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Feeding and Fluids in the Premature and Sick Newborn in the Low-Middle Income Countries

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1. Introduction

1.1 Overview of the feeding principles in premature and sick infants

There are many appropriate feeding regimes in neonatal nurseries around the world. (Adamkin, 2005; Chan, 2001; Gomella,2004; Eyal, & Zenk, 2004; Klingenberg, Embleton, Jacobs, O'Connell, & Kuschel, 2011; McCormick et al, 2010; WHO, 2007) Exact regimes are not as important as following basic principles of feeding these fragile infants. These principles include the following components below.

Start feedings as early as it is safe to do so. This is especially important because most nurseries in low-middle income countries (LMICs) do not have access to total parenteral nutrition (TPN). Although controversial and not consistently practiced in high-income countries (Klingenberg, et al., 2011) infants in LMICs who are stable should begin feedings on day 1 or 2 at the latest. In very low birthweight infants, who are too ill to feed on day 1, it is helpful to give intravenous (IV) fluids on day 1 and then begin an intravenous to enteral titration on day 2. Generally feeds should be advanced as rapidly as tolerated, especially in locations without TPN. Once on full feeds and off intravenous fluids, most infants will require about 160-200 ml/kg/day (and occasionally more) to meet their caloric needs and ultimate weight gain goals of about 15g/kg/day (Gomella, et al., 2004). As stressed, later in the chapter, the first feedings ideally should be colostrum. The exact volume needed for adequate weight gain after the initial expected drop in weight in the first 7-14 days of life (up to 21 days in very small infants) will depend on the caloric content of the mother's breastmilk or substitute feedings. Mothers' breastmilk can vary in caloric content from about 14 to 35 calories per ounce depending on the fat content of her breastmilk (Meier et al., 2002). For detailed information on how to determine the caloric content of breastmilk see the Textbook of Global Child Health (AAP) (Slusher T et al, 2012) .

Preterm infants less than 1200 grams require gavage feedings every 2 hours; ≥ 1200 g-1500g generally require gavage feedings every 2-3 hours; infants >1500-2000 grams can be given a combination of gavage and oral feedings (cup and spoon or dropper) every 3 hours. Infants

greater than 2000 grams who are neurologically intact can generally be fed at the breast or via cup and spoon if unable to feed at the breast due to either infant or maternal problems (guidelines adapted from Gomella et al for LMICs) (Gomella, et al., 2004). When first beginning feeding at the breast, most premature infants will require supplementation with cup and spoon feeds because of insufficient milk transfer to support adequate weight gain. Bottle feedings should be strongly discouraged in LMICs because of the difficulty of keeping them clean and their association with diarrheal diseases and death in these environments (Alrifai et al, 2010; Eshete, 2008; Ghosh et al., 1997).

Advance feedings as rapidly as is safe to do so. Generally this works best if there is a specific protocol that the nurses can follow without additional orders. Guidelines about when to deviate from these protocols and when to call the physician for feeding problems should also be in place. For infants less than 1000 grams birthweight, begin at 1cc every 1-2 hours and advance by 1-2cc every 24 hours if tolerated; for birth weight 1000g-1500 grams start at 1-2cc every 2 hours if possible (every 3 hours may be required depending on nursing shortages) and advance by 1-2cc every 12 hours; for birth weight greater than 1500 grams to 2000 grams start at 2-3cc/feed every 3 hours and advance every 8-12 hours; for birth weight greater than 2000 grams-2500 grams and unable to feed at the breast start at 5cc and advance by 5cc every 6-8 hours; for birth weight greater than 2500 grams and unable to feed at the breast start at 10cc every 3 hours and advance by 10-15cc every 3-6 hours (adapted from Zlatkin and Perman) (Zlatkin, 1988).

All breastfeeding babies should get Vitamin K_1 at birth and be supplemented with Vitamin D (Leung & Sauve, 2005). Additionally, iron supplementation should be started in all breastfed premature infants as soon as they are tolerating feeds and in term breastfed infants by four months of age(Baker & Greer, 2010).

1.2 Addressing feeding problems

Observe for signs of feeding intolerance including signs of necrotizing enterocolitis (NEC). Some of the signs of feeding intolerance include increasing abdominal distention, increasing gastric aspirate (especially if > than 30% the previous feeding), bilious vomiting and bloody stools (Gomella, et al., 2004). Isolated delayed gastric emptying should not be used as the only criteria for initiating, advancing, or withholding feeds (Adamkin, 2005). This practice can lead to excess delays in reaching appropriate caloric goals with consequent poor weight gain. If the infant has only increasing abdominal distention or gastric aspirate, without other signs of NEC, it may be appropriate to hold 1-2 feedings and then resume feedings at a smaller volume and increase slowly to reach caloric goals. If the infant has other signs of NEC or a surgical abdomen such as abdominal tenderness, edema of the gut wall, thrombocytopenia, X-ray changes consistent with NEC or a surgical abdomen, feedings will need to be held, IV fluids and/or total parental nutrition (if available) started along with other appropriate care as indicated by the disease process including antibiotics, nasogastric decompression and surgical consults.

Recognize the importance of distinguishing between swallowed blood and true gastrointestinal bleeding. Feedings do not need to be held for swallowed blood. Bloody gastric aspirates are not a sign of NEC but may be associated with swallowed maternal blood, gastric irritation, hypothermia, thrombocytopenia, and gastric ulcers. However, if

available, it is appropriate to begin ranitidine and give Vitamin K_1 (if not previously given) in infants with gastrointestinal bleeding not of maternal origin. Consider a second dose of Vitamin K_1 if bleeding is severe.

Recognize contraindications for beginning enteral feeds and/or continuing or advancing feeds. Absolute contraindications include a complete obstruction at any level unless the obstruction is caused from a meconium ileus, which may be alleviated non-surgically; severe hemodynamic instability, and confirmed necrotizing enterocolitis. In the absence of TPN, supporting these infants for more than 1-2 weeks on IVF's alone is difficult. Therefore, feedings should be started or re-started as soon as it is safe to do so. Signs that it is safe to attempt feedings include a soft, non-distended, non-tender abdomen with bowel sounds present and minimal gastric drainage.

2. Routes of feeding (gastric tube verses cup verses at the breast)

Oral feeding of the preterm infants is a challenge to the provider, the mother and the family. The maturation of feeding skills occurs in the last trimester of pregnancy and therefore, preterm infants are born deficient in the skills necessary for effective feeding including the ability to latch, to suck effectively, and to coordinate sucking, swallowing and breathing. Due to early delivery and complicated by interventions including suctioning, intubation, and ventilation, as well as neurologic, gastroenterological and cardiac status, the development of appropriate skills may be delayed, or significantly affected. The motor activities necessary for feeding, sucking, swallowing and breathing, develop in utero and are observed developing as early as 10-12 weeks gestation with the infant opening the jaw and 3-4 weeks later beginning suckling with fingers in the oral cavity. Breathing movements and swallowing begin as early as the 12th week of life. By the 28th week of gestation the jaw is observed in rhythmic movements with alveolar ridge stimulation. As the infant matures in utero, so do the behaviors necessary to sustain feeding. By the 28th-33rd week of gestation, suckling bursts can appear erratic and non-rhythmical. A mature suck, swallow, pause pattern is not observed until 35 to 36 weeks of gestation. This consistent rhythmic organization of suckling coordinated with swallowing and respirations is often considered a hallmark for neurologic maturation (adapted from Delaney and Anderson)(Delaney & Arvedson, 2008). Even when able to suckle, preterm infants have limited fat suckling pads in the cheeks, which impact the ability to maintain suction and duration of feeding.

Prior to initiating oral feeding, an evaluation of the infant's feeding skills should be performed by an experienced observer (Nightlinger, 2011). The respiratory rate during rest and sleep in the past several days should be noted. Infants who are tachypneic or have frequent apneic spells are at risk during oral feedings. Presence of excessive oral secretions with drooling or choking spells may be an indication of poor swallowing or anatomical abnormalities that need to be evaluated. Any abnormalities of the tongue, palate or lips should be noted as they may affect the method of feeding.

An oral-digital exam may be helpful in assessing readiness for feeding. The examiner presents his or her gloved finger in the mouth of the infant, with the pad of the examiners finger toward the palate. It is not unusual to find the tongue elevated posteriorly pressed against the hard palate. As the jaw opens wide for feeding, this initiates a drop in the tongue

and one can observe central grooving as the side of the tongue elevates, surrounding the nipple or examiner's finger. The observer should see or feel the tongue move in a peristalsis motion not retracting and protruding. There should be a smooth peristaltic rhythm to the suckle with pausing, while suction is felt on the finger. Persistent retraction of the tongue, lack of seal or suction, sustained milk leakage, during oral feedings, hyperactive gag reflex, jaw gapping with loss of suction, or jaw tightening, and jaw or tongue undulations are adversely affect feeding. If persisting, these may be signs of neurologic deficits or swallowing disorders rather than prematurity (Nyqvist et al, 2001;Guilleminault et al, 1984).

Feeding regimens typically begin with gastric tube feeding in infants under 1500 grams. The determination of when to transition to oral feeds and how to begin oral feeding depends on the clinical status of the infant and the nursery specific protocols. Studies have shown that many neonatal units have no set policy for breastfeeding and that neonatal nurses have not received training in breastfeeding techniques (Cricco-Lizza, 2009; Siddell & Froman, 1994). This lack of training translates into poor and erroneous feeding information, lack of guidance for mothers and families, introduction of artificial feeds, and ultimately the possibility of breastfeeding failure for the mother and infant (Buckley & Charles, 2006; Grossman et al., 2009; Manganaro et al., 2009).

Work has been done by Nyqvist and Anderson (Nyqvist et al,2010) and de Aquino(de Aquino & Osorio, 2009) identifying a developmental care approach to feeding. This involves teaching staff and mothers to identify behavioral cues, stress cues, periods of wakefulness, feeding readiness and alertness. Reactions to overstimulation including excessive crying or staying asleep are behavioral cues of disorganization of state. Identifying these cues helps mothers and caregivers to adjust the environment and the feeding as needed for the infant. Thus feeding success is on a continuum of small developmental increments beginning with early tube feeding with gradual introduction of the breast through Kangaroo Mother Care (KMC) (Nyqvist, 2004) [see Figure 1.]. Skills are acquired slowly and will likely be associated with ups and downs, which should not be regarded as a failure. Mothers should be actively encouraged during this process. It is appropriate to allow the infant to lick or suckle the breast at each feeding even before effective suckling develops. This continuum begins with the preterm infant in developmentally appropriate positioning from the day of birth, which affords the infant the best opportunities to develop physiologically appropriate skills for readiness for feeds.(de Aquino & Osorio, 2009) Kangaroo Mother Care [i.e. the infant unclothed except for a hat and skin to skin against the mother's chest with the infants back covered with a blanket] should be initiated as soon as possible. KMC promotes temperature stability, steady growth, early and prolonged duration of breastfeeding, parental ability to respond to infant cues and enhanced attachment. KMC also reduces length of hospital stay, maternal postpartum depression symptoms, pain and incidence of infection.(Hake-Brooks & Anderson, 2008; Nyqvist et al, 2010) KMC allows the mother to spontaneously offer her breast and the infant to readily feed when awake and alert (Kliethermes et al, 1999; Nyqvist, 2010). Nyqvist noted that some very preterm infants have the capacity for early development of oral motor competence that it sufficient for establishment of full breastfeeding even at a low post-menstrual age(Nyqvist, 2008). De Aquino (de Aquino & Osorio, 2009) evaluated feeding retrospectively for infants who were tube fed at breast with expressed breastmilk. At discharge, 100% of the infants who were

tube fed at the breast, were exclusively breastfed with appropriate weight gain, supporting breast feedings supplemented with oral gastric tube feedings as an efficient method in the feeding transition of preterm infants (de Aquino & Osorio, 2009).

The impact of cup feeding or bottle feeding on weight gain, oxygen saturation, and breastfeeding rates of preterm infants was examined in 34 bottle-fed and 44 cup-fed preterm infants (Rocha et al, 2002). No significant differences between groups were found with regard to time spent feeding, feeding problems, weight gain, or breastfeeding prevalence at discharge or at 3-month follow-up. Possible beneficial effects of cup feeding were lower incidence of desaturation episodes and a higher prevalence of breastfeeding at 3 months of age (Rocha, et al., 2002).

Fig. 1. Kangaroo Mother Care

In another study Abouelfettoh (Abouelfettoh et al, 2008) evaluated the use of cup feeding as an exclusive method of feeding preterm infants during hospitalization and its impact on breastfeeding outcomes after discharge. Sixty preterm infants averaging 35weeks gestation and birth weight of < 2150 grams participated in the study. Control group infants received only bottle feedings during hospitalization and the experimental group received only cup feedings during hospitalization. At six weeks of life the cup fed infants had significantly more mature breastfeeding behaviors than bottle fed infants and had a significantly higher proportion of breast feedings one week after discharge (Abouelfettoh, et al., 2008).

Meier (Meier et al., 2000) reported outcomes for 34 preterm infants whose mothers used silicon nipple shields during breast feedings. The mean milk transfer was significantly greater for feedings with the nipple shield (18 vs. 4 ml), with all 34 infants consuming more milk during breastfeeding. Major factors limiting the use of breast shield in LMIC are availability of shields, costs, concerns about cleanliness, and promoting bottle-feeding. However, as with many technologies used in high-income countries, it may be appropriate to have shields available in the special care baby nurseries for use before discharge of the infant from the nursery.

3. Monitoring for appropriate growth and responding appropriately to poor weight gain and growth

Observe for adequate weight gain which is generally about 15g/kg/day. However, the smaller the baby the slower the initial weight gain and the longer it is expected to take to get back to birth weight. In LMIC's where TPN is generally not available using the older growth chart from Dancis et al (Dancis et al, 1948) (see Figure 1.) may be more appropriate than using newer growth charts included in current neonatal handbooks and textbooks. Premature infants should ideally be weighed on the same scale daily (or at a minimum of every 2-3 days) and plotted on their individual growth chart. Adjustments to feedings should be made if the infant falls off the growth curve for more than 2 days.

Preterm nutritional guidelines and growth goals are currently based on the reference standard of intrauterine growth and fetal nutrient accretion rates (McLeod & Sherriff, 2007). This standard is difficult to achieve for this high-risk population especially in LMICs. If postnatal growth fails, preterm infants are at higher risk for adverse neurological outcomes and compromised health. The nutrient deficit occurring in the early weeks post delivery, when the infant is medically fragile, is difficult to overcome. Weight, length and head circumference measurements remain important clinical indicators of growth, but composition of weight gain is emerging as a necessary measure in determining the adequacy of nutrition intake and growth (McLeod et al, 1994). The need to monitor weight for estimation of fluid balance is a different task than monitoring for growth, and the practitioner needs to be aware of both issues. As noted on the growth chart (Dancis, et al., 1948), most preterm infants have a precipitous drop in weight in the first 7-14 days of life due to diuresis; the smaller the infant, the greater the percent of weight loss and the longer the time to regain birth weight. It is helpful to document this weight loss on a growth chart and establish the rate of growth from the lowest weight's plotting point(Zorlu, 2011). If early weight loss is not plotted, weight gain in the first several weeks of life appears inadequate. Inadequate growth is also identified by a lower growth rate than that required to follow the growth curves on the chart (Pridham et al., 2011).

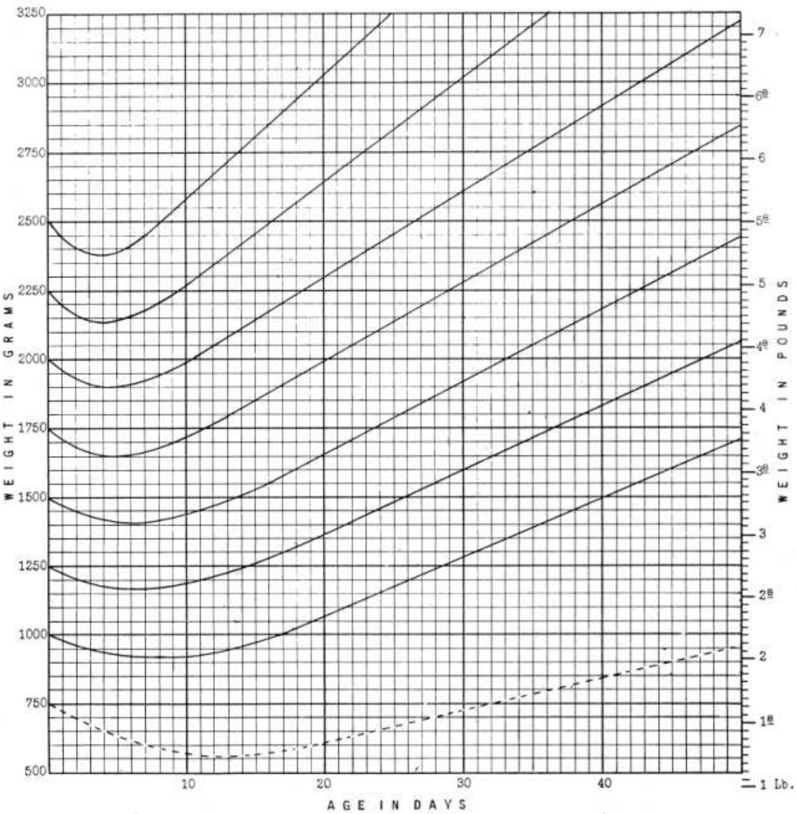
If growth is poor, it is important to evaluate the cause. It may simply be that the infant is getting inadequate calories. This can be addressed as noted below by increasing the volume and/or fat content of the breastmilk, ideally by improved breastmilk expression techniques and/or increasing the fat content of the feeds or lacto-engineering (discussed later in this chapter). Rarely, it may be appropriate, if available, to add breast milk fortifiers and/or supplemental artificial feeds. Additionally, fat malabsorption, chronic lung disease, fluid restrictions and increase in energy expenditure may all contribute to poor growth. In infants feeding at the breast, weighing the infant pre-feed and post-feeds has been discussed in the

literature and used in clinical practice for the last decade (Funkquist et al, 2010). Data by Hasse supported the use of pre- and post-feeds weighing as accurate, and an objective assessment of breastmilk intake (Haase et al, 2009), although this requires very accurate scales, not usually available in LMICs.

4. Breast milk use in premature and sick infants

4.1 Advantages of breastmilk

Breastmilk is the best food available for infants and should be strongly supported and encouraged worldwide. No substitute provides the same benefits as breastmilk to the infant. The many benefits are appropriately summarized in this table adapted from a wall hanging in Swaziland (Table 1.). These benefits of breastfeeding are also summarized in an article by Leung et al(Leung & Sauve, 2005) that highlights nutritional, immunological, anti-infective advantages of breastmilk, as well as the enhanced cognitive development and prevention of allergies, obesity, diabetes, and possibly sudden infant death and later hypertension.



From: Dancis J, O'Connell JR, and Holt LE. J Pediatrics 1948; 33:570-572.

Fig. 1. Expected Neonatal Weight Changes based on Birth Weight.

For the premature infant the benefits are even more numerous and as summarized in an article by Meier, et al (Meier , 2010) the use of breastmilk also reduces the risk of a multitude of problems including necrotizing enterocolitis, nosocomial infections and re-hospitalizations in this vulnerable population.

Breast Feeding is BEST	
Best for Baby	Fresh milk never goes off (never spoils)
Reduces Allergies	Emotionally bonding
Economical	Easy, once established
Antibodies-greater immunity	Digested well
Stool inoffensive-rarely constipated	Immediately available-no mixing required
Temperature ideal	Nutritionally optimal
	Gastroenteritis greatly reduced

Table 1. Breast Feeding is BEST

When using breastmilk, use the colostrum first. Do not dilute breastmilk. In many cultures, discarding colostrum is common (Okolo et al, 1999; Rogers et al., 2011; Tiwari et al,, 2009). Education regarding the importance of giving the colostrum and not discarding the colostrum should be emphasized. As also noted in these studies (Okolo, et al., 1999; Rogers, et al., 2011; Tiwari, et al., 2009) and many others, pre-lacteal feedings are also common,(Ahmed et al, 1999; Chandrashekhar et al., 2007; Darmstadt et al., 2007; Lakati et al, 2010) are associated with increased morbidity and mortality(Engebretsen et al, 2008;Leach et al., 1999) and should be discouraged.

4.2 Breastmilk production

The challenge of producing sufficient quantities of breastmilk to support the growth of the preterm infant falls largely on the mother of the medically fragile infant. However, health care providers can help educate these mothers in improved expression techniques and thus, relieve some of this burden. Some mothers presented with the challenge of providing expressed breastmilk for their fragile infant have feelings of helplessness, powerlessness and inadequacy arising in an extremely vulnerable period for the mother-baby breastfeeding pair(Boucher et al, 2011; Rossman et al., 2011). The importance of initiating early breastmilk expression by hand and/or pumping cannot be emphasized enough. Creating nursing routines that document breastmilk expression and frequency into the regular record of care for the postpartum mother, legitimizes this cause and empowers the nurse to begin helping the mother down the lactation pathway. This journey of providing milk, a life saving substance for the infant, is one the entire nursery must take part in. Protocols and procedure as well as policies regarding breastfeeding, milk expression including pumping, milk storage and handling, will clarify each participants role in providing this life saving white gold to fragile infants (Dougherty & Luther, 2008). Breastmilk expression regimens that mimic the feeding behaviors of full term infants are best for establishment of lactogenesis (Slusher et al., 2007). This includes frequent expression of milk every two hours beginning as soon after delivery as possible, ideally within the first two hours. Recovery from birth can be arduous and pumping is often viewed as something a mother does once she feels

healthy. This attitude, thereby, delays breastmilk expression by hours or days and mothers lose the natural window and hormonal levels necessary for ease of transition from colostrum to mature milk (Chen et al, 2001). When breastmilk expression is begun in the second hour of life or as soon thereafter delivery as is possible, mothers experience prolactin surges and prolactin cell receptor proliferation that promotes quick and efficient milk flow (Meier et al 2011). Trophic feeds for sick infants can then be managed with mothers' own milk, thereby avoiding the risk of artificial feeds in the immature gut. As noted by Slusher et al (Slusher, 2011) many mothers can express enough breastmilk by hand expression and this method should be supported and encouraged for most mothers. If a mother's milk supply is inadequate or decreasing over time, high quality hand pumps are also useful, especially in hospitals without consistent electricity. However, breastmilk expression protocols should include procuring a hospital grade pump (double pump) especially in referral hospitals as they do increase total maternal milk volume expressed (Slusher, et al., 2007; Slusher, et al., 2011) and can prove to be invaluable in those mothers who have an inadequate or decreasing milk volume with hand expression and hand pumps. Teaching the mother to combine hand expression and breast massage with pumping helps increase the expression of hind milk and avoids the problem of overly full breasts (Renfrew MJ, 2009). A combination of techniques, hand expression along with pumping may actually prove to be optimal (Morton et al., 2009). Fitting the pump breast shield to the mother's breast is an important part of providing the proper equipment for the mother who is expressing milk for her infant via an electric breast pump. The breast shield, the portion of the pumping kit that actually fits on the breast, must have adequate room for the nipple to move easily in the tunnel portion of the shaft. If this opening is too small or too large, then the mother may experience trauma to the breast or nipple and reduced milk flow. Persistent use of inappropriate breast shields may limit milk production and lead to early weaning. Mothers should be advised to pump regularly every 2-3 hours, as well as given advice that if it appears that they will be traveling or busy during the scheduled pumping time to pump early rather than miss the pumping session. If mother's feel they cannot pump the entire pumping session of 15- 20 minutes or two minutes beyond the time she no longer sees milk, then she should pump as long as possible for that pumping and then try to pump more frequently and more efficiently later to make up for the limited pumping session earlier in the day. Mothers who have prolonged pumping sessions beyond 20 minutes typically do not produce more milk and may have more nipple soreness. It is the repeated removal of milk from the breast that creates the stimulus for higher milk yield. There are large variances of how much milk the breast is able to store as well as how much milk the mother is able to pump. Mothers who appear to have plenty of milk but pump limited amounts may have mechanical problems with the pump, the wrong size breast shield, may be more successful hand expressing or need a different environment to promote let down.

4.3 Breastmilk storage

Milk storage containers are best when made of polypropylene, hard sided plastic or glass with a solid lid. Avoid open containers, containers closed with a bottle nipple, and polyethylene soft-sided storage bags (Cossey et al, 2011; Manohar, Williamson, & Koppikar, 1997). These bags often sequester nutrients and may split or tear. Concern has been

expressed about regarding bacterial contaminant in breastmilk and the need for random culturing of milk. A recent analysis by Schandler demonstrated that breastmilk cultures are not predictive of infection in premature infants (Schanler et al., 2011) and therefore, are not recommended. Ideally, storage facilities in the nursery should be readily available for refrigerating freshly pumped milk and freezing extra milk while the infant is nil per os (NPO) or not consuming the amounts the mother is pumping. Even when such facilities are not available, or when her infant is taking only small volumes of milk at each feeding, the mother still needs to express until the breast is emptied. Emptying or nearly emptying the breast at each expression session increases milk production and increases the likelihood that the mothers of these infants will continue to be able to have enough milk to exclusively breastfeed their infants after discharge from the nursery (Chapman & Perez-Escamilla, 2000; Daly et al, 1996; Neville, 1999). Breast feeding mothers know when most of the milk has been extracted as the breast feels soft and lighter in weight.

Unrefrigerated breastmilk can be generally be given to infants for up to 3-4 hours (6 hours if very clean conditions) when stored at room temperature (ABM, 2010). Breastmilk may be safely refrigerated however, the suggested times vary widely depending on the study and the conditions of refrigeration from 3-8 days (ABM, 2010). If facilities exist for freezing expressed breast milk and keeping it frozen (consistent power), it may be frozen in the back of the freezer for at least 3 months (ABM, 2010). If fresh milk is not available, then refrigerated mother's milk should be given. Give frozen milk to infants who have exhausted both fresh and refrigerated supplies.

4.4 Increasing the caloric content of breastmilk

One major advantage of having extra milk at each breastmilk expression session is the opportunity to alter the caloric content of the milk by pumping the milk in two or even more aliquots. The first milk that the mother expresses is low fat, low calorie foremilk and can be set aside or stored for later use if those facilities are available. The later milk is higher fat, higher calorie milk or hindmilk and can be fed to the infant preferentially and improves the growth rate of the infant. This process is called "lacto-engineering" and is described in detail in the AAP book "Textbook of Global Child Health"(Slusher T, 2012). If time for teaching and staffing allow, both mothers and health care providers can be taught to determine the caloric content of breastmilk using a simple hematocrit spinner and reader. This process determines the creamatocrit or cream content of the milk and is discussed in detail by Slusher and Lucas (Lucas, 1978; Slusher et al, 2012). If this is not possible, mothers can be taught to watch their milk as they express it and to change containers when it begins to thicken and feed the second milk to their infants. For infants feeding at the breast, the first milk extracted from the breast is high in lactose, is sweet to the infant and entices the infant to feed more. The last milk in the breast or expressed near the end of the pumping or feeding session is high in fat and can be over 30 calories per ounce (Bishara et al 2008; Ogechi et al, 2007; Slusher et al., 2003). Feedings of hind milk alone contribute to weight gain in the infant (Ogechi, et al., 2007). Hind milk feeding is often employed for the infant unable to tolerate advancing volumes of feed or who demonstrates inadequate growth (Griffin et al, 2000; Lucas, 1978). Other additives have been utilized to promote growth in breastfed infants. These additives include human milk fortifiers, powdered formula and exogenous oil to

improve caloric and nutrient intake. Each of these has disadvantages especially in LMICs. The cost of commercial breastmilk fortifiers is prohibitive in LMICs, artificial milk is expensive and easily contaminated during mixing, and oils may be poorly absorbed and adhere to tubing (Hamosh, 1987; Mehta, Hamosh et al, 1988). Supplementing breast milk involves not only the direct cost of the formula or supplement but also that of training the mothers in techniques for feeding their infants without compromising breastfeeding or increasing the risk of infectious diseases (Griffin, et al., 2000; Lucas, 1978; Ruiz et al, 2002).

4.5 Increasing breastmilk volumes

Bishara (Bishara et al, 2009) determined factors associated with foremilk volume (milk produced in the first 3 minutes of pumping), hindmilk volume (remainder of milk produced), and total milk volume produced by mothers of very preterm infants at 3 weeks postpartum. Milk volumes were not associated with mother's age, race or ethnic background, education, parity, reported pre-pregnancy body mass index, previous breastfeeding experience, frequency of milk pumping, longest time between pumps, infant birth weight, or multiple births. However, degree of pre-maturity (<26 weeks vs. 26 to 27 weeks) was significantly related to the relative proportion of foremilk/hindmilk volumes (Bishara, et al., 2009).

Increasing breastmilk volume is a challenge to all mothers who provide milk for their infants. The best practice is to prevent low milk supply by expressing breastmilk as soon as possible after delivery preferably within 2 hours. During the early hours after birth this may require the assistance of nursing personnel, depending on the physical condition of the mother. Slusher and her research team physically assisted mothers who were too sick to hold the pumping equipment or physically participate in the pumping (personal communication). Instruction in assisting mothers should be included in training protocols for obstetric and neonatal staff. Some mothers of preterm infants express minimal milk volumes in the first few days of life and will need encouragement to continue expressing until their milk volume increases. Documentation of breastmilk expression, including method, by nursing staff and giving data in report to oncoming staff helps to establish a team approach to pumping and milk collection. Inadequate milk production needs to be investigated. Most mothers experience inadequate production due to improper removal of milk or a number of reasons which may include: infrequent pumping, shortened pumping, inadequate removal of hind milk, medications including birth control commencement, uterine hemorrhage, and thyroid conditions. Inadequate breast pumps and mechanical pump problems may also be at fault for inadequate milk removal and subsequent limited production. Correcting these problems may increase milk production (Hill et al., 2009). Mothers need encouragement, support, and an observation of breastmilk expression techniques to establish and build a supply. Advise the mother to eat as nutritious and high caloric diet as feasible, and drink fluids to thirst.

Galactogogues (ABM 2011) have been used to help preterm and term mothers create more milk. These include both herbal remedies and prescribed medications that stimulate milk receptor cells or prolactin surges. Galactogogues typically will not produce more milk if the regular removal of milk is not occurring. Establishing a good milk removal routine is paramount in addressing low milk supply. Combining hand expression and pumping

may increase milk expression (Morton, et al., 2009). Many mothers find that seeing more milk with pumping or hand expression is the best motivator for pumping more. Galactogogues based on herbs and other natural substances include fenugreek, galega (goat's rue) and milk thistle (Zuppa et al., 2010). Mothers with ragweed and peanut allergies should be advised to avoid fenugreek. Principle prescription medications contributing to increased milk supply include metoclopramide (Betzold, 2004) and domperidone (Wan et al., 2008). The latter is more effective, is associated with fewer side effects, and is preferred throughout much of the world. Galactogogues may be started at any time during the pumping process and should not be withheld as a last resort. The use of galactogogues should be limited to those situations in which reduced milk production from treatable causes has been excluded.

Occasionally hormonal imbalances in conditions such a polycystic ovarian syndrome, thyroid disorders, insufficient glandular development of the breast, breast reduction surgeries or breast lumpectomy may reduce the ability for the breast to make milk (Andrade et al, 2010).

4.6 Alternate feedings in premature and sick infants

As previously noted, the preferential milk for the preterm infant is, of course, his or her own mother's milk fed fresh to the infant. Options if the mother does not wish to breastfeed or has an absolute or relative contraindication to breastfeeding include primarily donor milk, wet nurses and artificial feeds. Donor breastmilk is considered an important adjunct to infant feeding in many high-income countries where donor milk is both screened carefully and stored properly making it an unlikely source of feedings in LMICs. Likewise, wet nurses should be screened for infections to ensure their breast milk is safe. Wet nurses cannot be recommended in LMICs when this screening is unavailable. Preterm formula, if available, can be offered if breastmilk feedings are not an option. Milk based formula is preferred. Special nutrient and caloric enriched formulas that support good growth and development are available for use in preterm infants in the first six months of life (Jeon et al., 2011). In most LMICs, availability and cost mean that powdered artificial feedings designed for term infants are the only alternate infant food available to both premature and term infants for whom breastmilk is not an option. When using powdered formula it is essential that it be prepared hygienically with good hand washing, clean water (ideally boiled) and clean utensils. There is a very small risk of bacterial contamination in powdered milk formula with Enterobacter sakasakii, a rare opportunistic pathogen associated with meningitis, necrotizing enterocolitis and sepsis (Gurtler et al, 2005; Palcich et al., 2009). As pointed out in a study in Tanzania, this is of particular concern in the preterm, but can occur at any age (Gurtler, et al., 2005; Mshana et al., 2011). Therefore, breastmilk is preferred in the neonatal period particularly for preterm infants. Most other homemade formulas, including animal milks, are less ideal for the neonate than formula designed for infant feedings and should only be used as a last resort, especially during the neonatal period. As mentioned earlier, cups and spoons should be encouraged instead of bottles in any LMIC where hygiene is often not ideal.

4.7 Breastmilk and the HIV positive mother

Breastmilk was recognized to be a leading cause of maternal-to-child transmission (MCTC) of HIV early in the epidemic (Kreiss, 1997; Ogundele & Coulter, 2003; Ruff, 1994). Initial

efforts to curtail this mode of transmission were focused heavily on substitute feedings for breast milk. Breastfeeding was strongly discouraged and heroic efforts were made to get breastmilk substitutes into LMICs. Unexpectedly, this effort was met with at least as many infants dying in the substitute feeding group as were dying in the breastmilk group due to an unacceptably high incidence of illnesses including diarrhea in the substitute feeding group.(Horvath et al., 2009; Rollins, 2007; Thior et al., 2006) In some studies (Shapiro et al., 2007) discontinuing breastfeeding was considered to be the primary risk factor for death. Additionally, mothers may choose to breastfeed because breastfeeding is culturally acceptable: and not breastfeeding can lead to discrimination or stigmatization (Cavarelli & Scarlatti, 2011; Sadoh & Sadoh, 2009) Unfortunately, women given breastmilk substitutes often choose to give mixed feedings with breastmilk and breastmilk substitutes. This combination of mixed feedings is identified as the most risky choice with the highest incidence of maternal to child transmission (MTCT) of HIV (Coutsoudis et al., 2001).

Researchers and clinicians alike continue to struggle with the best feeding options and other interventions in low-resource settings to curtail MTCT of HIV (Kuhn et al., 2008). Significant strides have been made in recent years. All involved continuing to emphasize educating mothers on their infant feeding choices and supporting those choices whatever they are. If the mother concurs, the current recommendation is to support breastfeeding unless breastmilk substitutes are acceptable, feasible, affordable, sustainable and safe (AFASS)(WHO, 2010). Because exclusive breastmilk feedings are associated with the lowest incidence of HIV transmission, exclusive breastmilk feedings are recommended for the first six months of life (WHO, 2010). After six months of life complimentary foods should be added as appropriate. Breastmilk feeding should continue along with these complimentary foods unless breastmilk substitutes are now AFASS. At any point during the breastfeeding period that breastmilk substitutes become AFASS, the transition to breastmilk substitutes should be supported. This approach still has a significant ongoing risk of MTCT of HIV unless antiretroviral drugs are included in the regime (Cavarelli & Scarlatti, 2011; Horvath, et al., 2009; McIntyre, 2005). Additionally, boiling expressed breastmilk may be an option for some mothers where artificial feeds are not available (Cavarelli & Scarlatti, 2011; Savage & Lhotska, 2000).

Recent advances in making antiretroviral drugs available and affordable to HIV+ mothers who choose to breastfeed have decreased the risk of transmission of HIV through breastmilk. If fully implemented, the WHO recommendations could potentially reduce the risk to 5% or less from the background risk of 35% in breastfeeding infants (WHO, 2010). The risk of MTCT of HIV can be reduced by using either maternal ARV prophylaxis (WHO Option A) initiated as early as 14 weeks gestation and then daily infant nevirapine throughout the period of breastfeeding and one week beyond or maternal ARV treatment (WHO Option B) of HIV during pregnancy and continuing through breastfeeding and 1 week beyond as recommended by the WHO publication "Antiretroviral Drugs for Treating Pregnant Women and Preventing HIV Infection in Infants: Recommendations for a Public Health Approach" 2010 version (summarized in table 2. below) (WHO, 2010). However, it is agreed that all HIV infected pregnant women with CD4 cell count < 350 cells/mm^3 should receive antiretroviral treatment for their own health and for prevention of MTCT (WHO, 2010). Some protocols include an option B+ in which mothers who don't meet the criteria for ARV treatment themselves, are continued on ARV's for life after beginning ARV's during

pregnancy and breastfeeding instead of stopping them one week after weaning from breastfeeding (Ciaranello et al., 2011). For many LMICs daily nevirapine is more economical and therefore, more feasible than treating the mothers with ARV's but either regime decreases MCTC and can be supported with current evidence-based studies. For details of these regimes and others consult a pediatric HIV specialist and an up to date source of recommendations of ARV's for the prevention of MCTC. All recommendations regarding MCTC are frequently changing, therefore, all health care providers treating HIV+ mothers and their infants should check current recommendations from WHO, UNICEF and other updated sources.

Antiretroviral (ARV)-prophylaxis options recommended for HIV-infected pregnant women who do not need treatment for their own health	
Maternal AZT + Infant ARV prophylaxis **(Option A)**	Maternal triple ARV prophylaxis **(Option B)**
Mother	Mother
Antepartum twice-daily AZT starting from as early as 14 weeks gestation and continued during pregnancy. At onset of labour, sd-NVP and initiation of twice daily AZT + 3TC for 7 days postpartum (Note: If maternal AZT was provided for more than 4 weeks antenatally, omission of the sd-NVP and AZT + 3TC tail can be considered; in this case continue maternal AZT during labor and stop at delivery).	Triple ARV prophylaxis starting from as early as 14 weeks of gestation and continued until delivery, or if breastfeeding, continued until 1 week after all infant exposure to breast milk has ended. Recommended regimes include: ATZ + 3TC + LPV/r or AZT + 3TC + ABC or AZT + 3TC + EFV or TDF + 3TC (or FTC) + EFV
Infant	Infant
For breastfeeding infants Daily NVP from birth for a minimum of 4 to 6 weeks, and until 1 week after all exposure to breast milk has ended.	Irrespective of mode of infant feeding Daily NVP or twice daily AZT from birth until 4 to 6 weeks of age
Infants receiving replacement feedings only Daily NVP or sd-NVP + twice daily AZT from birth until 4 to 6 weeks of age	
ARV-antiretroviral; AZT-zidovudine; 3TC-lamivudine; NVP-nevirapine; sd-NVP-single dose nevirapine; LPV/r- lopinavir/ritonavir; EFV-efavirenz; FTC-emtricitabine;	

WHO. Antiretroviral Drugs for Treating Pregnant Women and Children and Preventing HIV Infection in Infants Recommendations for a public health approach 2010 version. 2010;
http://www.who.int/hiv/pub/mtct/PMTCTfactsheet/en/

Table 2.

4.8 Contraindications and relative contraindications to breastmilk feeding

There are few conditions in which breastfeeding is not recommended for the infant or for the mother. Unless alternate feedings are acceptable, feasible, affordable, sustainable, and safe (AFASS), HIV positive mothers are encouraged to breastfeed. An infant diagnosed with galactosemia, a rare metabolic disease should not breastfeed. Mothers with certain untreated

infections (e.g. tuberculosis) should not breastfeed at the breast but may be able to use expressed breastmilk depending on the particulars of their disease. Infants of mothers with Hepatitis B carriage may breastfeed provided their newborns are immunized against Hepatitis B immediately after birth as soon as dry and stable(IOM, 2011) . For specific situations consult an infectious disease specialist or the Red Book(AAP, 2009). Any mother using illicit drugs, taking cancer chemotherapy agents such as antimetabolites, or undergoing radiation therapy, generally should not breastfeed. Nuclear medicine studies vary in their components and advice should be sought in particular for the radioactive component of the scan (AAP, 2001; Hale, 2010).

4.9 Team approach and education: Supporting and encouraging breastfeeding

Breastfeeding incidence and duration rates are significantly affected by maternal educations and staff education (Brent et al, 1995). It is important to focus on providing evidenced based education and support regarding breastfeeding practices in special care baby units to mothers as well as all staff interfacing with the mother and baby (Meier, 2010). In a USA study, Hallbauer found that infants with a lower weight and gestational age, who had prolonged stays in the neonatal intensive care unit were less likely to be breast-fed after discharge (Hallbauer et al, 2002). This suggests that efforts to promote breast-feeding in the neonatal unit were ineffectual or inadequate. The author suggests that in order to remedy this situation it is necessary to keep the mother-infant pair together, to promote breastfeeding before and immediately after delivery and to train staff in the management of lactation (Hallbauer, et al., 2002). Family-centered care has been implemented in many neonatal intensive care units throughout the U.S. and is invaluable in helping families, whose infants require hospitalization, cope with the stress, fear, and altered parenting roles that may accompany their child's condition and hospitalization (Mulasky, 2005). In high-income countries, a combination of breastfeeding management and family centered training for neonatal intensive care unit staff enhances the care of these medically fragile infants and their families. In LMICs family centered care is the norm and essential in providing care for their family members. Mothers already play a vital role in the care of their premature and sick infants and in many of these LMICs and stay either with the infant in the nursery or nearby. However, education and support in the feeding and care of their infant is crucial to providing optimal growth, development and exclusive breastfeeding for these most vulnerable infants.

Statistics specific for infants graduating from special care baby units in low-middle income countries is lacking. However, since breastfeeding is the norm in these countries it is likely that most infants go home with at least partial breastmilk feeds. The larger problem is promoting exclusive breastmilk feedings for the first six months of life. This is challenging especially in HIV positive mothers. Mixed feedings are common and misconceptions about the adequacy of mothers' own milk are widespread. There is an ongoing need to continually promote and reinforce the Baby Friendly Hospital Initiatives (UNICEF, 2009). Abolyan found the Baby Friendly training among staff increases breastfeeding rates as well as maternal satisfaction (Abolyan, 2006). Breastmilk is the life saving choice for infant feeding in high-risk special care baby nurseries and should be the standard of care for these infants. However, this must be balanced with the needs of the individual infant and, when appropriate, alternative feedings recommended (i.e. some infants of HIV+ mothers,

orphaned or abandoned infants, infants who are failing to thrive despite their mothers efforts to produce adequate breastmilk). All policies, procedures and training regarding infant feeding should promote, protect and support breastfeeding for the mother and their infants whenever possible.

5. Indications for and appropriate intravenous fluids in premature and sick infants

The goals of IV fluid therapy are to maintain adequate hydration, appropriate electrolyte balance and sufficient carbohydrate intake to support basic metabolic processes and avoid hypoglycemia. Fluid and electrolyte requirements for newborns change with advancing gestational age and postnatal age as total body water decreases, extracellular fluid volume contracts, renal tubular reabsorption of free water, sodium, and bicarbonate improves, and skin matures. Extremely preterm infants are at especially high risk for excessive rate of water loss through their very thin skin. Transepidermal water loss immediately after birth at 26 weeks gestation is 60 $g/m^2/h$ decreasing to approximately 25 $g/m^2/h$ by 32 weeks and to 10 $g/m^2/h$ by 40 weeks post-menstrual age (Seri I, 2005). A 25-27 week gestation infant placed in 50% humidity on the first day after birth may lose 129 ml of water/day through the skin alone (Modi, 2005). The skin matures quite rapidly so that even in the most immature infants born at 26 weeks gestation, the transepidermal fluid loss has decreased to about 43 ml/day by one week after birth. Antenatal steroids accelerate skin maturation in the preterm infants, thereby reducing postnatal transepidermal water loss.

In the healthy term infant the immediate post-delivery period is characterized by a negative fluid and sodium balance. Hormonal changes associated with labor and delivery initiate a postnatal diuresis over the first 2-3 days at which time fluids should be limited so as not to impede this process. Normally during the first 1-3 days oral intake via breastfeeding is limited. Consequently, isotonic contraction of extracellular fluid volume occurs. The result in the healthy term newborn is an appropriate weight loss over the first several days after birth of 1-2% per day for a total weight loss of 5-10%(Kalhan , 2001). Birth weight is usually regained by day 7. Preterm infants are born with relatively more total body water to excrete, immature renal function, and greater transepidermal water loss. Therefore, they have a substantially greater initial weight loss, up to 15% over the first week, and regain birth weight between the second and third week after birth. In both term and preterm infants, weight gain over the first few days is abnormal and represents fluid and sodium retention due either to excessive administration of fluid or to neonatal conditions which compromise organ function or increase capillary leak.

5.1 Fluid requirements

Fluid requirements are influenced by clinical and environmental conditions. Insensible, evaporative fluid losses are increased by low humidity environments (<50%), care under radiant warmers, high ambient temperature, phototherapy, non-humidified respiratory gases, skin defects or breakdown (e.g., omphalocele, gastroschisis, burns), fever, and tachypnea. Gastrointestinal losses are readily evident when due to diarrhea or nasogastric drainage, but may be unapparent when due to third spacing associated with necrotizing enterocolitis or to large evaporative losses during GI surgery. Environmental factors such as clothing, high

humidity, care in a double walled incubator, skin ointments, and humidified respiratory gases all decrease insensible losses. Some clinical problems decrease fluid requirements due to organ injury (e.g., birth asphyxia) or the underlying pathophysiology (RDS, PDA).

Taking the normal adaptive changes into account, IV fluid administration in the first few days should be limited and then gradually increased to maintenance volumes over the next several days. Urine output should normally be at least 2 ml/kg/hour after the first day. Daily fluid intake will vary depending upon gestational age and medical condition. Extremely preterm infants have very high insensible water loss due to epidermal immaturity and will need a higher fluid intake to compensate for their transepidermal water loss. However, excessive fluid and sodium administration at this time is associated with complications, particularly in preterm infants, such as pulmonary edema, increased respiratory distress, patent ductus arteriosus and a greater risk of bronchopulmonary dysplasia. Because of the contraction of total body water, Na supplementation is not needed until 3-4 days after birth.

For term infants begin IV infusion rates at 60-80 ml/kg/day on days 1-3, increasing slowly by 10-20 ml/kg/day to 100 ml/kg/day. On days 3-7, if clinically stable with appropriate weight loss of 1-2% per day, continue increasing total fluid intake (IV + PO) by 20 ml/kg day up to a maximum of 180 ml/kg/day. After day 7, do not exceed a maximum fluid intake (IV plus PO) of 180 ml/kg/day until the infant is off IV fluids and entirely on ad lib oral feeds.

The fluid requirement for premature infants varies depending upon the degree of prematurity, as well as environmental factors and clinical problems that increase or decrease insensible fluid loss. In general, on days 1 and 2 after delivery, infants with birth weights < 1000 g require 100-150 ml/kg/day; infants with birth weights 1001-1500 require 60-100 ml/kg/day ; and infants with birth weights >1500 require 60-80 ml/kg/day. For all infants total fluids (IV + PO) are gradually increased by 10-20 ml/kg/day to reach 150-160 ml/kg/day by 7-10 days of age. When growing, and without medical complications, premature infants may tolerate up to 180 ml/kg/day. Providing preterm infants with humidified incubators or placing them under small plastic tents will decrease insensible loss and total fluid requirements. Fluid intake should be based on birth weight until birth weight is regained. In general, too much fluid is more deleterious than too little fluid It is better to err on the side of cautious fluid administration.

For all infants, be sure to include the volume of oral feeds when calculating the daily total intake/day. If receiving only intravenous (IV) fluids write the order to indicate how much is to be given each hour. If the infant is also receiving oral feeds, an IV+ PO order will avoid inadvertently giving too much or too little fluid as IV and/or PO volumes are changed (ex. if the infant is receiving a total of 360 ml of fluid/day and is being fed every q 3 hours: "Give 20 ml D5W IV + 25 ml breastmilk PO/NG every 3 hours = 45 ml q3 hours= 360 ml/day total.") Rewrite the order to maintain the appropriate interval volumes as IV and PO intakes change.

5.2 Glucose

Begin with a glucose infusion rate of 6 mg/kg/min given as D5W if birth weight is < 1000g and 8 mg/kg/minute as D10W if birth weight is greater than 1000 g. Increase the glucose

infusion rate by 3-6 gm/kg/day (10-20 kcal/kg/day) to a maximum of 12-14 mg/kg/min. Keep the serum glucose less than 150 mg/dL. It is helpful to calculate the glucose infusion rate (GIR) in mg/kg/minute [(% glucose X ml/kg/day) /24 hours per day/60 minute per hour] and the caloric intake (Cal/kg/day) provided (IV glucose =3.4 Cal/gm). A GIR of 4-6 mg/kg/minute approximates basal hepatic glucose production. About 50 Cal/kg/day are needed for maintenance of weight and basic metabolic function (Kalhan SC, 2001). This level of caloric intake is barely achievable using D10W at maximum fluid volumes. Initiation of enteric feeds is necessary as soon as possible in order to provide enough calories and nutrients for growth.

5.3 Electrolytes

In the first 3 days after birth, electrolytes are not needed and IV fluids containing only 5% or 10% glucose (D5W or D10W) are adequate. Sodium (Na) supplementation (3-4 mEq/kg/day) should be started by day 3 to avoid hyponatremia and help establish the positive sodium balance needed for growth. Nasogastric and ostomy drainage contain a considerable amount of NA (45-140 mmol/L) which can generally be replaced with equal amounts of 1/3-1/2 NS. Potassium (K) can also be added (1-2 mEq/kg/day) on day if urine output is adequate and the infant is not yet taking enteric feeds. Adding 10 mEq K/1000ml of IV fluid provides 1 mEq K/100 ml which is adequate for most infants. Since inadvertent administration of excess potassium may be fatal, potassium should be added to IV fluids only when necessary and the preparation carefully checked by two nurses.

5.4 Types of IV fluids

If stock IV solutions are not available, adding 25 ml of Ringers Solution or Ringers Lactate to 100 ml of D5W or D10W will approximate ¼ NS and deliver 3-4 mEq Na/100ml (Slusher et al, 2011). If only D5W is available, an appropriate amount of D50W can be added to the D5Wsolution to make D10W as described in detail in the AAP book"Textbook of Global Child Health" (Slusher T, 2012). Care must be taken to maintain sterility when mixing IV solutions together. All fluids except for acute volume expansion should contain glucose.

Total parenteral nutrition (TPN) containing protein and lipid in addition to glucose, is necessary to achieve adequate intravenous caloric and nutrient intake when enteric feeds are not possible. TPN has dramatically improved the survival following neonatal surgical procedures such as diaphragmatic hernia, tracheoesophageal fistula, omphalocele, gastroschisis and bowel resection associated with prolonged inability to take enteric feeds. However, TPN is associated with a much higher risk of sepsis because the solution itself is an excellent culture medium and infusion lines, especially if centrally placed, are at high risk for contamination. Although used routinely to support nutrition for sick newborns in developed countries, TPN solutions require preparation and administration under strictly controlled, aseptic conditions with appropriate facilities and staff.

5.5 Methods of fluid administration

IV fluids are best given continuously by infusion pumps. Alternatively a non-mechanical drip set with a buretrol may be used. Accidental acute fluid overload may be life threatening. It is therefore critical to limit the amount of fluid that can be rapidly infused by

filling the pump syringe, pump chamber or buretrol with only 2-4 hours of IV fluid. When continuous infusion is not possible, IV fluid can be given intermittently as frequent, small boluses every 2 hours. However, intermittent bolus administration of glucose increases the risk of hyperglycemia and hypoglycemia, acute changes in serum osmolality and risk infection from frequent entry into the IV line. This method of IV fluid administration should be used only if safer methods of IV infusion with pumps or drip sets are unavailable.

5.6 Routes of fluid administration

IV fluids may be given by peripheral or central lines. Do not exceed D12.5W when using a peripheral IV or D20W if using a central venous line. NS, 1/2NS or D5W can be used in central arterial lines; hypertonic solutions should be avoided.

5.7 Monitoring fluid status and electrolytes

Monitoring fluid and electrolyte balance is essential. All fluid intake should be systematically recorded including IV infusions, medications, blood products, and feeds. Passage of urine and stool should also be recorded. Whenever possible urine output should be measured. Any drainage from NG tubes and chest tube should be measured and recorded. Vital signs including heart rate, respiratory rate, temperature and blood pressure should be recorded at least once or twice per day. A careful daily physical exam should include evaluation of capillary refill, skin turgor, mucous membranes, and the anterior fontanel. An accurate, unclothed, daily weight is one of the best ways of assessing overall fluid balance in the first several days after birth. Obtaining a daily weight in preterm infants, especially those who are extremely immature, must be balanced against the difficulty of doing so, the accuracy of the scale and potential complications which may occur during the process of weighing (e.g., hypoxia, hypothermia, exposure to contaminated surfaces). If possible, serum electrolytes should be checked using small capillary blood samples every 24-48 hours during the first week or until stable. At a minimum Na and K should be checked on days 3 and 7. The normal serum sodium level is Na 132-144 mmol/L; the normal K level is 3.8-5.7 mmol/L(Modi, 2005).

5.8 Complications

Common complications of IV fluid therapy include hyponatremia (< 130 mmol/L), hypernatremia (> 150 mmol/L), hyperglycemia (> 150 mg/dl), hypoglycemia (< 40 mg/dl) if fluids are abruptly discontinued, accidental fluid overload, and skin injury due to IV infiltration. Avoiding severe burns due to IV infiltration requires frequent inspection of the IV infusion site. Treat IV infiltration in an extremity by elevating the limb. If circulation to an area on the infiltrated extremity is compromised, warm the opposite extremity which will help reflexly dilate blood vessels in the affected limb without increasing oxygen demand. If the skin is broken down, the area should be treated as a burn.

5.9 Fluid requirements in common neonatal conditions

Birth asphyxia is often associated with renal insufficiency due to acute tubular necrosis resulting in severe oliguria or anuria. In this circumstance, fluid intake should be limited to insensible loss, approximately 30 ml/kg/day on day 1 in term infants. Fluids intake is

liberalized slowly as urine output improves. A tight nuchal cord may result in hypovolemia when venous return from the placenta to the fetus via the umbilical vein is obstructed. Affected infants have poor capillary refill, tachycardia, may have weak pulses, and often have respiratory distress. These infants usually respond promptly with improved perfusion and resolution of respiratory distress and tachycardia after volume expansion with boluses of 10 ml/kg normal saline IV boluses up to a total of 20-30 ml/kg. A symptomatic patent ductus arteriosus is common in preterm infants, especially if fluid administration has been excessive. Indomethacin, used to pharmacologically close the ductus, is associated with transient oliguria, fluid retention and hyponatremia. Extremely premature infants (24-27 weeks gestation) have very high transepidermal free water loss and renal immaturity in the first several days after birth that increase the risk of hypernatremia and hyperkalemia. Changes in weight and electrolytes must be closely monitored and fluid intake adjusted accordingly. Respiratory distress syndrome is associated with increased pulmonary fluid and failure to diurese until 3-4 days after birth at which time the respiratory disease improves. Use of diuretics is ineffective in hastening the spontaneous diuresis. Immediately after gastrointestinal surgery, infants are often oliguric or anuric. Usually this is due to intravascular volume depletion from large, intraoperative insensible fluid losses from the exposed gut and/or post-operative third. The appropriate treatment is volume expansion, not administration of a diuretic. In shock, due to acute blood loss, the best treatment is immediate volume expansion with blood products.

6. Diagnosis and treatment of hypoglycemia in sick and premature infants

Glucose production in the fetus is normally very low, and most glucose for fetal energy utilization is obtained from the maternal circulation via facilitated diffusion across the placenta (Hay, 2006). Under normal circumstances, birth represents the beginning of a transition period when the neonate will develop the ability to maintain glucose homeostasis independently. Serum glucose levels fall initially, reaching a nadir around 2-3 hours of age. Catecholamine release, cortisol surge, insulin production, enhanced glycogenolysis and gluconeogenesis are a few of the important hormonal and metabolic events taking place that ultimately lead to activation of independent glucose production in the normal neonate. Serum glucose concentrations will rebound within the first 4 hours after birth from this physiological nadir. With established feedings, the serum glucose level will continue to stabilize over the first 24 hours of life.

Routine glucose monitoring is not recommended in the normal, healthy, term neonate (Committee on Fetus and Newborn, 2011). However, there are specific neonatal populations that are at increased risk of developing hypoglycemia and warrant close observation and monitoring. Glucose homeostasis is the result of a balance between energy production and energy utilization. When this balance is skewed, hypoglycemia results. Preterm infants, small for gestational age (SGA) infants, and very low birth weight (VLBW) infants have an impaired ability to produce glucose due to limited hepatic stores available for glycogenolysis. Illness in any neonate increases metabolic demand and energy utilization. Infection, asphyxia, and hypothermia thus increase the risk of neonatal hypoglycemia. Infants of diabetic mothers (IDM) and large for gestational age infants have increased metabolic demands secondary to macrosomia. Prolonged hyperglycemia in utero leads to abnormal glucose metabolism in the IDM after birth. IDMs have higher levels of circulating

insulin, lower serum glucose levels, lower availability of alternative fuels, and impaired counter-regulatory hormones, all of which contribute to a high risk of neonatal hypoglycemia, often developing immediately after birth earlier than what is seen in other at risk populations (Martin, 2011; Peace O, 2010).

The overall incidence of neonatal hypoglycemia is difficult to define. Studies have reported incidence rates from 0.4% to 29% during the first 24 hours of life depending on the study population and level of serum glucose used to define clinically significant hypoglycemia (Burdan DR, 2009; Depuy AM, 2009; Johnson, 2010; Najati N, 2010). The risk of hypoglycemia is higher in resource poor countries, even in populations not characteristically thought of at risk. A study in Nepal among term infants born by uncomplicated delivery in a hospital setting found 10% with serum glucose <37 mg/dl (<2.0 mmol/l) and over 50% with at least mild hypoglycemia <50 mg/dl (<2.8 mmole/L) within the first 24 hours of life (Pal Deb, 2000). Contributing factors that are often more common place in resource poor countries include lack of prenatal care, poor maternal nutrition, and delayed feeding practices.

Neonatal hypoglycemia may have long-term sequelae. Hypoglycemia is often associated with hypoxemia, respiratory compromise, prematurity and other problems of the ill or premature infant. This can make it difficult to associate neurodevelopmental outcomes with hypoglycemia alone. Generally, transient hypoglycemia in an otherwise healthy neonate has a good prognosis whereas recurrent, severe, or prolonged hypoglycemia has been associated with poor developmental outcomes ranging from attention disorder to cerebral palsy (Martin et al, 2011).

6.1 Signs and symptoms of hypoglycemia

Signs and symptoms of neonatal hypoglycemia are subtle and nonspecific. Jitteriness, irritability, feeding difficulty, apnea, hypothermia, cyanosis, tachycardia, lethargy, floppiness, eye rolling or tachypnea could all be signs of symptomatic neonatal hypoglycemia. Diagnosis is confirmed with the identification of a low serum glucose, and resolution of symptoms after glucose administration. Because the symptoms are nonspecific, consideration should be given to other diagnoses as well, including sepsis and asphyxia. More severe signs, including seizures and coma, often result from recurrent and/or prolonged hypoglycemia. Seizures and coma are not as quickly or easily reversed with glucose administration (Martin et al, 2011).

Serum glucose levels are among the most common laboratory tests performed on neonates. Hypoglycemia is common, easily confirmed by laboratory testing, and the symptoms are reversible if intervention occurs in a timely manner. Any infant with nonspecific signs of illness should raise concern for possible neonatal hypoglycemia.

6.2 Glucose values and Interpretation

The definition of clinically significant hypoglycemia is not known. There is no current research to indicate a level of serum glucose that consistently leads to permanent neurologic injury. Instead, general consensus and an operational approach guides management and treatment decisions in neonatal hypoglycemia.

Serum glucose levels between 40-50 (2.2-2.7 mmol/l) during the first 4 hours of life is generally regarded as normal, less than 35 mg/dl is regarded as abnormal. After reaching a physiologic nadir, infants' serum glucose levels should stabilize. As a result, glucose levels >45 mg/dl is considered normal in infants 4-24 hours of age (Martin et al, 2011).

6.3 Treatment options for hypoglycemia

Treatment begins with prevention and screening of at risk infants. Early breastfeeding, ideally within the first hour following birth, and frequent feedings every 2-3 hours, can avoid severe neonatal hypoglycemia. Delayed neonatal feedings for up to several days is sometimes practiced in developing countries. This places all infants, but especially the ill and preterm infant at risk for significant and prolonged hypoglycemia. Known at risk infants should be screened for hypoglycemia by 3 hours of age and sooner if clinical concerns arise.

Neonatal hypoglycemia is treated by replenishing the substrate supply. The preferred method is by breastfeeding. As mentioned, frequent feeding helps maintain euglycemia. Infant formula, or expressed breastmilk, can also be given by bottle, cup or gavage as necessary. This provides immediately accessible glucose through carbohydrate metabolism, as well as fats and protein for glycogenesis and maintenance of glucose stores during times of fasting. Enteral glucose administration via breastmilk, formula, or D5W should be used in mild to moderate neonatal hypoglycemia.

The goal is to achieve a balance of energy production with energy utilization through frequent bolus feeds occurring every 2-3 hours, for a total fluid goal of 60 ml/kg on the first day of life. Once feeds become well established, continued persistent hypoglycemia is an indication of an underlying metabolic or endocrine disorder.

Intravenous glucose should be used if the neonate is symptomatic or if moderate to severe hypoglycemia is identified, which can be defined as a serum glucose <25 mg/dl during the first 4 hours of life, <35 mg/dl from 4-24 hours of age. Intravenous dextrose should also be given to the infant manifesting late stage symptoms of coma and/or seizures. Intravenous dextrose is given as a small bolus of 2 ml/kg of D10W followed by a maintenance glucose infusion rate (GIR- see Equation I for calculating) of 5-7 mg/kg/minute. Although suboptimal, in the rare occasion that intravenous fluids are not available for the treatment of symptomatic or moderate to severe hypoglycemia, D5W at 10 ml/kg by gavage can be given orally or by naso-gastric tube. Hyperosmolar glucose solutions (D25 and D50) should not be used in neonates and have been associated with intracranial hemorrhage and rebound hypoglycemia (Marx JA, 2010). Available solutions should be diluted to a concentration of D10.

$$\mathrm{GIR}\ (\mathrm{mg/kg/minute}) = \frac{(\%\ \text{dextrose concentration x total ml / kg / day})}{144}$$

6.4 Summary

Neonatal hypoglycemia is the result of abnormal glucose metabolism after birth. It is a manifestation of the imbalance between energy production and energy utilization. While the incidence of hypoglycemia is unknown, it is potentially more common in resource poor countries, and known to occur at higher rates in susceptible populations such as the ill or

preterm neonate. The neonatal brain is the primary consumer of serum glucose, and is at risk during periods of energy depletion. As such, prolonged, recurrent, or severe hypoglycemia may result in neurologic sequelae. Identification of at risk infants, close monitoring and prevention strategies, prompt recognition and effective treatment can be achieved in the developing world.

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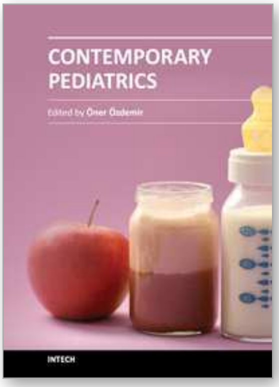

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Book Contemporary Pediatrics with its 17 chapters will help get us and patients enlightened with the new developments on the contemporary pediatric issues. In this book volume, beyond classical themes, a different approach was made to current pediatric issues and topics. This volume, as understood from its title, describes nutritional infant health and some interesting topics from pediatric subspecialties such as cardiology, hemato-oncology and infectious diseases.