before thawing and feeding is suggested.

C. Pacifiers. In term infants, early (2-5 days) vs late (> 4 weeks) pacifier use has been shown to be detrimental to exclusivity and duration of breastfeeding in term infants (Howard 2003, Dewey 2003). In preterm infants, non-nutritive sucking has been associated with decreased hospital stay and faster transition from gavage to bottle feeding (Pinelli 2001a). There is controversy about whether the use of pacifiers while gavage feeding is associated with more rapid gastric emptying and more rapid weight gain (Premji 2000). Recent studies have not demonstrated any detrimental effect on short or long term breastfeeding rates in preterm infants (Collins 2004). When the mother is absent, a pacifier may be beneficial for soothing, when other techniques are not available or are ineffective. Pacifiers should not be used to delay feedings, even in anticipation of the mother’s arrival. Crying in a term infant is a late sign of hunger (AAP 2005). A fretful infant expends calories better reserved for growth, and an exhausted infant is less capable of feeding at the breast.

D. Total Nutrient Admixture (TNA or “3 in 1 Parenteral Nutrition”): Total Nutrient Admixtures (TNAs), also called 3-in-1 or All-in-One solutions make
use of the fact that under certain conditions the glucose/amino-acid solution may be mixed with intravenous fat emulsion and administered to the patient in one bag. These admixtures, commonly used in adults and pediatrics, have been successfully used by some NICUs under carefully controlled conditions using manufacturer and published data on emulsion stability specific for pediatric/neonatal aminoacid formulations (Bullock 1992).

E. Discontinuation of parenteral nutrition, with removal of central catheters, as soon as adequate enteral nutrition is established.
At some point in the progression from parenteral to enteral nutrition, every infant reaches a point where the advantages of more parenteral nutrition are outweighed by the risks of continued central vascular access and infection. Central lines are a clear risk factor for infection, and there is some data to suggest that 21 days is a “break point” at which the risk of line-associated sepsis increases significantly (Chathas 1990). Of particular concern for protracted use of parenteral nutrition are the data which link Intralipid® administration to a significantly increased risk of coagulase negative Staphylococcus sepsis (Freeman 1990, Avila-Figueroa 1998). Although we are unaware of any good data from controlled trials on when to discontinue parenteral nutrition, an “expert opinion” strategy would suggest that when an infant is tolerating 80-100 kcal/kg/d of enteral nutrition, and there are no other risk factors, it should be possible to discontinue all parenteral nutrition and continue advancing enteral nutrition (Kilbride 2003, Kuzma-O'Reilly 2003).

F. Use of insulin to control hyperglycemia and provide adequate calories
While most neonatologists would agree that glucose levels associated with significant glycosuria, and a concomitant osmotic diuresis, should be avoided, there is no consensus about milder levels of hyperglycemia. Most experts agree that glucose levels above 220 mg/dL should be avoided. Whether glucose should be “tightly” controlled to avoid levels of 140-220 mg/dL remains entirely untested. There are data from both adult and pediatric intensive care units, which suggest a relationship between hyperglycemia and increased morbidity and mortality, although whether there is a causal relationship is still unknown (Izquierdo 2005, Faustino 2005). Hyperglycemia is a significant problem in extremely low birth weight infants, with the degree of hyperglycemia apparently inversely related to birth weight (Farrag 2000). The mechanism of this hyperglycemia is complex, and includes abnormalities in both glucose production and in insulin metabolism. In VLBW infants, gluconeogenesis is actually increased, and is relatively independent of serum glucose levels. The rate of glucose production appears to be inversely related to weight, with the smallest infants making the most glucose (Keshen 1997). At least part of the hyperglycemia seen in extremely low birth weight infants is due to decreased insulin production in the presence of high glucose levels. In addition, the very preterm infant has a decreased response to insulin (Farrag 2000). The end result of this, and of possibly other mechanisms, is persistent hepatic glucose production despite high levels of circulating glucose (Farrag 2000, Ziegler 2002).
It is clear that insulin administration is an effective tool for decreasing serum glucose levels in VLBW infants (Vaucher 1982, Collins 1991, Thabet 2003). Unfortunately, there are no data on the long-term effects of prolonged exogenous insulin administration to the VLBW infant on health later in life. There is, however, reason to be concerned that protracted exposure of the VLBW infant to high glucose levels may “program” the infant’s glucose/insulin homeostasis system abnormally (Farrag 2000, Schwitzgebel 1998). Given the profound effects of a hyperglycemic environment of the developing fetus of a diabetic mother, there may be reason to be concerned about protracted exposure of the VLBW infant to hyperglycemia and/or exogenous insulin. Similarly, the possible link between in utero growth retardation and later diabetes raises serious concerns about the importance of maintaining normal glucose homeostasis (Farrag 2000).

Ziegler recommends starting insulin if an infant is hyperglycemic while receiving > 6 mg/kg/hr of glucose, and discontinuing insulin if an infant is able to tolerate 50-60 kcal/kg/d of glucose without hyperglycemia (Ziegler 2002). However, this recommendation does not address the management of the infant who does not tolerate more than 60 kcal/kg/d of IV glucose, but who is not growing appropriately. We suggest that, with careful consideration and monitoring, insulin might be used with even higher glucose infusion rates, if that is needed to provide good growth.

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