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Nutritional Management of the Extremely Low Birth Weight Infant: An Evidence Based Clinical Practice Guideline

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NUTRITIONAL MANAGEMENT OF THE EXTREMELY LOW BIRTH WEIGHT INFANT: AN EVIDENCE BASED CLINICAL PRACTICE GUIDELINE

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ABSTRACT

Premature birth has risen steadily over the last decade resulting in an increased number of infants needing neonatal intensive care. The demand for neonatal intensive care has lead to many improvements in the delivery of such care with an increase in the survival of the smallest and most premature infants. However, most of these infants are being discharged from neonatal intensive care units (NICU) with severe extrauterine growth restriction (EUGR).

Extremely low birth weight (ELBW) infants born at 23-27 weeks gestation and who have a weight of less than 1,000 grams are at the highest risk for EUGR because of their low birth weight and extreme prematurity. The need for prolonged mechanical ventilation and blood pressure support delays the ELBW infant from receiving needed amounts of early nutrition during the first few weeks of life. This lack of early nutrition leads to large and ongoing energy and protein deficits, which have been cited as the leading cause of EUGR in the ELBW infant. Despite current evidence that supports the administration of early aggressive nutrition in the ELBW infant to improve extrauterine growth, clinical practice remains largely unchanged.

The Institute of Medicine (IOM) in its 2008 report states that the use of evidenced based clinical practice guidelines (CPG) has the potential to reduce undesirable practice variation thereby eliminating the use of ineffective interventions. Developing evidenced based CPGs utilizing a systematic, rigorous and transparent process will serve to standardize practice while improving clinical outcomes. Therefore, the purpose of this doctoral project is to provide an evidence based CPG on the nutritional management of the ELBW infant. The CPG includes evidence based recommendations that are centered

on promoting adequate extrauterine growth during the NICU stay in order to prevent EUGR in the ELBW infant.

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CHAPTER 1

BACKGROUND, PROBLEM and PURPOSE

Premature birth has risen steadily over the last decade resulting in an increased number of infants needing neonatal intensive care. The demand for neonatal intensive care has lead to many improvements in the delivery of such care with an increase in the survival of the smallest and most premature infants. However, most of these infants are being discharged from neonatal intensive care units (NICU) with severe extrauterine growth restriction (EUGR) putting them at risk for poor neurodevelopment and severe handicaps later in life (Hans, Phylipow, Long, Thureen & Georgieff, 2009; Kashyap, 2007; Martin, et al., 2009; Stephens, et al., 2009; Vlaardingerbroek, van Goudoever & van den Akker, 2009).

EUGR occurs when a premature infant's growth falls below the 10^{th} percentile of that for a normal fetus at the same gestational age (Clark, et al., 2003; Coverston & Schwartz, 2005; Yu, 2005). The infants at highest risk for developing EUGR are those classified as extremely low birth weight (ELBW). ELBW infants born at 23-27 weeks gestation and who have a weight of less than 1,000 grams are at high risk for EUGR because of their low birth weight and extreme prematurity.

The extreme prematurity of the ELBW infant's organs and organ systems limits their ability for transition to extrauterine life. Many ELBW infants require prolonged mechanical ventilation due to their immature lungs, blood pressure support due to their

immature myocardium, and parenteral nutrition due to their immature gastrointestinal system (Gleason & Devaskar, 2012). The need for such support delays the ELBW infant from receiving needed amounts of early nutrition during the first few weeks of life resulting in poor growth (Stephens et al., 2009).

In utero, the ELBW infant would be receiving twice the amount of amino acids needed for protein accretion with the excess amount being oxidized for energy production (Adamkin, 2005). Glucose would be delivered at a rate that meets fetal energy expenditure and would be controlled by maternal glucose concentration (Clark et al., 2003). Lipid uptake would be minimal and be done at a rate that meets the essential needs for neuron development (Hay, 2006)

In contrast, during the first weeks of extrauterine life amino acids are withheld or given in minimal amounts due to concern for the ELBW infant's ability to catabolize early amino acids (Adamkin, 2005; Hay, 2006). Glucose is given as the sole source of energy resulting in concentrations that are too high for the ELBW infant, leading to hyperglycemia (Hay, 2006). Intralipids are held due to hyperglycemia and the risks of lung injury and kernicterus (Clark, et al., 2003).

Postnatal nutrition regimens utilizing glucose as the sole energy source and lacking adequate amounts of protein result in large protein and energy deficits in the ELBW infant. These deficits may reach up to 300kcal/kg and 12g/kg of protein within the first week of life leading to altered growth at the cellular and systemic level (Clark et al., 2003). The cumulative and ongoing deficits of energy and protein are cited as the leading cause of EUGR in the ELBW infant (Adamkin, 2005; Clark et al., 2003; Coverston & Schwartz, 2005; Ehrenkranz, 2007; Hay, 2006).

Extensive research has been conducted to determine the best nutritional regimen for preventing EUGR in the ELBW infant. Data from randomized controlled trials (RCT) strongly suggests providing nutrition that mimics the intrauterine environment may improve energy intake and prevent protein loss, thereby improving growth in the ELBW infant (Ibrahim, Jerondi, Baier, Dhanireddy & Krouskop, 2004; Wilson, et al., 1997). Despite these data providing strong evidence for improving EUGR, clinical practice remains largely unchanged.

Bloom et al. (2003) found a wide variation in postnatal weight gain among 51 NICUs within a healthcare network leading them to conduct a quality improvement project. Upon further review of each NICU, it was noted that systems of care and standards of practice varied based on healthcare provider habit or history of the unit. Hans et al (2009) believe this type of practice is due to a lack of knowledge, systematic planning and practice implementation. Whereas, Ehrenkranz (2007) & Martin et al. (2009) believe this type of practice is due to the lack of evidence based CPGs. Therefore, the purpose of this doctoral project is to provide an evidence based CPG on the nutritional management of the ELBW infant.

The aim of this CPG is to guide clinical practice in the nutritional management of the ELBW infant from birth to hospital discharge. The evidence based recommendations address fluid and electrolyte management, energy and mineral intake, glucose administration, early aggressive nutrition, enteral feedings, and nutritional assessment. These recommendations are centered on promoting adequate extrauterine growth of the ELBW infant in order to prevent or at least decrease EUGR.

CHAPTER 2

REVIEW OF THE LITERATURE

This chapter is presented in three parts. Part I presents an overview of evidence based practice (EBP), Clinical practice guidelines (CPG) and CPG development, formulation of clinical questions, systematic reviews, and evidence grading. Part II presents an overview of clinical situations that must be considered in the nutritional management of the ELBW infant. Part III provides evidence tables developed from a review of the literature detailing the supportive data for this doctoral project.

The review of the literature was completed using Pubmed, The Cochrane Database of Systematic Reviews, and Cumulative Index to Nursing and Allied Health Literature (CINAHL) electronic databases. The literature search was restricted to include articles in the English language but no restrictions were placed on publication date or type of research study. Search terms included laboratory assessment, nutritional assessment, growth and growth assessment, premature infant, low birth weight infant, very low birth weight infant, and extremely low birth weight infant.

PART I: OVERVIEW

EVIDENCE BASED PRACTICE

In *Crossing the Quality Chasm: A New Health System for the 21st Century*, the Institute of Medicine (IOM) (2001) points out that the U.S. healthcare system lacks sufficient design to promote quality care due to an abundance of research not being translated into practice within a timely manner. This report is credited with highlighting the need for EBP, which is a problem solving approach that integrates the best evidence from systematic research with clinical expertise and patient values to make clinical care decisions (Fineout-Overholt, Levin & Melnyk, 2004; Mateo & Kirchhoff, 2009; Newhouse, Dearholt, Poe, Pugh & White, 2007). Generally, EBP is considered a process that includes: asking a clinical question in the PICO format, utilizing systematic reviews to evaluate and summarize the evidence, translating the evidence into CPGs and evaluating the outcomes (Fineout-Overholt, et al., 2004) The aim of EBP is to decrease variation in clinical practice that utilizes the best evidence to improve clinical care processes and outcomes.

CLINICAL PRACTICE GUIDELINES

A CPG is a set of systematically developed statements designed to guide clinicians and patients in their decisions about the appropriate health care for specific clinical conditions (IOM, 2008). The recommendations included in a CPG should be linked to the scientific research that supports them which is identified through a rigorous process of systematic review and appraisal of the literature (Hargrove, Griffer & Lund, 2008; Melnyk, 2004; Poolman, Verheyen, Kerkhoffs, Bhandari & Schunemann, 2009; Turner, Misso, Harris & Green, 2008).Moreover, CPGs developed utilizing the evidence

obtained from systematic reviews may serve as key resources to translate the evidence for clinical practice, thus decreasing ineffective variation in practice and improving clinical outcomes.

CLINICAL PRACTICE GUIDELINE DEVELOPMENT PROCESS

The purpose of a CPG is to give clinicians and patients statements regarding the best evidence for making clinical health care decisions. However, many CPGs are being developed by national agencies and special interest groups leading to a decentralized process for CPG development creating bias and inherent problems with the final product (Bondmass, 2009; Clutter, 2009). In 2008, the IOM published *Knowing What Works in Health Care: A Roadmap for the Nation*, which called attention to the lack of standardization in the process for developing a CPG.

In 2008, the IOM recommended that clinical recommendations in CPGs be developed by a panel of experts who are knowledgeable of the clinical problem and are capable of understanding the relevant research in order to make a sound judgment. The process should also include two separate grading systems; one to grade the quality of evidence and one to grade the strength of evidence. Furthermore, the IOM (2008) pointed out that using a standardized transparent and scientifically rigorous process would result in trusted CPGs that would discourage undesirable practice variation while encouraging the use of interventions that are known to be effective.

CLINICAL QUESTION

The first step in developing a CPG is asking a clinical question, which needs to be as specific as possible, since it will drive the strategies used to search the evidence (Newhouse et al., 2007). The PICO format is most commonly used to narrow the clinical

question and clearly identify the problem and key words that may be used for searching the evidence. PICO stands for **P** patient **I** intervention **C** comparison with another intervention and **O** outcomes. Asking clinical questions in this format allows one to conduct a comprehensive literature review in a systematic way to identify clinical research studies that truly answer the question.

SYSTEMATIC REVIEW

Systematic reviews are a summary of the research evidence in evaluating clinical interventions intended to treat and/or prevent disease (Stevens, 2008). The systematic review process includes retrieving, critically appraising and synthesizing randomized controlled trials to answer a clinical question (Melnyk, 2004). According to the IOM (2008) conducting systematic reviews delineates what is known and not known about the effectiveness of a health intervention. Systematic reviews are considered to be the strongest level of evidence, which should be used when making clinical decisions.

GRADE SYSTEM

The GRADE (Grades of Recommendation, Assessment, Development and Evaluation) System provides a comprehensive, precise and transparent method for grading the quality of evidence and the strength of recommendations included in CPGs (Brozek et al., 2009; Guyatt, 2011). GRADE categorizes evidence as high, moderate, low and very low depending on a study's methodology, consistency, precision and directness. The strength of a recommendation is categorized as strong or weak depending on the desirable effects of the intervention.

The GRADE system provides a simple and transparent but rigorous approach to grading the quality of evidence and the strength of recommendations when developing

CPGs. The use of such a simplistic and transparent system to develop CPGs not only meets the IOM's recommendations but the use of GRADE makes it easier for patients and their healthcare providers to interpret recommendations in a CPG when making clinical care decisions (Guyatt, 2008).

Part II: THE EXTREMELY LOW BIRTHWEIGHT INFANT

The ELBW infant is usually born during the last part of the second trimester or the early part of the third trimester (23-27 weeks gestation). The second and third trimesters of pregnancy are characterized as a time in gestation when increased growth and development of the fetus is occurring (Gleason & Devaskar, 2012). An infant born during this time in gestation has underdeveloped organs and organ systems. The immaturity of the ELBW infant and the limited ability of their organ systems to regulate body function pose unique clinical situations that must be considered when caring for such infants (Lee & Jain, 2000).

Fluid & Electrolyte Balance

The ELBW infant has a large amount of total body water due to a lack of fat tissue and a larger amount of lean body mass. At 24 weeks gestation, the fetus is estimated to have a total body water content of 90%, which is mostly contained in the extracellular space (Fusch & Jochum, 2005). This amount of fluid in the extracellular space results in a larger fluid load for the ELBW infant's immature kidneys to excrete during postnatal diuresis.

Postnatal diuresis occurs in three phases: the pre-diuretic phase, diuretic phase, and post-diuretic phase. The pre-diuretic phase occurs during the first 24-48 hours of life and is characterized by low urine output due to a fall in glomerular filtration rates (GFR) (Lee & Jain, 2000). Oliguria during the pre-diuretic phase is usually prolonged in the ELBW infant due to a lower fractional excretion of sodium (FENa) and the presence of respiratory distress (Fusch & Jochum, 2005). As respiratory distress resolves and FENa improves urine output starts to increase and is followed by the diuretic phase, which may

last 2-4 days. The diuretic phase is marked by high urine output and insensible water loss due to extracellular fluid volume contraction (Lee & Jain, 2000). During the diuretic phase, the ELBW infant is at high risk for fluid and electrolyte imbalances due to the large amount of insensible water loss (IWL) via the immature epidermal skin layer , which is estimated to be as high as 5-7ml/kg/day (Baumgart, 2008; Fusch & Jochum, 2005).

Fluid and electrolyte balance during the diuretic phase of postnatal diuresis is critical in the ELBW infant. Failure to replace IWL will result in dehydration and hypernatremia whereas failure to administer adequate sodium at a time of high FENa results in hyponatremia (Bhatia, 2006). Potassium balance is also affected by the amount of IWL and the ELBW infant may experience non-oliguric hyperkalemia that occurs when intracellular potassium shifts out of the cell due to the contraction of the extracellular fluid compartment (Baumgart, 2008). The increased level of extracellular potassium coupled with the ELBW infant's diminished capability of excreting potassium during the diuretic phase of postnatal diuresis leads to further elevation of potassium levels and the possibility of cardiac arrhythmias (Lee & Jain, 2000).

The post diuretic phase of postnatal diuresis usually occurs within 1-2 weeks of life when urine output normalizes and the infant reaches a steady state of fluid balance (Fusch & Jochum, 2005). This phase marks the completion of extracellular fluid volume contraction, a decrease in total body water, and an increase in cell mass (Lee & Jain, 2000). Postnatal diuresis results in a large amount of fluid loss and postnatal weight loss for the ELBW infant. Although weight loss is expected during postnatal diuresis the

ELBW infant loses 5-10% more of their birth weight than preterm infants born at higher gestational ages (Fusch & Jochum, 2005).

Energy Requirements

The ELBW infant has a large body surface area relative to body mass and is poorly insulated due to their thin skin and lack of subcutaneous fat stores leading to rapid heat loss and the need for increased energy to maintain a normal body temperature (Lee & Jain, 2000). IWL during postnatal diuresis further increases the energy needed for the ELBW infant to maintain their own temperature (Hay, 1994). Although placing ELBW infants in heated and humidified double walled isolettes improves thermoregulation their energy requirements to promote growth an adequate weight are higher than the average growing premature infant (Carr, Denne & Leitch, 2000).

Glucose Management

Glucose is the predominant source of energy provided to the ELBW infant postnatally. In-utero, glucose is delivered via the placenta at a rate that meets fetal energy needs and is dependent on maternal glucose concentrations with glycogen stores increasing throughout gestation (Clark et al., 2003). Birth of the ELBW infant results in minimal to no glycogen stores and poor glucose synthesis due to immature enzymes responsible for gluconeogenesis (Thureen & Hay, 2008). Decreased glycogen stores and inadequate glucose synthesis place the ELBW infant at high risk for hypoglycemia especially when faced with the stress from hypothermia, respiratory distress, and possible sepsis (Lee & Jain, 2000).

The ELBW infant's risk of hypoglycemia and high energy needs leads the clinician to administer high rates of glucose. The inability of the ELBW infant to regulate

insulin production and glucose synthesis due to stress results in glucose intolerance and hyperglycemia (Hay, 1994). Hyperglycemia in the ELBW infant leads to a hyperosmolar state, osmotic diuresis and further fluid and electrolyte imbalances (Lee & Jain, 2000).

Respiratory Complications

Managing early fluid and electrolyte imbalances in the ELBW infant can be quite difficult especially when the treatment for respiratory distress syndrome (RDS) and patent ductus arteriosus (PDA) involves restricting fluid intake for a period of time (Baumgart, 2008). RDS is a lung disease seen only in premature infants due to a lack of surfactant production. Surfactant is a phospholipid produced by type II pneumocytes, which are first seen at 24 weeks gestation and mark the beginning of saccular development of the lungs (Jobe, 2008) The saccular phase of lung development is when gas exchange begins to occur and defines the viability of an ELBW infant (Rutter & Post, 2008).The lack of surfactant in the ELBW infant adversely affects pulmonary function due to an increase in atelectasis, poor pulmonary compliance and necrosis of epithelial tissue in the lungs (Lee & Jain, 2000). Synthetic surfactant does exist and rapidly improves pulmonary function once it is given. But, positive pressure and mechanical ventilation are still needed to support the ELBW infant.

Prolonged mechanical ventilation with positive pressure results in remodeling of the ELBW infant's lung tissue (Rutter & Post, 2008). Positive pressure destroys epithelial tissue in the lung causing pulmonary edema from leakage of protein and extravascular fluid into the terminal conducting airways (Lee & Jain, 2000). Continued exposure to positive pressure ventilation promotes further destruction to lung tissue resulting in chronic lung changes and the development of bronchopulmonary dysplasia (BPD).

BPD is the need for oxygen at 36 weeks postconceptual age (PCA) along with chest x-ray findings of pulmonary fibrosis and emphysematous changes (Walsh, 2008). The cause of BPD is multi-factorial and is the result of immature lungs damaged by mechanical ventilation and oxygen toxicity resulting in inflammation and cellular injury from oxygen radicals (Belik, 2008; Oh et al., 2005). Inflammation and cellular injury increase the need for ventilation causing a continual cycle of inflammation, cellular injury and pulmonary edema.

Developing BPD can be prevented if appropriate management strategies of RDS are utilized within the first few weeks of life. Treatment of RDS focuses on surfactant administration to decrease alveolar surface tension and improve pulmonary compliance (Jobe, 2008). The use of fluid restriction is meant to prevent pulmonary edema thereby reducing the need for high amounts of positive pressure and prolonged mechanical ventilation that lead to the development of BPD (Oh et al., 2005).

Cardiovascular Complications

The development of BPD may also be influenced by the presence of a PDA within the first few weeks of life (Stephens et al., 2008). A PDA occurs when the fetal shunt called the ductus arteriosus (DA) fails to close after birth. In utero, blood enters the pulmonary artery from the left ventricle but is shunted through the DA due to high resistance in the pulmonary vasculature (Lee & Jain, 2000). After birth, the pulmonary vasculature decreases significantly in response to a high oxygen environment leading to closure of the DA (Gleason & Devaskar, 2012). The ELBW infant is born with RDS and lacks sufficient intra-arterial oxygen concentrations and arterial musculature to close the DA resulting in a PDA (Baumgart, 2008).

A PDA allows oxygenated blood from the aorta to shunt across the DA into the lungs resulting in pulmonary edema. The shunting of blood across the DA results in hypotension and decreased systemic perfusion. A PDA left untreated may result in congestive heart failure and decreased kidney perfusion resulting in low urine output (Baumgart, 2008).

The treatment of a PDA is aimed at closing the DA. Medications can be given that work to decrease prostaglandin synthesis thought to be a contributor in the persistence of a PDA after birth. However, initial fluid restriction during the first few days of life is recommended to prevent fluid volume overload that may occur before postnatal diuresis takes place (Stephens et al., 2008).

Gastrointestinal Complications

Fluid volume overload during the first week of life has been associated with an increased risk for necrotizing enterocolitis (NEC) (Bell & Accargeui, 2010). NEC is a disease more commonly seen in premature infants and its incidence increases as gestational age decreases (Neu, 2008). The exact pathogenesis of NEC is currently unknown. But certain factors are known to be associated with its development, which includes: an immature gastrointestinal system with a decreased barrier function, presence of an infectious organism, commencement of enteral feedings that provide a substrate for infection, and a possible ischemic or thromboembolic event (Lee & Jain, 2000; Neu, 2008).

The clinical manifestations of NEC are characterized by abdominal distension and tenderness, feeding intolerance with large feeding residuals, bloody stools, bowel perforation, and intestinal necrosis. The diagnosis of NEC is done with abdominal x-ray

where pneumatosis intestinalis, or gas in the bowel wall, is seen (Neu, 2008). Treatment of NEC involves antibiotic therapy, gastric decompression, and in the most severe cases surgical resection of the necrotic bowel with ilieostomy.

The severity of NEC and its associated morbidity and mortality have resulted in care providers withholding enteral feedings during the first few weeks of life in the ELBW infant (Adamkin, 2005). Withholding feedings to prevent NEC for long periods of time has been known to cause intestinal atrophy and further delay the development of the ELBW infant's gastrointestinal system (Neu, 2008). Prolonged periods of NPO status require the ELBW infant to receive total parenteral nutrition (TPN) for weeks and even months at a time placing them at risk for poor growth and nutritional deficiencies.

Metabolic Complications

One of the most common nutritional deficiencies seen in the ELBW infant is osteopenia of prematurity. Osteopenia of prematurity is a metabolic bone disease due to poor bone mineralization in the premature infant (Greer, 2008). The disease is characterized by calcium, phosphorus and vitamin D deficiencies. The disruption in mineral supply that occurs upon birth results in a bone remodeling process that increases bone resorption thereby decreasing bone density in the ELBW infant (Rigo, Pieltain, Salle & Senterre, 2007). Failure to provide adequate calcium, phosphorus and vitamin D exacerbates bone resorption leading to bone mineral content changes and possible fractures.

Neurodevelopment

Failure to provide adequate nutritional support in the ELBW infant not only results in poor bone mineralization but it decreases extrauterine growth resulting in poor

neurodevelopmental outcomes. Ehrenkranz et al. (2006) found that when extrauterine growth was increased from 12 to 21 grams/kg/day the incidence of cerebral palsy, abnormal neurologic examination and impaired neurodevelopment fell significantly. Stephens et al. (2009) found that the early administration of energy and protein in ELBW infants improved their neurodevelopmental outcomes. An increase of 10kcal/kg/day improved performance on the mental development index (MDI) by 4.6 points and for every gram/kg increase in protein intake MDI scores improved by 8.6 points (Stephens, et al., 2009).

Neurodevelopment is perhaps the most important outcome for the ELBW infant since they are born with an immature brain and nervous system. Intraventricular hemorrhage (IVH) is common in the ELBW infant due to their inability to regulate cerebral blood flow resulting in the rupture of blood vessels located in the germinal matrix, which is a highly vascularized area of the brain that regresses in size as gestation progresses and fully involutes at 34-36 weeks (Lee & Jain, 2000). In addition, malnutrition during a time of early brain development leads to the overall decrease in brain cells leading to memory loss, behavior issues and learning deficits (Ehrenkranz et al., 2006).

PART III: EVIDENCE TABLES

Fluid & Electrolyte Management

PICO Question: What type of fluid and electrolyte regimen meets the fluid and electrolyte needs of the ELBW infant?

Search terms: fluid intake, water intake, electrolyte requirement, sodium intake, potassium intake, fluid and electrolyte management, premature infant, low birth weight infant, very low birth weight infant, and extremely low birth weight infant

Summary of findings:

A systematic review of premature infants and two observational studies in ELBW infants supported fluid restriction to prevent PDA, NEC, and BPD. Two RCTs were done in ELBW infants and found sodium restriction during the first few days of life promotes postnatal diuresis. An observational study in ELBW infants found that potassium should also be held in the first few days of life due to the risk of non-oliguric hyperkalemia. However, no studies were found that addressed daily maintenance requirements for sodium or potassium supplementation so, recommendations from the 2004 American Academy of Pediatrics (AAP) Committee on Nutrition were used.

Insensible Water Loss

PICO Question: Does humidification improve fluid and electrolyte management of the ELBW infant?

Search Terms: insensible water loss, fluid and electrolyte management, premature infant, low birth weight infant, very low birth weight infant, and extremely low birth weight

Summary of findings:

Clinical trials to determine the use of humidity to improve fluid and electrolyte balance in the ELBW are lacking. Two retrospective chart reviews were done after humidified isolettes were implemented in two different NICUs with similar findings of improved fluid and electrolyte management along with a decrease in insensible water loss.

Table 1: Fluid & Electrolyte Management

Author/Year	Study Design Level of Evidence		Study Purpose/Study Sample Study Intervention/Study Outcome	Results	GRADE Quality of Evidence
Fluid Management					
Bell & Acarregui 2010	Systematic Review	I	**Purpose:** To investigate the effect of water intake on postnatal weight loss. The risks of dehydration, PDA, NEC, BPD, IVH and death in premature infants. **Sample:** 5 RCTs including preterm infants born at less than 37 weeks gestation**.** **Intervention:** Varying intakes of water given intravenously. **Primary Outcomes:** postnatal weight loss, dehydration **Secondary Outcomes:** PDA, NEC, BPD, oxygen requirement at 28 days of life and 36 weeks PCA, IVH, and death before discharge.	Fluid restriction resulted in a higher postnatal weight loss. The risk of PDA, NEC, and death was significantly lower with fluid restriction. Water intake had no significant effect on BPD or IVH in premature infants. Fluid restriction had a non-significant trend toward dehydration.	High **Study Limitations** None
Oh et al., 2005	Retrospective Review of RCT	IV	**Purpose:** To determine the association between fluid intake and postnatal weight loss on the development of BPD among ELBW infants. **Sample:** 1,382 ELBW infants born from October 1999-August 2001 included in the Neonatal Research Network Study on Glutamine Supplementation. **Intervention:** Varying fluid and sodium intake determined by the attending neonatologist. **Outcomes**: weight loss, BPD, and death	Higher fluid intake given during the 2nd to 10th day of life was associated with the development of BPD. Infants given a higher amount of fluid had less weight loss and a significantly higher risk of BPD and death.	Low **Study Limitations** Retrospective Review
Stephens et al., 2008	Retrospective Cohort	IV	**Purpose:** To determine the effect of fluid intake on PDA, BPD and caloric intake in the ELBW infant. **Sample:** 204 infants born at less than 32 weeks gestation and less than 1,250 grams. **Intervention:** Infants were divided into 3 groups based on the amount of fluid intake prescribed by the attending neonatologist **Outcomes:** PDA, BPD, and caloric intake	Infants who required the highest fluid intake were of lower gestational age and birth weight and had increased rates of PDA. The amount of fluids given during the first 3 days of life and during the first week of life was significantly associated with higher rates of BPD and PDA. Fluid intake (>170ml/kg/d) administered in the first few days of life is significantly associated with higher PDA rates. No difference in caloric intake was found.	Low **Study Limitations** Retrospective Chart Review
Insensible Water Loss					
Gaylord, Wright, Lorch, Lorch & Walker, 2001	Retrospective Chart Review	IV	**Purpose:** To compare fluid and electrolyte management in ELBW infants nursed in humidified versus non-humidified isolettes. **Sample:** 155 ELBW infants admitted the NICU over a 4 year period. **Intervention:** care provided in a humidified versus a non-humidified isolette. **Primary Outcomes:** total daily fluid requirement, weight, urine output, serum electrolytes, incidence of PDA and BPD.	Infants who were not cared for in humidified isolettes had higher fluid intake, less hourly urine output and more likely to have hypernatremia, hyperkalemia, and azotemia. No difference in the incidence of BPD or PDA between the groups. A higher number of gram negative isolates were found in the group who received humdification.	Low **Study Limitations** Retrospective Chart Review

Kim, Lee, Chen & Ringer, 2010	Retrospective Chart Review	IV	**Purpose:** To identify changes in temperature, fluid and electrolyte management, growth and short term outcomes in ELBW infants nurse in humidified hybrid incubators compared to a cohort of patients cared for in a non-humidified incubator. **Sample:** 182 ELBW infants admitted to the NICU over a 3 year period. **Intervention:** care provided in a hybrid humidified isolette versus non-humidified isolette. **Primary Outcomes:** temperature control, fluid intake, electrolyte balance, growth velocity. **Secondary Outcomes:** mortality, PDA, BPD, NEC, IVH and sepsis.	Infants who received care in the hybrid humidified isolette had less fluid intake, urine output, insensible water loss, weight loss, and hypernatremia during the first week of life. Infants in the hybrid humidified isolette had less lab draws for electrolytes and less blood transfusions. Infants in the hybrid humidified isolettes had a higher incidence of hyponatremia on postnatal day 1 and higher growth velocity. Benefits were of the humidified hybrid isolette were more pronounced in infants with weight less than 750 grams. No difference in sepsis, NEC, IVH, or BPD, but infants who received care in a non-humidified isolette had an increased incidence of severe BPD and need for mechanical ventilation.	Low **Study Limitations** Retrospective Chart Review
Sodium Supplementation					
Costarino, Gruskay, Corcoran, Polin & Baumgart, 1992	RCT	II	**Purpose:** To compare a salt restricted parenteral fluid regimen to a salt supplemented regimen. **Sample:** 17 infants born at less than or equal to 28 week gestation with a birth weight less than 1,000 grams **Intervention:** Sodium supplementation with 3-4meq/kg/day given for 5 days (treatment) versus no sodium given for 5 days (control). **Outcomes:** sodium intake, fluid intake, urine output, FENa, and GFR.	Sodium supplementation resulted in sodium balance of zero during the first 5 days of life. Sodium restricted infants had high rates of sodium excretion promoting a negative sodium balance. Increased fluid intake was noted in infants supplemented with sodium. Infants who were sodium restricted were more likely to have a normal serum osmolality and a decreased incidence of BPD. Both groups had neither dilute nor concentrated urine and had a high rate of FENa.	High **Study Limitations** None
Shaffer & Meade, 1989	RCT	II	**Purpose:** To assess extracellular fluid volume regulation in very low birth weight infants. **Sample:** 20 infants with a birth weight between 700 and 1,500 grams. **Intervention:** 3meq/kg/day of sodium versus 1meq/kg/day given intravenously or by mouth. **Outcomes:** sodium intake, sodium balance, body water composition	Serum sodium levels increased significantly in both groups. Body weight decreased in both groups during the first 5 days of life. ECFV* decreased in both groups during the first 10 days of life and stabilized. Sodium balance was negative in both groups but became positive by 10 days of age. Sodium excretion was higher in the 3meg/kg/day group during the first 10 days of life; after days 20 and 30 with no difference. Urine sodium and FENa increased in the 3meq/kg/day group between days 1 and 5 of life whereas urine sodium and FENa decreased in the 1meq/kg/day group. Hyponatremia occurred more often in the 1meq/kg/day group.	Moderate **Study Limitations** No discussion of blinding or allocation concealment

Potassium Supplementation					
Lorenz, Kleinman & Markarian, 1997	Observational Cohort	IV	**Purpose:** To characterize potassium metabolism during the three phases of fluid and electrolyte homeostasis. **Sample:** 31 infants with birth weight less than 1,000 grams **Intervention:** Use of potassium plasma concentration, potassium intake and output, and renal clearances to determine potassium metabolism **Primary Outcomes:** serum potassium values.	Potassium values increased initially after birth despite potassium supplementation. Serum potassium levels peaked upon postnatal diuresis and decreased significantly once postnatal diuresis was complete. Infants who developed hyperkalemia were noted to have higher serum potassium levels within 12 hours of birth. Potassium excretion decreased after postnatal diuresis despite an increase in potassium supplementation.	Low **Study Limitations** None

Note. ECFV=extracellular fluid volume

Mineral Requirements

PICO Question: What intake of calcium, phosphorus, and magnesium is required to meet the needs of the ELBW infant and promote bone mineralization?

Search Terms: calcium intake, phosphorus intake, magnesium intake, mineral intake, bone mineralization, osteopenia of prematurity, premature infant, low birth weight infant, very low birth weight infant and extremely low birth weight infant.

Summary of findings:

The recommended intake of calcium, phosphorus and magnesium has been estimated based on intrauterine accretion rates (AAP Committee on Nutrition, 2004). One RCT in infants less than 1,200 grams investigated using higher intakes of calcium and phosphorus in parenteral nutrition to improve mineral retention and bone mineral content and found administering higher rates of calcium and phosphorus in TPN improved early and long term bone mineralization.

Table 2: Mineral Requirements

Author/Year	Study Design Level of Evidence		Study Purpose/Study Sample Study Intervention/Study Outcome	Results	GRADE Quality of Evidence
Prestidge, Schanler, Shulman, Burns & Laine, 1993	RCT	I	**Purpose:** To determine the accumulative effects of increasing the quantities of calcium and phosphorus in TPN. **Sample:** 24 infants with birth weight less than 1,200 grams expected to have parenteral nutrition for at least 3 weeks. **Intervention:** Standard concentration of calcium (1.25mmol) and phosphorus (1.5mmol) in parenteral nutrition versus High concentration of calcium (1.7mmol) and phosphorus (2mmol) in parenteral nutrition. **Outcomes:** retention of calcium and phosphorus and BMC*.	Improved calcium and phosphorus retention was significantly higher in the HIGH group. Serum calcium, magnesium, parathyroid hormone, 25-hydroxyvitamin D, and osteocalcin were similar in both groups. Serum phosphorus levels were significantly higher in the HIGH group. BMC* and the rates of increase in BMC* were improved between weeks 1 and 4, 1 and 8, and 1 and 26 weeks PCA* in the HIGH. TPN used in this study contained cysteine	High **Study Limitations** None

Note. BMC=bone mineral content

Energy Requirements

PICO Question: How many calories are needed to meet the energy expenditure of the ELBW infant?

Search Terms: energy intake, caloric intake, energy expenditure, energy balance, premature infant, low birth weight infant, very low birth weight infant, and extremely low birth weight infant

Summary of Findings:

Evidence is lacking to determine the energy requirements for the ELBW infant with most of the studies being conducted in healthy growing premature infants. One observational study compared energy expenditure in a group of ELBW infants to a group of critically ill term infants and found that energy expenditure in the ELBW was much higher than current estimates. A RCT investigated energy intake along with varying amounts of protein intake and found that a higher caloric intake of greater than 70kcal/kg/day given with 2.7-3.5g/kg/day of protein leads to improved nitrogen retention and increased weight gain. Expert opinion recommends providing enough caloric intake to mimic intrauterine growth rates with energy requirements estimated utilizing the studies included in the evidence table (Hay, 2005; Leitch & Denne, 2005).

Table 3: Energy Requirements

Author/Year	Study Design Level of Evidence		Study Purpose/Study Sample Study Intervention/Study Outcome	Results	GRADE Quality of Evidence
Carr, Denne & Leitch, 2000	Observational Cohort	IV	**Purpose:** To compare total daily energy expenditures and energy intakes in extremely premature infants to critically ill and healthy term infants. **Sample:** 10 ELBW infants less than 28 weeks gestation. **Intervention:** Measurement of total energy expenditure and total body water using a double labeled water method in ELBW and term infants given varying caloric intake. **Primary Outcomes:** total energy expenditure, total body water, energy intake.	Total energy expenditure was higher in the extremely premature infant and estimated to 84.1±33.3kcal/kg/day.	Low **Study Limitations** Study findings were in abstract form only.
Zlotkin, Bryan & Anderson, 1981	RCT	II	**Purpose:** To evaluate the individual and combined effects of energy and nitrogen intake on nitrogen retention and growth. **Sample:** 22 appropriate for gestational age premature infants greater than 4 days of age. **Intervention:** Group 1: 50kcal/kg/d + 80mg/kg/d N* Group 2: 50kcal/kg/d + 640mg/kg/d N* Group 3: 80kcal/kg/d + 320mg/kg/d N* Group 4: 80kcal/kg/d + 480mg/kg/d N*Group 5: 80kcal/kg/d + 640mg/kg/d N* Group 1 & 2 received glucose as sole energy source. Group 3-5 were randomly assigned and received energy as glucose plus IL*. **Outcomes:** N* balance and weight gain.	Increased non-protein energy resulted in improved nitrogen retention and weight gain. Increasing nitrogen intake while leaving energy intake constant had no effect on nitrogen retention. Increasing energy intake along with nitrogen intake correlated significantly with improved nitrogen retention. Providing energy intake of greater than 70kcal/kg/day and 2.7-3.5g of protein/kg/d resulted in duplication of intrauterine nitrogen accretion rates.	Moderate **Study Limitations** Lack of blinding. No discussion of allocation concealment

Note. IL=intralipid, N=nitrogen

Glucose Management

PICO Question: What glucose infusion rate meets the needs of the ELBW infant? Should hyperglycemia in the ELBW infant be treated with glucose restriction or insulin infusion?

Search Terms: glucose infusion rate, glucose infusion, intravenous glucose, hyperglycemia, premature infant, low birth weight infant, very low birth weight infant, and extremely low birth weight infant

Summary of findings:

Clinical trials are lacking to determine the appropriate glucose infusion rate for the ELBW infant so, experts suggest utilizing intrauterine glucose infusion rates as a guide for administering glucose to the ELBW infant (AAP Committee on Nutrition, 2004; Hay, 2005). Two systematic reviews were found, one that addresses the prevention of hyperglycemia and one that addresses the treatment of hyperglycemia. Findings in these systematic reviews confirm the lack of evidence in determining the appropriate glucose infusion rate for administering glucose and in treating hyperglycemia in the ELBW infant. The use of insulin to prevent hyperglycemia is not recommended due the high rate of death before 28 days of age associated with using insulin as a prophylaxis against hyperglycemia.

Table 4: Glucose Management

Author/Year	Study Design Level of Evidence		Study Purpose/Study Sample Study Intervention/Study Outcome	Results	GRADE Quality of Evidence
Sinclair, Bottino & Cowett, 2011	Systematic Review	I	**Purpose:** To assess the effects of interventions for prevention of neonatal hyperglycemia in infants with birth weights less than 1,500 grams receiving or intending to receive total or partial parenteral nutrition **Sample:** 4 RCTs involving infants less than 32 weeks gestation and birth weight less than 1,500 grams receiving or intended to receive parenteral nutrition without hyperglycemia at the start of the study. **Intervention:** Restriction versus no restriction of glucose infusion. Insulin therapy versus restriction in the rate of glucose infusion. Insulin therapy versus no restriction in the rate of glucose. **Primary Outcomes:** mortality, neurodevelopmental impairment, growth at 36 weeks PCA, blood glucose concentrations **Secondary outcomes:** caloric intake, cumulative parenteral glucose intake, hypoglycemia, nitrogen accretion, sepsis, NEC, CLD*, length of hospital stay, and levels of insulin growth factor.	Insufficient evidence exists to inform clinical practice on the rate of glucose infusion. Insulin decreases blood sugar levels but its use to prevent hyperglycemia is not recommended for practice as it is associated with death before 28 days of age.	High **Study Limitations** None
Bottino, Cowett & Sinclair, 2011	Systematic Review	I	**Purpose:** To examine the effects of interventions for treating neonatal hyperglycemia in the very low birth weight infant who is receiving total or partial parenteral nutrition. **Sample**: 2 RCTs involving infants with birth weight less than 1,500 grams and born at less than 32 weeks gestation. **Intervention:** Reduction of glucose infusion rate versus no reduction in glucose infusion rate. Insulin infusion versus no reduction in glucose infusion rate. Insulin infusion versus reduction in glucose infusion rate. **Primary outcome:** all cause mortality, neurodevelopmental impairment, severe IVH, ROP*, bacterial and fungal sepsis **Secondary outcomes:** time to resolve hyperglycemia, recurrent episodes of hyperglycemia, hypoglycemia, caloric intake, NEC, duration of mechanical ventilation, CLD*, and length of hospital stay.	Insufficient evidence exists to determine if treatment interventions for hyperglycemia are associated with an increased risk of morbidity or mortality. Insulin infusion was associated with a higher intake of energy and glucose resulting in improvement in short term growth, but the importance of these outcomes could not be determined.	High **Study Limitations** None

Note. CLD=chronic lung disease, ROP=retinopathy of prematurity

Early Aggressive Nutrition

PICO Question: Does an early aggressive nutrition plan that includes early administration of amino acids, intralipids, and minimal enteral feedings improve growth of the ELBW infant?

Search Terms: total parenteral nutrition, amino acid intake, protein intake, intravenous amino acids, intravenous fat emulsion, intralipid, intravenous fat, lipid infusion, parenteral lipid, lipid emulsion, trophic feedings, minimal enteral feedings, growth, premature infant, low birth weight infant, very low birth weight infant, and extremely low birth weight infant.

Summary of findings:

Clinical studies to determine the best nutritional method for promoting growth in the ELBW infant are minimal. Most studies include very low birth weight (VLBW) infants who weigh less than 1,500 in order to obtain an adequate sample size. Two RCTs have shown that an early aggressive nutritional regimen leads to an improved caloric intake within the first few days of life as well as a positive nitrogen balance. In one of the RCTs early aggressive nutrition was associated with improved growth within the first week of life and prior to discharge.

Part of early nutrition requires the administration of amino acids and intralipids shortly after birth. Eleven RCTs have been conducted to examine the effect of early administration versus the late administration of amino acids in premature infants with birth weights ranging from 500 grams to 2,000 grams. The early administration of protein has been shown to prevent catabolism, promote nitrogen balance and protein synthesis without increasing blood urea nitrogen (BUN) levels and disrupting acid base balance. A

systematic review of early intralipid administration found that no adverse effects were associated with intralipid administration but its use could not be recommended for promoting short term growth.

Minimal enteral feedings (MEF) or trophic feedings are the last component of an early aggressive nutrition plan. In a systematic review trophic feedings were found to have no statistical effect on growth or development, but no harm or adverse effects including NEC were found to be associated with administering trophic feedings. These findings were further supported in another systematic review that found delaying enteral nutrition did not reduce the risk of NEC.

Table 5: Early Aggressive Nutrition

Author/Year	Study Design Level of Evidence		Study Purpose/Study Sample Study Intervention/Study Outcome	Results	GRADE Quality of Evidence
Early Aggressive Nutrition					
Ibrahim, et al., 2004	RCT	II	**Purpose:** To determine if early aggressive TPN vs. late TPN will improve nitrogen and energy balance. To determine if any complications with early aggressive TPN will occur. **Sample:** 32 infants with birth weights between 501 to 1250 grams and gestational ages of 24 to 32 weeks. **Intervention:** Early TPN: 3.5g/kg/d of AA* +3g/kg of IL* within 2 hours of birth versus Late TPN: Dextrose and 2g/kg AA* at 48h of life + 0.5g/kg of IL* 48h after, which both increased by 0.5g/kg/d to a max of 3.5g/kg AA* and 3g/kg IL* **Primary outcomes:** Nitrogen balance and caloric intake. **Secondary outcomes:** BPD, IVH, PDA, ROP*, and sepsis.	Early TPN= higher nitrogen retention, higher caloric intake within 5 days of life and greater mean serum bilirubin levels with no clinical difference. Late TPN group= higher mean serum glucose concentrations. No difference in complications.	Moderate **Study Limitations** No blinding of intervention
Wilson et al., 1997	RCT	II	**Purpose:** To improve energy intake in sick VLBW infants; to decrease growth problems, lessen pulmonary morbidity, shorten hospital stay, and avoid possible feeding related morbidities with an early aggressive nutrition regimen. **Sample:** 125 infants with birth weight less than 1,200 grams or infants with birth weights of 1,200 to 1,499 grams requiring mechanical ventilation within 24 hours of birth **Intervention:** Control group: Glucose alone until DOL 3 AA* 1g/kg/d on DOL 3 advanced by 0.5/g/kg/d to max of 2g/kg/d; IL* 0.5g/kg/d on DOL* 5 advanced by 0.5g/kg/d to max of 2g/kg/d Enteral feeds introduced when clinically stable. Treatment Group: Glucose +AA* at 0.5g/kg advanced by 0.5g/kg/d to a max of 3.5g/kg/d; IL* 0.5g/kg/d started DOL* 2 advanced by 0.5g/kg/d to max of 3.5g/kg/d. Enteral feeds 0.5ml/h at 12h of life. **Outcomes:** time to regain birth weight, days of oxygen therapy, days of mechanical ventilation and days to discharge.	Infants who received early aggressive nutrition had higher energy intake with less weight loss after birth and took less time to regain their birth weight. Infants in the treatment group had improved weight gain, length and head circumference at discharge. No difference was found in length of stay or pulmonary morbidities.	High **Study Limitations** Interventions were unable to be blinded but clinical outcomes were pre-defined to help control for blinding. Observers of biochemical and radiological data were blinded to group assignment.
Early Administration of Protein					
Anderson, Beiber & Heird, 1979	RCT	II	**Purpose:** To determine the efficacy of two isocaloric nutrition regimens administered intravenously. **Sample:** 14 preterm infants appropriate for gestational age whose clinical condition precluded oral feedings for at least 5 days. **Intervention:** IV glucose vs. glucose + 2g/kg/day of AA* given for 5 days. **Outcomes:** electrolytes, BUN, acid base status, plasma AA* levels, nitrogen balance.	Infants who received AA* had positive nitrogen balance. Infants who received glucose alone had significantly lower total essential AA* and total AA* concentrations. Infants who received AA* developed essential fatty acid deficiency.	Moderate **Study Limitations** No blinding and no discussion of allocation concealment

Blanco et al., 2011	RCT	II	**Purpose:** To examine changes in plasma AA* levels over time when ELBW infants are provided standard AA* supplementation or an early and high AA* supplementation. **Sample:** 62 ELBW infant less than 12 hours of age. **Intervention:** AA* at 0.5g/kg/day started within 24 to 36 hours of life and advanced by 0.5g/kg/day to a maximum of 3g/kg/d and continued for 7 days vs. AA* at 2g/kg/day started within 24 hours of life and advanced by 1g/kg/day to a maximum of 4g/kg/day and continued for 7 days. **Outcomes:** AA* Levels	Total AA* concentrations, including essential and nonessential AA* concentrations were higher in the early and high AA* group. Essential and total AA* concentrations were higher at day 1 and 3 in the early and high AA* group. Non-essential AA* concentrations were only different on day 3 in the early and high AA* group.	High **Study Limitations** None
Clark, Chase & Spitzer, 2007	RCT	II	**Purpose:** To measure the effects of 2 distinct strategies for parenteral nutrition on neonatal growth and blood AA* profiles. **Sample:** 122 infants born at 23-29 6/7 weeks gestational age **Intervention:** 2.5g/kg/day of AA* (started at 1g/kg/d and advanced by 0.5g/kg/d-low group) vs. 3.5g/kg/day of AA* (started at 1.5g/kg/d and advanced by 1g/kg/d-high group). IL* started at same time as TPN at 0.5g/kg/d and advanced by 0.5/kg/d. GIR* rate 8-12mg/kg/min; no use of Insulin. AA* limited to 1g/kg/d for low AA* group; 2g/kg/d for high AA* group when feeds at 80-100ml/kg/d. Completed treatment once on full feedings. **Outcome:** growth and plasma AA* levels.	No difference between the two groups for growth or morbidities; Infants in the high AA* group had higher AA* levels than the low AA* group.	High **Study Limitations** None
Murdock, Crighton, Nelson & Forsyth, 1995	RCT	II	**Purpose:** To compare the biochemical tolerance of 3 different parenteral nutrition regimens administered within the first 48 hours of life. **Sample:** 29 infants with birth weight less than 2,000 grams who could not receive enteral feedings directly after birth. **Intervention:** 10% glucose infusion vs. 10% glucose infusion + AA* vs. 10% glucose infusion + AA* + IL* **Outcomes:** AA* profile, cholesterol, triglycerides, acid base status, glucose levels.	Plasma AA* fell immediately in the glucose only group. Hypoglycemia occurred more frequently in the glucose + AA* group and the least commonly in the glucose +AA*+ IL*. No difference in the groups for triglyceride and cholesterol levels within 48 hours of administering IL*.	Moderate **Study Limitations** No blinding or discussion of allocation concealment
Poindexter, Langer, Dusick & Ehrenkranz, 2006	RCT	II	**Purpose:** To determine whether early administration of parenteral AA* is associated with better growth and neurodevelopmental outcomes **Sample:** 1,018 infants with birth weight of 401 to 1,000 grams and enrolled within 72 hours of life. **Intervention:** Administration of 3g/kg/day or greater of AA* within first 5 days of life (early) vs. less than 3g/kg/day of AA* given in the first 5 DOL* (late). **Outcomes:** growth (weight, length and head circumference) and neurodevelopmental outcomes.	Significant difference in weight, length and head circumference at 36 weeks post conceptual age in favor of early AA* group. The odds of having a weight less than the 10th percentile was 4 fold higher in the late AA* group with male infants twice as likely to have a head circumference below the 10th percentile. No difference was found in neurological or developmental outcomes or growth parameters between the 2 groups at 18 months corrected age.	High **Study Limitations** None

Rivera, Bell & Bier, 1993	RCT	II	**Purpose:** To provide information on the safety and efficacy of AA* administration to low birth weight infants during the first 3 days of life. **Sample:** 23 preterm infants with RDS requiring mechanical ventilation and indwelling arterial catheters during the first 3 days of life. **Intervention:** Glucose alone vs. glucose +1.5g AA*/kg/day administered on the first day of life. **Outcomes:** nitrogen balance, AA* levels, protein kinetics, electrolytes, ammonia, and BUN levels.	Infants who received AA* had positive nitrogen balance, whole body protein balance as a result of increased protein synthesis. Early administration of AA* was deemed safe with no differences in electrolytes or ammonia, BUN levels.	Moderate **Study Limitations** No blinding
TeBraake, Van Den Akker, Wattimena, Huijmans & Van Goudoever, 2005	RCT	II	**Purpose:** To test the administration of 2.4grams AA*/kg/d in VLBW infants to see if it is safe and results in positive nitrogen balance. **Sample:** 135 premature infants with birth weight equal to or less than 1500 grams. **Intervention:** Administration of 2.4g/kg/d of AA* within 2H of birth and 5.5mg/kg/min of Glucose (treatment group) versus glucose at 5.5mg/kg/day after birth, with administration of 1.2g/kg/d AA* on the first day of life and advancement to 2.4g/kg/d on the third day of life (control group). **Outcomes:** Nitrogen balance, AA* concentrations, metabolic acidosis, and glucose levels.	Treatment group had more infants who received prenatal steroids. Treatment group had higher BUN levels on Day 2 with no difference in levels on Day 4. Treatment group had improved nitrogen intake, positive nitrogen balance on day 2, and higher AA* levels. No adverse effects were found between the two groups.	Moderate **Study Limitations** Caregivers were not blinded to the intervention and infants in the treatment group received more prenatal steroids.
Thureen, Melara, Fennessey & Hay, 2003	RCT	II	**Purpose:** To assess the safety and efficacy of early AA* intake mimicking intrauterine accretion rates **Sample:** 28 infants with birth weight less than or equal to 1,300 grams and requiring mechanical ventilation. **Intervention:** 1g/kg/d of AA* versus 3g/kg/d of AA* given intravenously. **Outcomes:** protein balance, acid base status, and BUN levels.	Infants receiving 3g/kg/d of AA* had increased protein accretion through increase protein synthesis rather than through the prevention of protein breakdown. No significant difference in metabolic acidosis, use of sodium bicarbonate or BUN levels.	Moderate **Study Limitations** Lack of blinding and no discussion of allocation concealment
Van Goudoever, et al., 1995	RCT	II	**Purpose:** To gain information on protein kinetics after AA* supplementation. **Sample:** 18 preterm infants less than 2,000 grams needing mechanical ventilation and umbilical catheters. **Intervention:** Glucose only (control) vs. Glucose + AA* delivered after birth. **Outcomes:** nitrogen balance, protein synthesis, AA* profile, blood pH, BUN and glucose levels.	No difference in blood pH, base excess, urea concentration or glucose levels. Total AA* concentration and essential AA* concentration were significantly lower and below references ranges in the control group. Nitrogen retention was improved in the treatment group. Improved protein balance due to enhanced protein synthesis rather than increased protein breakdown. Cysteine levels were highly predictive for protein synthesis in the treatment group.	Moderate **Study Limitations** Lack of blinding and no discussion of allocation concealment

Van Lingen, Van Goudoever, Luijendijk, Wattimena & Sauer, 1992	RCT	II	**Purpose:** To evaluate the effect of AA* administration given during the second day of life on protein turnover and nitrogen balance. **Sample:** 18 preterm infants appropriate for gestational age **Intervention:** Glucose alone was administered to both groups on the first postnatal day. Group A: glucose + AA*+IL* versus Group B: glucose + IL* until postnatal day 4 when AA* were added to the regimen. **Outcomes:** protein turnover and nitrogen balance.	Group A had higher protein flux and higher protein synthesis. No difference in protein breakdown between the 2 groups. Administration of AA* resulted in positive nitrogen balance. No adverse effects of AA* administration were found.	Moderate **Study Limitations** Lack of blinding and no discussion of allocation concealment
Early Administration of Intralipids					
Simmer & Roa, 2009	Systematic Review	I	**Purpose:** To assess the effect of early administration of IL* on growth, the risk of CLD* and other respiratory morbidities, NEC, IVH, ROP*, PDA, sepsis, thrombocytopenia, jaundice, and death in premature infants being fed parenterally. **Sample:** 7 RCTs assessing the effect of early versus late administration of IL* **Intervention:** Early introduction of IL* (less than 5 DOL*) versus late introduction of IL* (greater than 5 DOL*) **Primary Outcomes:** weight, length, head circumference, incidence CLD*, death **Secondary Outcomes:** respiratory morbidities, NEC, PDA, ROP*, IVH, sepsis, thrombocytopenia, and jaundice.	The early administration of IL* has no statistically significant effect on short term nutrition or other clinical outcomes. Neither benefits nor adverse outcomes were found in administering IL* early. The use of early administration of IL* cannot be recommended for short term growth or to prevent mortality or morbidity in premature infants.	High **Study Limitations** None
Minimal Enteral Feedings (MEF)					
Bombell & McGuire, 2009	Systematic Review	I	**Purpose:** To determine the effect of trophic feedings on feeding tolerance, growth and development, the incidence of NEC, infection, and mortality. **Sample:** 8 RCTs investigating trophic feedings in infants less than 32 weeks gestation and weighing less than 1,500 grams at birth. **Intervention:** Early trophic feeding (milk volumes up to 24ml/kg/day) within 4 days of birth continued for at least 7 days vs. enteral fasting for 1 week. **Primary Outcomes:** feeding tolerance, NEC. **Secondary Outcomes:** mortality prior to discharge, growth, neurodevelopment, infection, hyperbilirubinemia, and duration of hospital say.	Trophic feedings do not have a statistically significant effect on feeding tolerance, growth and development, NEC, infection or mortality. Trophic feedings were not associated with clinical harm.	High **Study Limitations** None

Morgan, Young & McGuire 2011	Systematic Review	I	**Purpose:** To determine the effect of delaying the advancement of enteral feedings on the incidence of NEC, mortality and other morbidities in very low birth weight infants **Sample:** 5 RCTs with 600 premature infants less than 32 weeks gestation with birth weights less than 1,500 grams **Intervention:** Delayed advancement of enteral feeds (more than 4 days after birth) vs. early advancement of enteral feedings **Primary Outcomes**: NEC and all cause mortality during the neonatal period and prior to hospital discharge. **Secondary Outcomes:** growth (short term and long term), neurodevelopment, time to establish full enteral feeding, time to establish oral feedings, feeding intolerance, incidence of invasive infection and length of stay.	Delaying the advancement of enteral feedings does not reduce the risk of NEC, mortality or other morbidities.	High **Study Limitations** None

Note. AA= amino acids, CLD=chronic lung disease, DOL= day of life GIR=glucose infusion rate, IL=intralipids, ROP=retinopathy of prematurity

Enteral Nutrition

Human Milk

PICO Question: What type of feeding (human milk or formula) promotes growth and has the least adverse outcomes for the ELBW infant?

Search Terms: human milk, breast milk, formula, term formula, preterm formula, premature infant, low birth weight infant, very low birth weight infant, extremely low birth weight infant

Summary of findings:

No RCTs have been done comparing maternal human milk to formula due to the ethical implications of conducting such a study. A systematic review compared donor human milk to formula and found those infants fed formula had a higher incidence of NEC. The AAP Section on Breastfeeding (2005) developed a policy statement for exclusive human milk feeding of all newborns including premature infants until at least six months of age.

Table 6: Human Milk

Author/Year	**Study Design Level of Evidence**		**Study Purpose/Study Sample Study Intervention/Study Outcome**	**Results**	**GRADE Quality of Evidence**
Quigley, Henderson, Anthony & McGuire, 2008	Systematic Review	I	**Purpose:** To determine the effect of feeding with formula vs. donor human milk on growth and development and adverse outcomes in preterm low birth weight infants **Sample:** 8 RCTs with 1,107 clinically stable preterm infants born at less than 32 weeks gestational age. **Intervention:** Formula milk feeding versus donor human milk feeding **Primary Outcomes:** short and long term growth, neurodevelopmental outcomes at 12months, severe neurodevelopmental disability, cognitive and educational outcomes at more than 5 years of age. **Secondary Outcomes:** mortality, NEC, time to establish full feedings, feeding intolerance, sepsis.	Infants who were fed formula had higher rates of short term growth when compared to infants fed donor human milk. Formula feeding was associated with a higher risk of developing NEC. No effect was found on long term growth or development.	High **Study Limitations** None

Feeding Route

PICO Question: Should feedings in the ELBW infant be given through an orogastric or nasogastric feeding tube?

Search Terms: feeding tube, feeding methods orogastric (OG) feedings, nasogastric (NG) feedings, premature infant, low birth weight infant, very low birth weight infant, and extremely low birth weight infant

Summary of findings:

One systematic review found insufficient evidence to support the routine use of nasogastric or orogastric tube feedings in preterm infants.

Table 7: Feeding Route

Author/Year	Study Design Level of Evidence		Study Purpose/Study Sample Study Intervention/Study Outcome	Results	GRADE Quality of Evidence
Hawes, McEwan & McGuire, 2008	Systematic Review	I	**Purpose:** To determine the effect of feeding tube placement (nasogastric (NG) vs. orogastric (OG)) on feeding, growth and development, and adverse consequences in preterm or low birth weight infants. **Sample:** 2 RCTs of preterm infants less than 37 weeks gestational age or low birth weight infants less than 2,500 grams **Intervention:** Enteral feedings given via NG route versus the OG route **Primary Outcomes:** time to establish full enteral feedings, time to regain birth weight, growth assessed at intervals starting at 6 months of age. **Secondary Outcomes:** time to establish full oral feedings, time to extubation, time to be without oxygen supplementation, duration of hospital stay, and adverse events (apnea, pneumonia, NEC, gastric or esophageal perforation, nasal deformities, and neurodevelopmental outcomes)	Insufficient evidence to support routine use of either NG or OG route for feedings.	High **Study Limitations** None

Time of feeding administration

PICO Question: Should feedings in the ELBW infant be administered as an intermittent bolus or as a continuous infusion?

Search terms: feeding methods, continuous, intermittent, enteral nutrition, enteral feedings, premature infant, low birth weight infant, very low birth weight infant and extremely low birth weight infant

Summary of findings:

One systematic review found no difference in feeding administration on the incidence of NEC but insufficient evidence exists to recommend continuous feedings or intermittent bolus feedings. The American Dietetic Association (ADA) Pediatric Nutrition Practice Group (2009) points out that continuous feedings may be appropriate in the ELBW infant who exhibits signs of feeding intolerance or gastroesophageal reflux (GER).

Table 8: Timing of Feeding Administration

Author/Year	**Study Design Level of Evidence**		**Study Purpose/Study Sample Study Intervention/Study Outcome**	**Results**	**GRADE Quality of Evidence**
Premji & Chessel, 2011	Systematic Review	I	**Purpose:** To determine the effectiveness of continuous versus intermittent gavage feeding as a feeding strategy in preterm infants weighing less than 1,500 grams. **Sample:** 7 RCTs with 511 premature infants with birth weight less than 1,500 grams **Intervention:** Continuous enteral feedings vs. intermittent bolus enteral feedings **Primary Outcomes:** feeding intolerance, days to regain birth weight, age at full enteral feedings, age at discharge, somatic growth, and NEC **Secondary Outcome:** Apnea	No difference was found in continuous or intermittent enteral feedings on the time to reach full enteral feedings regardless of tube placement. The reports of NEC between the two methods of feeding were similar. Authors concluded not enough evidence exists to determine the best feeding method for preterm infants with birth weight less than 1,500 grams.	High **Study Limitations** None

Rate of Feeding Advancement

PICO Question: Should feedings be advanced at a slower or faster rate in order to promote growth and prevent NEC in the ELBW infant?

Search Terms: feeding advancement, growth, NEC, premature infant, low birth weight infant, very low birth weight infant, and extremely low birth weight infant.

Summary of findings:

One systematic review determined that the rate of feeding advancement did not increase the incidence of NEC and increasing feedings at a faster rate of 30-35ml/kg/day was associated with a decrease in the time to reach full feedings and regain birth weight. The authors of the systematic review recommended using caution when advancing feedings at a faster rate in the ELBW infant due to the small number of ELBW infants included in the systematic review.

Table 9: Rate of Feeding Advancement

Author/Year	**Study Design Level of Evidence**		**Study Purpose/Study Sample Study Intervention/Study Outcome**	**Results**	**GRADE Quality of Evidence**
Morgan, Young & McGuire 2011b	Systematic Review	I	**Purpose:** To determine the effect of slowly advancing enteral feedings on the incidence of NEC, mortality and other morbidities in very low birth weight infants. **Sample:** 4 RCTs with a total of 496 premature infants less than 32 weeks gestation and birth weight less than 1,500 grams **Intervention:** Advancement of feedings at a maximum rate of 24ml/kg/day vs. faster advancement (30-35 ml/kg/day) of feedings **Primary Outcomes:** NEC and all cause mortality during the neonatal period and prior to hospital discharge **Secondary Outcomes:** growth, neurodevelopment, time to establish full enteral feeding, feeding intolerance, infection and length of stay.	Slowly advancing enteral feedings does not reduce the risk of NEC but it decreases the amount of time for an infant to regain their birth weight and the amount of time to establish full enteral feedings. Length of stay was not affected by the rate of enteral feeding advancement.	High **Study Limitations** None

Human Milk Fortification

PICO Question: Does human milk fortification improve growth in the ELBW infant? Does fortification with higher amounts of protein improve growth in the ELBW infant?

Search Terms: human milk fortification, growth, enteral protein, protein, protein fortification, premature infant, low birth weight infant, very low birth weight infant, and extremely low birth weight infant

Summary of findings:

One systematic review done in preterm infants found that human milk fortification with a multi-component human milk fortifier is needed to improve growth and support bone mineralization. Another systematic review found that additional protein supplementation of 3-4g/kg/day is needed to promote adequate growth in infants weighing less than 2,500 grams once they are receiving full enteral feedings.

Table 10: Human Milk Fortification

Author/Year	Study Design Level of Evidence		Study Purpose/Study Sample Study Intervention/Study Outcome	Results	GRADE Quality of Evidence
Kuschel & Harding, 2009	Systematic Review	I	**Purpose:** To determine if human milk fortification with a multi-component fortifier improved growth, bone metabolism and neurodevelopmental outcomes without significant adverse effects in preterm infants. **Sample:**13 RCT with over 600 preterm infants **Intervention:** Fortified human milk feedings vs. non-fortified human milk feedings during the NICU stay. **Primary Outcomes:** growth to discharge, size at 12-18 months, bone metabolism, and neurodevelopmental outcomes **Secondary Outcomes:** fractures, nitrogen retention, adverse effects (hypercalcemia, GI* disturbances, feeding intolerance, diarrhea, NEC, blood pH, BUN levels, death).	Human milk fortification improves short term weight gain, linear and head growth as well as possible bone formation without adverse effects. No long term benefits of human milk fortification were found.	High **Study Limitations** None
Premji, Fenton & Sauve, 2010	Systematic Review	I	**Purpose:** To determine the effect of higher versus lower protein intakes of formula fed preterm infants on growth and neurodevelopment **Sample:** 5 RCTs of formula fed hospitalized infants less than 2,500 grams **Intervention:** higher enteral protein intake v lower enteral protein intake **Primary Outcomes:** growth, nitrogen utilization and accretion, IQ scores, 18month Bayley Scores, growth failure, phenylalanine levels **Secondary Outcomes:** gastric motility, days to full feedings, feeding intolerance, NEC, metabolic acidosis, serum albumin, sepsis, and diarrhea.	Increased protein intake (3-4g/kg/day) improved weight gain by 2g/kg/day, which was associated with increased lean body mass. No difference in phenylalanine levels. Limited evidence on long term outcomes and neurodevelopmental outcomes.	High **Study Limitations** None

Note. GI=gastrointestinal

Post Discharge Nutrition

PICO Question: Should the ELBW infant continue to receive fortified human milk after discharge to improve growth? Should the ELBW infant continue to receive premature infant formula after discharge to improve growth?

Search Terms: post discharge nutrition, human milk fortification, premature infant formula, infant nutrition, premature infant, low birth weight infant, very low birth weight infant, and extremely low birth weight infants.

Summary of findings:

The evidence for post discharge nutrition involves mostly premature infants without a focus on the ELBW infant. A case control study done in ELBW infants found an increase their total energy expenditure at discharge when compared to term infants. Two systematic reviews address post discharge nutrition in the premature infant, less than 37 weeks gestation. One systematic review compared fortified human milk to plain human milk after discharge and found an improvement in growth but the review was limited to 1 RCT. A second systematic review compared nutrient enriched premature infant formula to a standard term infant formula after discharge and determined the use of a nutrient enriched premature infant formula was not necessary after discharge in infants who were able to tolerate ad libitum feedings. The AAP Committee on Nutrition (2004) recommends premature infants especially those born at lower gestational ages receive fortified human milk or nutrient enriched premature formula until at least 9 months of age to meet their additional vitamin, mineral and caloric needs to promote adequate catch up growth.

Table 11: Post Discharge Nutrition

Author/Year	Study Design Level of Evidence		Study Purpose/Study Sample Study Intervention Study Outcome	Results	GRADE Quality of Evidence
Guilfoy, Wright-Coltart, Leitch & Denne, 2008	Case Control	IV	**Purpose:** To determine total energy expenditure in ELBW infants at discharge in comparison to term infants **Sample:** 10 ELBW infants on full feedings for at least 3 weeks and receiving fortified human milk or a post-discharge formula, 14 healthy term infants being breastfed at time of the study **Intervention:** Double labeled water method to determine energy expenditure **Outcomes:** energy expenditure	Total energy expenditure was significantly higher in the ELBW infant estimated to be greater than 90kcal/kg/day despite higher energy intake at about 130kcal/kg/day. The ELBW infant had more lean fat free mass than their term counterparts. Correction for fat free mass continued to show significantly higher energy expenditure in the ELBW infant. Weight gain in the ELBW infant was significantly higher than the healthy term infant.	Low **Study Limitations** None
Henderson, Fahey & McGuire, 2009	Systematic Review	I	**Purpose:** To determine the effects of nutrient enriched formula fed after discharge from the NICU on the preterm infant's growth and development **Sample:** 7 RCTwith 631 preterm infants partially fed formula following discharge from the NICU. **Intervention:** Nutrient enriched formula feedings versus standard term infant formula feeding. **Primary Outcomes:** short and long term growth, neurodevelopmental outcomes at 12months of age, severe neurodevelopmental disability, and cognitive and educational outcomes at more than 5 years of age. **Secondary Outcomes:** bone mineralization, feeding intolerance, clinical evidence of rickets, blood pressure readings, and BMI* at long term follow up.	Infants fed nutrient enriched formula ad libitum after discharge from the NICU had no statistical difference in growth, neurodevelopment, bone mineralization or feeding intolerance.	High **Study Limitations** None
McCormick, Henderson, Fahey & McGuire, 2010	Systematic Review	I	**Purpose:** To determine effect of plain human vs. multi-nutrient fortified human milk on growth and development of the premature infant **Sample:** 1 RCT of 39 preterm infants less than 33 weeks gestational age **Primary Outcomes:** growth during the study period, long term growth and growth restriction, neurodevelopmental outcomes, and education and cognitive outcomes at greater than 5 years of age **Secondary Outcomes:** bone mineralization, feeding intolerance, duration of breast feeding, and evidence of rickets, blood pressure values, and BMI* at long term follow up.	Feeding preterm infants with multi-nutrient fortified human milk improves growth during infancy but further trials are needed to confirm this finding and determine the long term effects.	High **Study Limitations** None

Note. BMI=body mass index

Nutrition Assessment

PICO Question: What parameters should be used to monitor growth in the ELBW infant? What laboratory assessments should be done to monitor the nutritional status of the ELBW infant? How often should laboratory assessments be done to monitor the nutritional status of the ELBW infant?

Search Terms: laboratory assessment, nutritional assessment, growth assessment, premature infant, low birth weight infant, very low birth weight infant, and extremely low birth weight infant

Summary of findings:

No clinical trials or observational studies have been done to address what parameters or laboratory data should be used to monitor nutrition in the ELBW infant. The ADA Pediatric Nutrition Practice Group (2009) provides recommendations for laboratory assessment of nutrition in premature infants. Moyer-Mileur (2007) provides recommendations for anthropometric measurements and laboratory assessment for monitoring nutritional status and growth in infants less than 1,500 grams.

CHAPTER 3

CONCEPTUAL MODEL

ACE STAR MODEL OF KNOWLEDGE TRANSFORMATION

The ACE Star Model of Knowledge Transformation provides a framework for understanding the concepts and processes utilized in the implementation and integration of EBP (Stevens, 2004). This model is a five point star that depicts the five different stages of knowledge transformation. The stages of knowledge transformation include discovery, summary, translation, integration and evaluation (Stevens, 2004). Each stage of knowledge transformation builds upon the previous stage of knowledge leading to newly discovered knowledge and information that may be used and implemented into clinical practice.

Discovery

The first stage of knowledge transformation or star point is discovery where new knowledge is generated (Stevens, 2004). In this stage, knowledge may be gained from conducting primary research studies or through a review of the literature to determine best clinical practices. The knowledge generated from either primary research studies or a literature review may then be used to guide clinical care decisions.

Summary

The second stage of knowledge transformation or star point is summary and is directly related to the EBP process. In this stage, primary research studies from a literature review are summarized into a meaningful and concise statement. The summary of evidence is usually done in the form of a systematic review or meta-analysis (Stevens, 2004). A systematic review or meta-analysis is considered to be the highest level and best

evidence that should be used to guide clinical practice (Melnyk & Fineout-Overholt, 2010).

Translation

The third stage of knowledge transformation or star point is translation. Translation is taking the summary of evidence in a systematic review or meta-analysis and developing a CPG to guide and standardize clinical practice (Stevens, 2004).

Integration

The fourth stage of knowledge transformation or star point is integration where new knowledge such as a CPG is implemented and used in clinical practice. Integration involves making and promoting change within the individual and the organization. Utilizing CPGs based on the highest level and quality of evidence promotes EBP in the clinical setting and will serve to improve clinical outcomes (Newhouse et al., 2007).

Evaluation

The last stage of knowledge transformation or fifth star point is evaluation. Evaluation involves assessing the outcome of the EBP change (Stevens, 2004). The outcomes may include clinical care outcomes, patient satisfaction, system efficiency or efficacy as well as a cost analysis. This final stage of knowledge transformation is imperative to the EBP process so that the desired effect or outcome may be evaluated and further clinical practice improvements can be made.

The ACE Star Model of Knowledge Transformation utilizes a five step process for understanding knowledge transformation, which can be applied to learning and implementing EBP. The third and fourth points of the ACE Star Model are the most congruent with the development and dissemination of this CPG. This guideline was

developed using the highest level of evidence available to guide neonatal health care providers in managing the daily nutrition of ELBW infants so that postnatal growth and neurodevelopment may be improved.

CHAPTER 4

PROJECT PLAN

ETHICAL CONSIDERATION

This doctoral project was submitted to the University of Nevada Las Vegas Institutional Review Board in April of 2011. The project was reviewed according to the federal regulatory statutes 45CFR46 and it was deemed exempt from needing IRB approval.

THE PROJECT

The EBP process was used in developing this CPG to address the nutritional management of the ELBW infant. The process included: developing a clinical question using the PICO format, completing an extensive review of the literature, categorizing the level of evidence, and evaluating the quality of evidence and strength of recommendations to be included in the CPG. The PICO questions and specific terms used to search the literature are included with the review of the literature and resulting evidence tables located in Chapter 2. Consistent with the conceptual framework for this project, systematic reviews were used where available.

The level of evidence was rated utilizing the Melnyk & Fine-Overholt (2010) Rating System for the Hierarchy of Evidence, which is the National Association of Neonatal Nurses (NANN) preferred model for rating level of evidence when developing a CPG. The quality of evidence and strength of recommendations were evaluated using the GRADE System, which meets the IOM's recommendations for evaluating the quality of evidence and the strength of recommendations used in developing CPGs.

EVALUATION

Peer review and evaluation of this CPG will be completed by two NANN members. The NANN members will be doctorally prepared neonatal nurse practitioners who have served on the NANN Board of Directors and various other NANN committees. Each reviewer will be asked to use the NANN Instructions for Writing Clinical Practice Guidelines to evaluate the CPG for content validity. The peer review period is expected to take three months and will commence upon successful defense of this doctoral project.

PRODUCT

According to the IOM (2008) CPGs should be developed by expert panels that have knowledge regarding the clinical situation and have the ability to interpret clinical research to make sound clinical judgments. The ultimate plan for this doctoral project is submission for publication, thereby transitioning this *project* into a *product* that may change practice. Pending expert review (described above) and revisions if needed, this CPG will be submitted to NANN for publication. Neonatal nursing practice is governed by NANN, who has published several CPGs to guide the clinical management of critically ill neonates. Therefore, NANN would be the most appropriate site for publication of this CPG.

CHAPTER 5

RESULTS

This chapter presents the evidence based recommendations for the nutritional management of the ELBW infant. The recommendations are included in the table below and have been organized according to the NANN Guidelines for writing CPGs. The practice recommendation column includes the guidelines for practice and the rationale or supporting evidence for each practice guideline. The level of evidence column indicates the strength of evidence for each guideline and is followed by the GRADE quality of evidence and strength of recommendation. References in support of the practice recommendations are included in the reference column.

Table 12: Practice Recommendations and Rationale

Practice Recommendation	Level of Evidence	Quality of Evidence	Strength of Recommendation	Reference
The overall nutritional management of the ELBW should be based on intrauterine nutrient accretion rates to promote a weight gain of 15-20g/kg/day. **Rationale:** Nutrient accretion rates are considered the best reference for growth of ELBW infants (AAP Committee on Nutrition, 1985). The intrauterine rates of accretion have been determined utilizing published data on the chemical analysis of the fetus in order to provide a reference fetus comparable to the premature infant and the ELBW infant (Ziegler, et. al, 1976).	VII	Very Low	Recommend	(AAP Committee on Nutrition, 1985; Ziegler, O'Donnell, Nelson & Fomon, 1976)
Fluid & Electrolyte Management				
Fluid intake will vary depending on the ELBW infant's gestational and postnatal age, disease process and severity of illness. Fluid intake for the ELBW infant should be restricted to meet the infant's physiologic needs. **Rationale:** Fluid restriction avoids excess water load on the immature kidney preventing fluid volume overload, which is associated with an increased incidence of NEC and PDA in premature infants. (Bell& Accareugi, 2010).	I	High	Strongly Recommend	(Bell & Accareugi, 2010)
Fluid intake for the ELBW infant during the first week of life should be based on the amount of insensible water loss and urinary output. Fluid intake should start at 60-80ml/kg/day on the first day of life and be advanced by 10-20ml/kg/day throughout the first week of life to a maximum of 160-170ml/kg/day. **Rationale:** Fluid management during the first week of life should allow for contraction of the extracellular fluid volume resulting in postnatal diuresis and a10-15% loss of birth weight. Failure to strictly manage fluid intake at such a critical time has been shown to increase the incidence of PDA and BPD in the ELBW infant (Oh et al., 2005; Stephens et al, 2008).	IV	Low	Recommend	(Oh et al., 2005; Stephens et al., 2008)
The ELBW infant should be placed in a double walled isolette with ambient humidity of 70%-80% to aid in insensible water loss and fluid and electrolyte balance. **Rationale:** The ELBW infant is born with an immature non-keratinized epidermis resulting in insensible water loss through the immature skin layer. In two retrospective cohort studies, placement of ELBW infants in humidity was found to decrease total fluid intake, improved electrolyte balance and improve growth (Gaylord, et al., 2001; Kim, et al., 2010).	IV	Low	Recommend	(Gaylord, et al., 2001; Kim, et al., 2010).
After the first week of life when postnatal diuresis is complete, the goal of fluid management should shift from replacing water loss to providing enough nutrients for adequate growth. The target fluid goal for promoting adequate growth should be: 140-160ml/kg/day and may be adjusted in 10-20ml/kg/day increments until reaching the fluid goal. **Rationale:** Adequate fluid intake after postnatal diuresis is essential for adequate nutrient intake and postnatal growth. The recommended fluid intake promotes weight gain consistent with intrauterine values (AAP Committee on Nutrition, 2004).	VII	Very Low	Recommend	(AAP Committee on Nutrition, 2004; Adamkin, 2009)

Sodium should be withheld during the first 5 days of life to promote postnatal diuresis. After diuresis, a recommended daily intake of sodium at 2-3meq/kg/day should be sufficient to meet the daily needs of the ELBW infant. **Rationale:** Sodium restriction during the first 5 days of age results in contraction of the extracellular fluid volume promoting postnatal diuresis (Shaffer & Meade, 1989). Infants who were supplemented with sodium within the first 5 days of life developed hypernatremia, required higher fluid intakes, and had a higher incidence of BPD (Costarino, et al., 1992).	II VII	Moderate Very Low	Strongly Recommend	(Costarino et al., 1992; Shaffer & Meade, 1989) (AAP Committee on Nutrition, 2004)
Potassium should be held during the first 5 days of life until postnatal diuresis is complete. An intake of 2-3meq/kg/day is recommended to the meet the daily needs of the ELBW infant. **Rationale:** The ELBW infant is at risk for developing non-oliguric hyperkalemia due to intracellular shifts in potassium during the first 5 days of life requiring potassium to be held (Lorenz et. al, 1997).	IV VII	Low Very Low	Recommend	(Lorenz et al., 1997) (AAP Committee on Nutrition, 2004; ADA Pediatric Nutrition Group, 2009)
Mineral Requirements				
Calcium, phosphorus, and magnesium should be administered at a rate that mimics intrauterine accretion. Calcium intake should be 60-90mg/kg/day, phosphorus intake should be 47-70mg/kg/day, and magnesium intake should be 4.3-7.2mg/kg/day when receiving parenteral nutrition. Calcium and phosphorus should be administered in a 1:1 molar ratio. The recommended intake for calcium, phosphorus, and magnesium increases once the ELBW infant is on full enteral feedings. Calcium intake should be 100-200mg/kg/day. Phosphorus intake should be 60-140mg/kg/day. Magnesium intake should be 7.9-15mg/kg/day. **Rationale:** Administering calcium, phosphorus, and magnesium to mimic intrauterine accretion rates improves bone mineral content decreasing the incidence of osteopenia of prematurity. In a RCT, administering higher doses of calcium and phosphorus within the first few days of life improved serum concentrations of phosphorus and bone mineral content from 1 week to 26 weeks postconceptual age (Prestridge et al., 1993).	II VII VII	High Very Low Very Low	Strongly Recommend	(Prestridge et al., 1993) (AAP Committee on Nutrition, 2004) (ADA Pediatric Nutrition Practice Group, 2009)
Energy Requirement				
Caloric intake for the ELBW infant should be supplied at the same intrauterine rate to promote optimal growth. Total caloric intake should be based on maintaining an energy balance of 25-30kcal/kg/day, which is estimated to be: 80kcal/kg/day to maintain body energy stores while receiving parenteral nutrition and should be the goal immediately after birth and within the first few days of life. 105-115kcal/kg/day (including 3.5g/kg/day of amino acids) to promote growth while receiving parenteral nutrition. 130-150kcal/kg/day to promote growth while receiving full enteral nutrition, additional protein may be needed to accompany the higher caloric intake. **Rationale:** Energy expenditure in the ELBW infant is estimated to be higher than the currently established values that are based on growing healthy premature infants (Carr, et al., 2000) Supplying additional calories along with an increased amount of protein has been shown to improve nitrogen retention leading to improved growth (Zlotkin, 1981).	II VI VII	Moderate Low Very Low	Recommend	(Zlotkin et al., 1981) (Carr et al., 2000) (Leitch & Denne, 2005; Hay, 2005)

Glucose Management				
Glucose intake for the ELBW infant shall be supplied at the same intrauterine rate to maintain adequate energy supply and should be administered directly after birth. Glucose infusion should start at: 5-7mg/kg/min and be advanced as tolerated by 1-2mg/kg/min to a maximum of 10-11mg/kg/day when receiving full parenteral nutrition. **Rationale** Glucose is the major source of energy for the fetal brain and is required to ensure adequate energy supply to the ELBW infant's brain. Insufficient evidence exists to determine the exact rate of glucose utilization but experts suggest using the fetal rate of glucose utilization as a guide for administering glucose to the ELBW infant (Hay, 2005; Sinclair et al., 2011).	I VII	High Very Low	Recommend	(Sinclair et al., 2011) (AAP Committee on Nutrition, 2004; Hay, 2005)
In the ELBW infant hyperglycemia occurs frequently during the first week of life due to glucose administration. Treatment of hyperglycemia may involve decreasing the glucose infusion rate or administering an insulin infusion but insulin should not be given to prevent hyperglycemia in the ELBW infant. **Rationale:** The exact cause of hyperglycemia seen in the ELBW during the first few days of life is still unknown but it is thought to be a result of glucose intolerance. Insufficient evidence exists to determine the exact method for treatment of hyperglycemia but insulin infusion to prevent hyperglycemia was found to be associated with an increase in death before 28 days of age (Bottino et al., 2011; Sinclair et al., 2011.)	I	High	Strongly Recommend	(Bottino et al., 2011; Sinclair et al., 2011)
Early Aggressive Nutrition				
Early aggressive nutrition should be administered to the ELBW infant. The nutritional plan should include early administration of amino acids, intralipids and minimal enteral feedings (MEF). **Rationale:** An early aggressive nutrition plan improves caloric intake within the first week of life and promotes nitrogen balance (Ibrahim et al., 2004; Wilson et al., 1997). In a RCT, a nutrition plan that included early administration of amino acids, intralipids and MEF was shown to improve weight, length and head circumference of infants less than 1,500 grams at discharge (Wilson, et al., 1997).	II	Moderate	Strongly Recommend	(Ibrahim et al., 2004; Wilson et al., 1997)
Amino acids should start right after birth at a rate of 3g/kg/day and should be increased by 0.5-1g/kg/day until reaching a maximum of 4g/kg/day. **Rationale:** Protein administration improves plasma amino acid levels, which promotes protein synthesis (Anderson, et. al, 1979; Blanco et al., 2011; Clark et al., 2007; Murdock et al., 1995; Rivera et al., 1993; TeBraake et al., 2005; Van Goudoever et al., 1995 Van Lingen et al., 1992) Giving protein at 3g/kg/day is considered to be safe and mimics protein accretion rates seen in-utero as well as improves glucose tolerance (Thureen et al., 2003). Administering protein right after birth is safe and effective in preventing catabolism, promoting nitrogen and protein balance without increasing blood urea nitrogen (BUN) levels or disrupting acid base balance (Anderson et al., 1979; Rivera et al., 1993; TeBraake et al., 2005; Thureen et al., 2003; Van Goudoever et al., 1995; Van Lingen et al., 1992). The early administration of protein to ELBW infants has been shown to improve weight, length, and head circumference at 36 weeks postconceptual age (Poindexter et al., 2006).	II	Moderate	Strongly Recommend	(Anderson et al., 1979; Blanco et al., 2011; Clark et al., 2007; Murdock et al., 1995;; Poindexter et al., 2006; Rivera et al., 1993; TeBraake et al., 2005; Thureen et al., 2003; Van Goudoever et al., 1995; Van Lingen et al., 1992;)

Intralipids should start within 24 hours after birth at a rate of 0.5-1g/kg/day and should be increased by 0.5-1g/kg/day until reaching a maximum of 3g/kg/day. Intralipids should be given continuously over 24 hours. **Rationale:** The administration of intralipids prevents essential fatty acid deficiency and improves glucose tolerance (Anderson, et al., 1979; Murdock et al., 1995). In a systematic review, early administration of intralipids was determined to be safe and have no adverse effects but could not be recommended for short term growth (Simmer & Rao, 2009). In a RCT, intralipids given as part of an early aggressive nutrition plan was found to improve growth of infants less than 1,500 grams within the first week of life and at hospital discharge (Wilson, et al., 1997).	I II	High Moderate	Strongly Recommend	(Simmer & Rao, 2009) (Anderson et al., 1979; Murdock et al., 1995; Wilson et al., 1997)
Minimal enteral feedings (MEF) should be started within the first 1 to 4 days of age at a rate of 10-25ml/kg/day. Minimal enteral feedings should be given for at least 5 to 7 days. **Rationale:** In a RCT, MEF when given as part of an early aggressive nutrition plan was found to improve enteral intake and feeding tolerance without increasing the incidence of NEC (Wilson, et al., 1997). Introducing MEF early within the first few days of life is further supported by two systematic reviews that found delaying feedings and the use of trophic feedings had no significant effect on the incidence of NEC (Bombell & McGuire, 2009; Morgan et al., 2011a).	I II	High High	Strongly Recommend	(Bombell & McGuire, 2009; Morgan et al., 2011a) (Wilson et al., 1997)
Enteral Nutrition				
Human milk should be used for enteral feedings in the ELBW infant. Donor human milk should be used when maternal human milk is unavailable or is contraindicated. In cases where human milk (maternal or donor) is unavailable a premature infant formula may be used for enteral feedings but the use of formula should not be the feeding of choice. **Rationale:** Human milk is species specific and all other formula preparations are substantially different making human milk uniquely superior for infant feeding (AAP Section on Breastfeeding, 2005). Human milk contains immunoprotective and growth factors that protect the immature gut mucosa of the ELBW infant. Infants fed formula instead of human milk (maternal or donor) are have an increased risk for developing NEC (Quigley et al., 2008).	I VII	High Very Low	Strongly Recommend	(Quigley et al., 2008) (AAP Section on Breastfeeding, 2005)
Enteral feedings may be administered through an oral or nasal gastric feeding tube. **Rationale:** The ELBW infant is not able to coordinate sucking and swallowing needed for oral nipple feedings placing them at high risk for aspiration. In addition, the ELBW infant's immaturity and severity of illness prevents them from being able to tolerate nipple feedings, which requires enteral feedings to be administered via a feeding tube. Evidence is lacking to support the routine placement of feeding tubes in the nose or mouth (Hawes et al., 2008). However, infants are obligate nose breathers and placing a feeding tube into their nares may lead to partial obstruction, increased airway resistance and increased work of breathing (Hawes et al., 2008).	I	High	Strongly Recommend	(Hawes et al., 2008)
Enteral feedings may be given every 2-3 hours as an intermittent bolus or continuously via a feeding pump. **Rationale:** Insufficient evidence exists to determine the best feeding method for the ELBW infant. In a systematic review no difference in the incidence of NEC or time to reach full feedings was found between intermittent or bolus feedings (Premji & Chessell, 2011). Continuous feedings may be warranted in ELBW infants with feeding intolerance or those with symptoms of gastroesophageal reflux (ADA Pediatric Nutrition Practice Group, 2009).	I VII	High Very Low	Strongly Recommend	(Premji & Chessell, 2011) (ADA Pediatric Nutrition Practice Group, 2009)

Advancement of enteral feedings should take into consideration the ELBW infant's gestational age and severity of illness. Enteral feedings may be advanced by 20-35ml/kg/day as tolerated until reaching full fluid intake at 140-160ml/kg/day. **Rationale:** Current evidence is lacking on the feeding advancement for the ELBW infant. In a systematic review, the rate of feeding advancement was not associated with an increased risk for NEC and slow advancement of feedings prolonged the need for parenteral nutrition and the time to regain birth weight in infants weighing less than 1,500 grams (Morgan et al., 2011b).	I	High	Strongly Recommend	(Morgan et al., 2011b)
Human milk (maternal or donor) should be fortified with commercially available human milk fortifiers. Fortification of human milk should be done gradually to prevent feeding intolerance and may begin with 22kcal/ounce when the infant is tolerating 100ml/kg/day of enteral feedings and advanced as tolerated to 24kcal/ounce when the infant is tolerating full enteral feedings at 140-160cc/kg. If human milk is unavailable, the infant may be given a premature formula and should be advanced to 24kcal/ounce premature formula in the same manner as the infant receiving human milk. **Rationale:** The composition of human milk varies from person to person with protein, fat, and mineral content decreasing throughout lactation. The reduction of protein, fat and minerals in human milk fails to meet the nutritional needs of the ELBW infant. Fortifying human milk with commercial human milk fortifiers provides the additional amount of energy and protein needed for growth while providing adequate amounts of calcium and phosphorus to improve bone mineral content in the ELBW infant (Kuschel & Harding, 2009). The addition of human milk fortifiers increases the osmolality of the human milk and may result in feeding intolerance (ADA Pediatric Nutrition Practice Group, 2009). Although human milk fortification is not associated with an increased risk of NEC (Kuschel & Harding, 2009) utilizing a step wise approach will help to prevent feeding intolerance and the need to stop feedings or decrease enteral intake.	I VII	High Very Low	Strongly Recommend	(Kuschel & Harding, 2009) (Adamkin, 2009; ADA Pediatric Nutrition Practice Group, 2009)
In addition to human milk fortification, enteral feedings should be supplemented with extra protein to reach a daily requirement of 3-4g/kg/day. If human milk is unavailable a premature infant formula with additional protein may be used. **Rationale:** The intrauterine accretion rate of protein to promote adequate growth is estimated to be 3-4g/kg/day. In a systematic review, protein supplementation of enteral feedings at intrauterine accretion rates was found to improve nitrogen balance and promote weight gain in infants less than 2,500 grams (Premji, et al., 2010).	I	High	Strongly Recommend	(Premji, et al., 2010)

Post Discharge Nutrition				
The ELBW infant should continue to receive fortified human milk after discharge to meet their high energy needs and to promote growth. In cases where human milk is unavailable the ELBW infant should continue to receive a premature infant formula after discharge. The amount of human milk fortification or caloric density of the premature infant formula should be adjusted to 22kcal/ounce just prior to discharge. The need for additional fortification should be based on the ELBW infant's disease process, weight gain, and history of osteopenia of prematurity. **Rationale:** The exact nutrient requirements for the ELBW infant have yet to be determined but it is clear that the ELBW infant continues to have a high energy need at time of discharge that must be met (Guilfoy, et. al, 2008). A systematic review of 1 RCT showed improvement in growth of premature infants fed fortified human milk upon discharge (McCormick, et al., 2010) In another systematic review, premature infants able to tolerate ad libitum feedings did not need a premature infant formula at discharge (Henderson et al., 2009). According to the AAP Committee on Nutrition (2004) human milk fortification or the use of premature infant formula should continue until at least 9 months of age to meet the additional vitamin, mineral, and caloric needs of infants born prematurely.	I IV VII	High Low Very Low	Strongly Recommend	(Henderson, et al., 2009; McCormick et al., 2010) (Guilfoy et al., 2008) (AAP Committee on Nutrition, 2004)
Nutritional Assessment				
Anthropometric measurements are used to monitor growth in all infants and should be done on a routine basis to monitor growth in the ELBW infant. Weight should be measured daily with use of a bed scale if possible due to the critical nature of the ELBW infant's illness. Weight gain should mimic the intrauterine growth rate of 15-20g/kg/day. Head Circumference should be measured weekly at the largest frontal occipital plan. Head circumference should increase by 0.9cm/week. Length should measured weekly using a recumbent length board to obtain the best measurement. Length should increase by 0.9cm/week. **Rationale:** Body weight is representative of total body mass and is reflective of changes in body composition to include lean tissue, fat, and the intracellular and extracellular fluid compartments (Moyer-Mileur, 2007). Head growth during infancy correlates well with overall growth and may indicate poor neurodevelopment if measurements are abnormal (Moyer-Mileur, 2007). Length is more closely associated with lean mass and is a better indicator of long term growth.	VII	Very Low	Recommend	(ADA Pediatric Nutrition Practice Group, 2009; Moyer-Mileur, 2007)

Laboratory data may be used to further assess the nutritional status of the ELBW infant. Recommendations for laboratory monitoring while receiving parenteral nutrition are as follows: Serum glucose should be monitored as needed based on severity of illness and disease process. Urine glucose should be monitored 1-3 times a day upon initiation of parenteral nutrition and then as needed once stable. Electrolytes and acid-base balance should be monitored daily upon initiation of parenteral nutrition and continue until energy and nutrient needs are met and stabilized. Once requirements are stable electrolytes may be monitored every 1-2 weeks as needed. Acid-base balance may be monitored as needed. Calcium, phosphorus, and magnesium should be monitored a 2-3 times a week during the initiation of parenteral nutrition and then every 1-2 weeks as needed. Triglycerides should be monitored with every rate increase and then every 1-2 weeks as needed while receiving intralipids. Blood urea nitrogen (BUN) and creatinine should be monitored a 2-3 times a week during the initiation of parenteral nutrition and then every 1-2 weeks as needed. Serum protein levels, liver enzymes, alkaline phosphatase, and blood cell count should be done to obtain a baseline at the start of parenteral nutrition and then every 2-3 weeks as needed. **Rationale:** Monitoring laboratory data on a regular basis during the initiation and continued use of parenteral nutrition aides allows the healthcare provider to assess the ELBW infant's response to parenteral nutrition and to identify any metabolic complications that may occur from the use of parenteral nutrition (Moyer-Mileur, 2007).	VII	Very Low	Recommend	(ADA Pediatric Nutrition Practice Group, 2009; Moyer-Mileur, 2007)
Recommendations for laboratory monitoring while receiving enteral nutrition are as follows: A baseline evaluation of serum and urine glucose, electrolytes, acid-base status, BUN, creatinine, calcium, phosphorus, magnesium, serum protein levels, liver enzymes, alkaline phosphatase, and blood cell count should be done upon reaching full enteral nutrition. Once the ELBW infant is stable on full enteral feedings with adequate nutrient and energy intake the laboratory assessment of electrolytes, calcium, phosphorus, BUN, creatinine, serum protein levels, liver enzymes, blood cell count may be done every 2-3 weeks and adjusted as needed based on clinical condition. **Rationale:** A routine monitoring schedule is not indicated when infants weighing less than 1,500 grams are clinically stable and receiving adequate nutrition (Moyer-Mileur, 2007). The recommendations can be used to monitor nutritional status and adjusted as needed based on the clinical condition of the ELBW infant.	VII	Very Low	Recommend	(ADA Pediatric Nutrition Practice Group, 2009; Moyer-Mileur, 2007)

CHAPTER 6

DISCUSSION and IMPLICATIONS for PRACTICE

The aim of this CPG is to provide evidence based practice recommendations on the nutritional management of the ELBW infant in order to promote adequate extrauterine growth and prevent or at least decrease EUGR. The need for improving EUGR in the ELBW infant has been well documented throughout the neonatal literature (Carroll, Slobodzian & Steward, 2005; Clark et al., 2003; Coverston & Schwartz, 2005; Yu, 2005) However, research to define the exact nutrient requirements needed to promote adequate extrauterine growth in the ELBW infant is limited.

Current nutritional management of the ELBW infant focuses on providing nutrition to promote weight gain that is similar to the intrauterine rate of 15-20g/kg/day, which has been recommended by the AAP (1985) as the gold standard for premature infant growth. In order to meet the AAP recommendations, ELBW infants have been fed diets high in fat and carbohydrates (Hay, 2006). This type of nutritional management has resulted in large protein and energy deficits that lead to poor extrauterine growth and EUGR in the ELBW infant (Clark et al., 2003; Stephens et al., 2009).

Strong evidence exists for providing early aggressive nutrition to prevent the protein and energy deficits that occur in the ELBW infant (Ibrahim et al., 2004; Wilson, et al., 1997). Most of the research has focused on early administration of amino acids with a number of the studies being conducted in infants less than 1,500 grams. However, the few studies conducted in ELBW infants have consistently shown that early administration of amino acids prevents catabolism, promotes protein synthesis and

establishes a positive nitrogen balance without adverse effects (Rivera et al., 1993; TeBraake et al., 2005; Thureen et al., 2003; Van Goudoever et al., 1995).

Energy requirements for the ELBW infant are still unclear and have been largely estimated from data obtained in healthy growing premature infants (Carr et al., 2000). Energy intake for the ELBW infant when receiving early amino acids has been estimated at 70-115kcal/kg/day (Carr et al., 2000; Hay, 2005; Leitch & Denne, 2005; Zlotkin et al., 1981) However, providing enough energy from non-protein sources is complicated by hyperglycemia and glucose intolerance in the ELBW infant (Hay, 2006). Administering intralipids in small doses along with amino acids has been shown to improve glucose tolerance (Anderson, et al., 1979; Murdock et al., 1995; Rivera et al., 1993; Thureen et al., 2003). Although early administration of intralipids has no adverse effects, the evidence to support its use to promote short term growth is conflicting (Simmer & Rao, 2009; Wilson et al., 1997).

Early administration of amino acids and intralipids are not the only components that make up an early aggressive nutrition plan. Trophic feedings or MEF have been shown to improve feeding tolerance and later feeding advancement (Wilson et al., 1997). In addition, the use of MEF has been shown in two systematic reviews to have no effect on the incidence of NEC (Bombell & McGuire, 2009; Morgan et al., 2011a). However, clinicians are still withholding feedings due to the fear of NEC (Adamkin, 2005, Ehrenkranz, 2007).

The exact pathogenesis of NEC is unknown but certain factors have been associated with its development (Neu, 2008). One of these factors is the commencement of enteral feedings thought to serve as a substrate for infectious organisms to multiply

(Lee & Jain, 2000). The use of formula has been shown to increase the incidence of NEC while human milk has been shown to decrease its incidence (Quigley et al., 2008). Despite this evidence to support exclusive human milk feeding and the recent advancements in providing donor human milk ELBW infants are still receiving premature infant formula as the feeding of choice.

It has been recognized that exclusive human milk feeding over time will not meet the nutritional needs of the ELBW infant (AAP Committee on Nutrition, 2004). Fortification of human milk with human milk fortifiers provides the additional nutrients needed to promote growth and bone mineralization in premature infants (Kuschel & Harding, 2009). However, continuing such fortification upon discharge is controversial. One systematic review suggests fortified human milk promotes growth after discharge but the review only included 1 RCT (McCormick et al., 2010) In another systematic review the use of a nutrient enriched premature formula after discharge had no effect on growth when compared to a standard term formula, but these findings were limited to infants who could tolerate ad libitum feedings (Henderson et al., 2009). Yet, the AAP (2004) recommends human milk fortification or a premature infant formula to meet the additional vitamin, mineral and caloric needs of the premature infant. Furthermore, Guilfoy et al. (2008) found that ELBW infants continued to have high energy expenditure at the time of discharge despite higher caloric intake of 130kcal/kg/day.

Determining the appropriate post-discharge nutritional regimen for the ELBW infant is an area needing further investigation. Especially when current evidence suggests additional protein supplementation of enteral feedings at 3-4g/kg/day is needed to promote weight gain in infants less than 2,500 grams (Premji et al., 2010). Bhatia (2005)

suggests that until optimal nutrition regimens are developed growth assessments need to be done at regular intervals with close attention to growth failure as well as growth excess.

Regular growth assessments are essential in the ELBW infant not only after discharge but throughout their NICU stay. Anthropometric measurements have been standardized in neonatal care whereas laboratory assessment varies depending on each NICU and healthcare provider. This variation in practice is most likely due to a lack of evidence to support how often laboratory assessments should be done (Moyer-Mileur, 2009). It is unlikely that a RCT will be done to provide strong evidence for routine laboratory assessments but observational or cohort studies to determine how often certain laboratory tests should be done would aid in the nutritional assessment of the ELBW infant.

Nutritional management of the ELBW infant is not an easy task and is further complicated by a lack of research done solely in this population of infants. Although, research done in the VLBW (less than 1,500 grams) infant may be applied to the care of ELBW infants their extreme prematurity and organ development must still be considered when providing such care. Therefore, this guideline should not be used without the careful examination of the ELBW infant's clinical condition and severity of illness.

IMPLICATIONS FOR PRACTICE

The development of this CPG provides neonatal healthcare providers with evidence based recommendations on the nutritional management of the ELBW infant and fulfills an existing gap in neonatal practice. The recommendations in the CPG are centered on improving extrauterine growth and therefore preventing or at least decreasing

EUGR. The publication and endorsement of this guideline by NANN will help to standardize nutritional management of the ELBW infant across the country and potentially improve growth and outcomes nationwide.

This guideline is the first evidence based CPG addressing the nutritional management of the ELBW infant. A lack of research done exclusively in the ELBW infant population has been highlighted with the development of this CPG. Strong evidence exists for the early administration of amino acids, intralipids and MEF or trophic feedings to prevent protein and energy deficits that lead to EUGR but maintaining growth with enteral nutrition is less clear especially after the ELBW infant is discharged from the NICU. Therefore, further studies are still needed to determine the nutrient requirements for maintaining adequate extrauterine growth of the ELBW infant.

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APPENDIX A: CURRICULUM VITAE

Dana J. Lunde, DNP, RNC, NNP-BC

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Las Vegas Nevada 89148 danalunde@gmail.com

Education

Doctorate of Nurse Practice 2012
University of Nevada- Las Vegas

Masters of Science in Nursing 2001
University of Texas-Houston Health Sciences Center

Bachelor of Science in Nursing 1999
University of Tulsa

Professional Experience

09/11-present
Neonatal Nurse Practitioner
Pediatrix Medical Group, Sunrise Children's Hospital NICU Las Vegas, NV

- Collaborate with a group of 7 neonatologists in the management of critically ill neonates in a 72 bed Level 3 unit with complete pediatric sub-specialty support with high frequency ventilation and nitric oxide.
- Perform required procedures in the care of critically ill neonates.
- Attend high risk deliveries for resuscitation and stabilization of critically ill neonates.
- Provide 24 hour in house coverage.

03/08-present
Clinical Practice Coordinator
Sunrise Children's Hospital Neonatal Intensive Care Unit Las Vegas, NV

- Program development
- Education of nursing staff and medical team members
- Policy and procedure review for the NICU
- Oversee clinical practices in the NICU
- Member of the Sunrise Children's Hospital & Medical Center IRB
- Participate in daily clinical rounds
- Consult on patients as needed

2007-2008
Neonatal Nurse Practitioner
Pediatrix Medical Group, Summerlin Hospital NICU Las Vegas, NV

- Collaborate with a group of 6 neonatologists in the management of critically ill neonates in a 30 bed Level 3 unit with complete pediatric sub-specialty support with high frequency ventilation and nitric oxide.
- Participate in ground transport of critically ill neonates for the city of Las Vegas.
- Perform required procedures in the care of critically ill neonates.

- Attend high risk deliveries for resuscitation and stabilization of critically ill neonates.
- Provide 24 hour in house coverage.
- Provide 24 hour out of house coverage for a level 2 nursery at sister hospital.

2003-2007
Neonatal Nurse Practitioner
Pediatrix Medical Group, Sunrise Children's Hospital NICU Las Vegas, NV

- Collaborate with a group of 8 neonatologists in the management of critically ill neonates in a 54 bed Level 3 unit with complete pediatric sub-specialty support with high frequency ventilation and nitric oxide.
- Participate in ground, helicopter, and fixed wing transport of critically ill neonates for the state of Nevada, western region of Arizona and eastern region of California.
- Perform required procedures in the care of critically ill neonates.
- Attend high risk deliveries for resuscitation and stabilization of critically ill neonates.
- Provide 24 hour in house coverage.
- Provide 24 hour out of house coverage for a level 2 nursery at sister hospital.

2002
Neonatal Nurse Practitioner
Saint Francis Hospital Eastern Oklahoma Perinatal Center Tulsa, OK

- Collaborate with a group of 4 neonatologists in the management of critically ill neonates in a 45 bed Level 3 unit with complete pediatric sub-specialty support and high frequency ventilation with nitric oxide and ECMO.
- Responsible for directing the daily medical management of the nurse practitioner team of patients and presenting them during daily rounds.
- Attendance at high risk deliveries for resuscitation and stabilization of critically ill neonates.
- Provided 24 hour in house coverage without attending in house back up.

1999-2001
Registered Nurse
Columbia Woman's Hospital Houston, TX

- Provided daily nursing care to critically ill neonates in a 76 bed combined level 2 and level 3 nursery with limited pediatric sub specialty support and high frequency ventilation with nitric oxide.
- Attendance at high risk deliveries to aid in the resuscitation and stabilization of critically ill neonates.

1998-1999
Senior Nurse Assistant
Saint Francis Hospital Eastern Oklahoma Perinatal Center Tulsa, OK

- Part of the nurse apprentice program for the NICU.
- Provided daily nursing care to a group of 3-4 growing preterm infants under the supervision of a registered nurse.
- Responsible for teaching and preparing parents for discharge from the NICU.

Licenses

- State of Nevada Advanced Practice Nurse Expires 03/2014
- State of Nevada Registered Nurse Expires 03/2014

- State of Nevada Board of Pharmacy License to Prescribe
  Expires 10/2012
- Controlled Substance Registration Certificate 02/2013

Certifications

- NCC Certification as a Neonatal Nurse Practitioner Expires 03/2014
- Neonatal Resuscitation Regional Instructor 08/2013
- Basic Life Support Provider Expires 07/2012
- STABLE Lead Instructor Expires 1/2014
- RTS Coordinator 01/2006

Professional Affiliations

- National Association of Neonatal Nurses
- National Association of Neonatal Nurse Practitioners
- Academy of Neonatal Nurses
- Nevada Advanced Practice Nursing Association
- AAP District VIII Section on Perinatal Pediatrics

Honors

- 2003 March of Dimes APN of the Year for Southern Nevada
- 2010 March of Dimes Educator of the Year for Southern Nevada
- Children's Heart Foundation of Nevada Executive Board Member-2011
- Planning Committee Co-Chairperson for 7th National Neonatal Nurses Meeting in Las Vegas, Nevada September 2007
- Planning Committee Member for 2010 NANN Conference in Las Vegas, Nevada
- Planning Committee Member for 2011 NANN Conference in Royal Caribe, Florida
- Planning Committee Chair- Elect for 2013 NANN Conference in Palm Springs, California
- Planning Committee Chair for 2014 & 2015 NANN Conference
- Speaker Bureau Abbott Nutrition 2012
- Speaker Bureau ONY Medical LLC 2009
- Editorial Consultant- *Neonatal Network: The Journal of Neonatal Nursing*

Publications

- Wing, D.M., Oertle, J., Cabioc, A., Evans, C., **Smith, D.,** Stangeby, B.: A Student Directed Community Project to Support Sexually Abused Women Veterans Suffering from Post Traumatic Stress Disorder. (2000). *Public Health Nursing*, 17(4), 239-24.,

- Wing, Donna Marie & **Smith, Dana J.**: Undergraduate Student-Faculty Publication Outside the Baccalaureate Curriculum. (2001). *Nurse Educator*, 26(6), 256-258.

Research Involvement

10/2005-05/2006 **Study Coordinator** at Sunrise Children's Hospital NICU for a multicenter, randomized, controlled trial entitled, **A Randomized, Double Blind, Placebo-Controlled Trial to Assess the Safety and Efficacy of Surfaxin (Lucinactant) In Very Low Birth Weight Infants At Risk for Developing Bronchopulmonary Dysplasia.**

06/2003-09/2004 **Study Coordinator** at Sunrise Children's Hospital NICU for a multicenter randomized controlled trial entitled, **A Double Blind, Randomized, Multicenter stratified study to Assess the Safety of an Intravenous Staphylococcus Aureus Immune Globulin(Human)[Altastaph] in Very Low Birth Weight Neonates.**

Doctoral Project

- Nutritional Management of the Extremely Low Birth Weight Infant: An Evidence Based Clinical Practice Guideline

Presentations

University of Tulsa

- Acid Base Balance Nursing Lecture (2002)
- Oxygenation Nursing Lecture (2002)
- Neurological Disruptions Nursing Lecture (2002)

University of Nevada Las Vegas

- Newborn Transition and Physical Assessment (2003-2006)

Mead Johnson Nutritionals /March of Dimes

- Nursing Grand Rounds: The Drug Exposed Neonate (2006)

Association of Neonatal Nursing

- Congenital Heart Disease at the 7th National Neonatal Nurses Meeting in Las Vegas, NV 2007

MedImmune Advocacy Group

- A Day in the Life of the Premature Infant in Las Vegas, NV 05/2009

ONY Medical LLC

- The Late Preterm Infant at John Muir Hospital Walnut Creek, CA 07/2009

National Association of Neonatal Nurses

- Neonatal Nutrition-2010 National Conference in Las Vegas, NV