JOHNS HOPKINS ALL CHILDREN'S HOSPITAL

Parenteral Nutrition for the Preterm Neonate Clinical Pathway

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All Children's Hospital

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Updated: January 2025

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Rationale:

Premature neonates, particularly those less than 30 weeks gestation, are born with minimal nutrient stores and rapidly developing deficits of energy and protein. This contributes to lower weight, length, and head circumference, which has long-term implications including impaired neurodevelopment. Gastrointestinal (GI) immaturity requires that full enteral nutrition be established over time. Parenteral nutrition (PN) provides a means to improve nutrient intake aiming to approach in-utero accumulation and is the established standard of care for neonates in the initial period after birth. Careful management of macronutrients and micronutrients in PN is essential to meet the unique needs of premature neonates to prevent metabolic derangements, electrolyte disturbances, nutrient deficiencies, and cumulative growth deficits.

This clinical pathway was developed by a consensus group of Johns Hopkins All Children's Hospital (JHACH) physicians, dieticians, and pharmacists to standardize the management of PN for preterm neonates.

Background / Published Data and Level of Evidence:

A. *Indication for PN*

PN is indicated for preterm neonates < 1,800 g to meet nutrient needs until adequate enteral feeding is established. It is recommended to promptly provide PN if the neonate is not expected to reach close to full enteral feedings within 3 days after birth.[1]

Central versus peripheral PN and osmolarity: the American Society for Parenteral and Enteral Nutrition (ASPEN) recommends not exceeding 900 mOsm/L in peripheral PN and at those recommendations are followed by JHACH. A 2021 study retrospectively looked at 618 PN days in 200 patients, comparing peripheral PN < 1000 mOsm/L and 1000 – 1250 mOsm/L, did not demonstrate any increase in line related complications with the higher osmolarity.[35]

B. *Phases of PN*

The premature neonate undergoes a wide range of physiologic changes during the first weeks of life that influence fluid and electrolyte requirements, nutritional needs including energy, and macronutrients and micronutrients.

There are three phases of PN management – initiation, transition/advancement, and growth.[2] During the first three days of life (DOL), the neonate undergoes contraction of extracellular fluid to promote postnatal diuresis and weight loss. Early initiation of PN is

directed at preventing a catabolic state. A transition period follows during which the neonate may have metabolic and physiologic instability and fluid management should promote a weight loss of no more than 15 – 20% of birthweight (BW) with reasonable electrolyte homeostasis.[3] Nutrients remain high as the neonate stabilizes and reaches the growth period. During the transition phase, the skin matures, and renal function improves. Once the neonate stabilizes, full nutritional needs should be met.

C. *Early provision of Amino Acids (Starter PN)*

Early administration of amino acid (AA) and dextrose solution reverses the catabolic process that begins immediately after the disruption of placental circulation. This practice correlates to increased protein synthesis and positive nitrogen balance.[4] A meta-analysis found that early provision of AA results in a lower maximum percent of BW lost (approximately 3% less) and a shorter duration of time to regain BW (by 2 – 3 days).[5] Use of Starter PN is generally well tolerated.[5] Higher AA intake correlates with higher blood urea nitrogen (BUN) levels. This is not a contraindication to administration of parenteral AA in the setting of normal renal function.[6] Higher BUN likely reflects post-natal fluid loss and inappropriate provision of parenteral calories.[7] There is no known recommended upper tolerable limit for BUN as it relates to PN AA dosing.

The relationship between parenteral AA dose and metabolic acidosis in premature neonates is not fully determined. Parenteral AA administered as TrophAmine® 10% are neutral in vivo and do not contribute to acidosis. Metabolic acidosis is a common abnormality early in the neonatal course and occurs independent of AA dose and is not, by itself, a reason to limit parenteral AA.[8] A study published by Bonsante et al in 2017 compared three groups of very premature neonates (< 30 weeks) in an observational study.[9] The group with the highest nutritional intake (dextrose, AA, and lipids) had significantly worsened metabolic acidosis in the first weeks of life (pH and base excess) requiring increased buffers.[9] The authors did not speculate on why improved nutritional intake contributed to acidosis and found less extrauterine growth restriction in those with higher nutrient delivery in the first week of life.[9] They recommended further study to prevent and treat acidosis in the very premature neonate.

D. *Energy (Calories)*

Parenteral energy requirements are determined to account for both losses (resting energy expenditure and metabolic demands) and growth requirements. Energy needs rapidly increase in the first week of life as the neonate reaches the growth phase. Insufficient calorie intake may support energy expenditures but not reach the level required for normal growth. This may lead to cumulative deficits. Most premature neonates need at least 110 – 130 kcal/kg/day for growth. A minimum of 30 – 40 kcal per 1 g AA is recommended to guarantee AA utilization. Optimal glucose and lipid intakes that maximize protein accretion and growth in preterm neonates have not been determined at various parenteral AA intakes.[41] Recommendations of proportions of non-protein caloric sources are 60 – 75% from carbohydrates and 25 – 40% from fat.[41]

E. *Macronutrients*

a. Glucose is the major fuel source for premature neonates with needs for homeostasis and growth up to twice that of term newborns. Extremely low birth weight (ELBW) and very low birth weight (VLBW) neonates are at risk for hypoglycemia (glucose less than 45 mg/dL) if sufficient glucose infusion is not provided.[10] Due to minimal lean and fat tissue stores, alternate substrates for energy metabolism (ketones and lactate) are not present. Lower hepatic glycogen stores and impaired gluconeogenesis limit endogenous glucose production.[11]

ELBW neonates are also at risk for hyperglycemia (defined as glucose > 145 mg/dL per the European Society for Pediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN)). The more traditional cutoff has been 180 mg/dL, but newer evidence suggests lower targets should be the goal due to increased morbidity and mortality in neonates with glucose higher than 145 mg/dL.[13] Reduced insulin response to elevated blood glucose levels, likely partial insulin resistance, and a lack of negative feedback on hepatic glucose production during PN dextrose infusion make the preterm neonate particularly susceptible.[11] Historically, a minimum glucose infusion rate (GIR) of 4 mg/kg/min was recommended to meet minimum glucose utilization needs to sustain the brain's metabolic needs. Newer evidence has demonstrated that cerebrospinal fluid (CSF) glucose is highly linear with serum glucose levels, suggesting that lower GIR may be indicated in some circumstances, with the recommendation of increasing or decreasing GIR to maintain euglycemia, rather than focusing on fixed GIR goals.[38,50,51] GIR is increased incrementally (2 mg/kg/min per day as tolerated based on serum glucose) until a goal of 8 – 12 mg/kg/min is achieved.[12] GIR greater than 12 mg/kg/min exceeds the maximum glucose oxidation point leading to fat synthesis and increased CO_2 production. With high-carbohydrate PN administration, excess acetyl coenzyme A (CoA) generated from glucose oxidation provides a substrate for fat synthesis within the liver or hepatic de novo lipogenesis increasing the risk of PN-associated cholestasis (PNAC).[39]

Excessive GIR also exacerbates glucose intolerance. Treatment with insulin may be warranted if euglycemia cannot be achieved by minimizing GIR. It is important to remember that insulin response is unpredictable in preterm neonates due to peripheral insulin resistance.[40]

b. AA (Protein) – A minimum of 2 g/kg/day is required to prevent negative nitrogen balance but this dose is insufficient for protein synthesis.[14] Doses as high as 3 g/kg/day on DOL 1 are considered safe.[1,15] Doses exceeding 3.5 g/kg/day for neonates on exclusive PN are not shown to be beneficial or indicated. Increased first-week protein and energy intakes are associated with higher Mental Development Index scores and a lower likelihood of length growth restrictions at 18 months. New concerns regarding protein above 3.5 g/kg/day resulting in

worse neurodevelopmental outcomes has prompted ASPEN and ESPGHAN to strongly recommend not exceeding 3.5 g/kg/day in PN.[1,16,41]

The essential AA in PN include isoleucine, leucine, lysine, methionine, phenylalanine, threonine, tryptophan, and valine. Other AA may be conditionally essential due to the premature neonate's limited ability to synthesize them. They include cysteine, glutamine, glycine, histidine, taurine, and tyrosine.

Cysteine is a conditionally essential AA in preterm neonates due to the biochemical immaturity of the enzyme cystathionase, which converts methionine to cysteine and ultimately to taurine. Typically, it is added to PN at a dose of 40 mg/g of AA. Adding L-cysteine as the hydrochloride (HCl) salt to the PN solution acidifies the solution, which improves calcium and phosphorus solubility.

c. Lipids – Intralipid® are a vital source of essential fatty acids for central nervous system development. Additionally, they are a concentrated source of energy needed for protein synthesis.[25] Provision of 2 g/kg initiated at birth is associated with improved nitrogen balance.[17,20, 21]

   Hyperlipidemia may contribute to hyperglycemia due to an increase in free fatty acids which may decrease peripheral glucose utilization and/or inhibit the effect of insulin to suppress hepatic glucose production.[18,25] Conversely, hypertriglyceridemia may occur because of lipogenesis due to excessive glucose intake. Premature neonates are also at risk for hypertriglyceridemia due to immature lipoprotein lipase.[19,24] In children, lipoprotein lipase is considered saturated when triglycerides (TG) exceed 400 mg/dL. A lower cut-off is recommended for preterm neonates based on the presumption that lipoprotein lipase is deficient.[26] Therefore, the upper limits for a TG level in premature neonates are unknown. Balancing energy needs with potential concerns of prolonged hyperglycemia, JHACH recommends stopping advancing intravenous (IV) lipids if the TG level is > 250 mg/dL and temporarily decreasing/stopping it if > 300 – 350 mg/dL. To prevent essential fatty acid deficiency (EFAD) a minimum linoleic acid intake of 0.25 g/kg/day is required (1.35 g SMOFlipid® per kg/day or 0.5 g Intralipid® per kg/day).[22,26]

   Intralipid® consists of 100% soybean oil. A composite IV lipid emulsion, SMOFlipid®, has a more favorable fatty acid composition with 30% soybean oil, 30% medium-chain triglyceride, 25% olive oil, and 15% fish oil. SMOFlipid®'s profile is desirable due to the presence of omega-3 fatty acids, which have anti-inflammatory properties as well as docosahexaenoic acid (DHA), and eicosapentaenoic acid (EPA), long-chain polyunsaturated fatty acids that promote retinal and brain development, fewer phytosterols, and more α-tocopherol than Intralipid®.[24]

Premature neonates have a high risk of developing PNAC, due in part to extended use of long-term PN. Intralipid® contributes due to several factors such as high linoleic acid, which converts to arachidonic acid (AA), a precursor to pro-inflammatory agents. Additionally, Intralipid® contains a high amount of phytosterols, that cannot be metabolized by humans and accumulate in the liver and bile. Phytosterols reduce bile excretion by acting on the nuclear farnesoid X receptor and inhibiting the bile salt export pump, leading to intrahepatic bile accumulation.[23]

Oxidation of polyunsaturated fatty acids (PUFAs) results in oxygen free radical formation, which can bind to deoxyribonucleic acid (DNA) and proteins causing cellular damage and death. α-tocopherol can scavenge free radicals from peroxidized lipids to prevent the propagation of oxidative lipid damage.[43] To minimize lipid peroxidation, parenteral lipids should ideally be light-protected, including bags, bottles, and tubing.

Studies comparing Intralipid® to SMOFlipid® in premature neonates do not indicate a reduced risk for developing PNAC and as a result, currently, it is not recommended to use one specifically to decrease the risk.[1]

Omegaven® is a 10% pure fish oil, Food and Drug Administration (FDA)-approved lipid emulsion for PNAC. It contains high amounts of omega-3 fatty acids, EPA, and DHA, but fewer omega-6 fatty acids than Intralipid® and SMOFlipid®, hence less pro-inflammatory and more anti-inflammatory fatty acids. Concerns that 1 g/kg/day, the FDA-approved daily dosing, can cause EFAD seem to be unfounded. This is despite low omega-6 fatty acids as neonates on fish oil monotherapy have stable triene to tetraene ratios (~ 0.02) and no biochemical or clinical evidence of EFAD even with long term therapy.[44]

F. *Electrolytes*

Sodium (Na) and potassium (K) supplementation is not generally required in the first 24 to 48 hours after birth as neonates are normally born with excessive extracellular fluid (ECF) and diuresis that occurs in the first DOL.

Newer evidence indicates that K supplementation is well tolerated earlier than previously thought when given in conjunction with early provision of AA shortly after birth. This is important, as K acetate or K phosphate can correct other metabolic disturbances such as metabolic acidosis or hypophosphatemia.

a. Sodium (Na) - It is recommended that serum Na is monitored daily in the first week of life with supplementation of 2 – 4 mEq/kg starting once the neonate has lost at least 6% of BW and Na levels are dropping. Limiting Na intake and avoiding excessive fluid intake early in the neonatal course is important to lower the risk for bronchopulmonary dysplasia (BPD). Hypernatremia (serum Na > 150 mEq/L) and loss of > 15 – 20% of BW (up to 20% expected with the lowest

gestational age (GA) due to higher total body water content) is associated with increased risk for intraventricular hemorrhage (IVH). This is more commonly caused by dehydration and not excessive exogenous Na sources. Concern for hypernatremia often limits the provision of Na during the transition period increasing the risk for Na depletion and hyponatremia and subsequently correlates to reduced growth outcomes. Target Na levels should be between 135 and 145 mEq/L long term, balancing fluid needs and risk of both hyponatremia and hypernatremia. A level less than 130 mEq/L is consistent with hyponatremia and Na depletion should be considered. However, serum levels are influenced by acute high Na intake, diuretic administration, or water overload. When assessing Na balance, it is important to consider all components: fluid intake, weight, urine output, humidity, and Na intake (from PN and other sources such as other intravenous fluids (IVF), IV flushes, and saline-containing boluses). After the first week of life, higher Na intake is associated with improved growth and mental development.[27]

b. Potassium (K) is the principal intracellular cation. VLBW neonates are at risk for hyperkalemia due to low renal excretion. This is a result of decreased expression and decreased function of Na-K-ATPase pump, decreased responsiveness to aldosterone, and lower glomerular filtration rate (GFR). The early provision of higher AA intake immediately after birth is effective to modify K metabolism, by reducing non-oliguric hyperkalemia and urinary K loss by protecting intracellular K. This suggests that K intake as early as DOL 1 is safe and well tolerated particularly if serum K is less than 5 mg/dL (on a venous or arterial sample) and urine output is greater than 1 mL/kg/hour. K dose of 2 – 3 mEq/kg/day is the average recommended dose to maintain serum values. Adding K early is essential to decrease the risk of refeeding syndrome, especially for intrauterine growth restriction (IUGR)/small for gestational age (SGA) neonates.[45]

c. Acetate is metabolized in the liver to produce bicarbonate on a 1:1 molar ratio. Metabolic acidosis commonly occurs in premature neonates because of decreased renal reabsorption of bicarbonate. Also, PN solution, which contains AA especially with the addition of cysteine hydrochloride, is acidic. The addition of acetate in the first few days is preferable to chloride (1 to 2 mEq/kg per day) as either a Na or K salt as it will correct and prevent the acidosis. Acid base balance may also be affected by chloride sources outside of PN such as saline flushes. Hyperchloremia can exacerbate acidosis.

d. ASPEN/ESPHGAN does not recommend Standard PN (excludes early PN) for premature neonates[1,16]

G. *Calcium, Phosphorus and Magnesium*

a. Calcium (Ca) - Premature neonates have inadequate Ca reserves. A majority of Ca is accumulated in the last trimester of pregnancy, which results in a Ca

accretion rate of 90 to 150 mg/kg per day with a peak of 150 mg/kg per day at 36 to 38 weeks gestation.

After preterm birth, it is difficult to achieve the intrauterine Ca accretion rate with either parenteral or enteral supplementation. The amount of Ca that can be added to PN solutions is very limited and retention rates of Ca rarely exceed 60 mg/kg per day, which affects the bone mineral content of growing preterm neonates.[46] Shortly after birth, serum Ca acutely declines because of reduced Ca intake, possible impaired response to parathyroid hormone, increased calcitonin levels, and increased urinary loss.

b. Phosphorus (P) - In premature neonates, serum P may be elevated after delivery due to decreased cellular uptake as well as decreased GFR resulting in a reduced P excretion. However, as GFR improves and the neonate enters an anabolic state, cellular P uptake increases. Hypophosphatemia (serum P < 5 mg/dL) in IUGR/SGA neonates and neonates born to mothers with preeclampsia (secondary to placental insufficiency) who receive early optimized protein nutrition support is common, and therefore early P addition is required as early as DOL 1 to decrease the risk of refeeding syndrome.[29,30,45] Without adequate P, hypophosphatemia results in impaired bone deposition.

   Bone mineral deficits - Premature neonates are prone to bone mineral deficits as the majority of mineral deposition occurs in the third trimester of pregnancy. Parenteral Ca and P, even when optimized, will not meet this need. It cannot meet intrauterine accretion rates due to limited solubility in PN. Neonates with prolonged PN are at high risk for bone mineral deficits, osteopenia of prematurity, rickets, and fractures. Bone under mineralization may affect chest wall stability leading to atelectasis and an increased risk of chronic lung disease (CLD). With conventional radiologic methods, decreases in bone mineral content are not detected until there is a 30% to 40% loss of bone mineral.[47]

   The ideal Ca to P ratio to promote optimal mineral retention is 2 - 3 mEq Ca to 1 mmol P (1-1.5:1 molar ratio)[46] with ratios of less, possibly disrupting mineral homeostasis. A molar Ca:P ratio below 1 (1.6 – 2 mEq Ca: 1 mmol P) can be indicated to reduce the incidence of early postnatal hypercalcemia and hypophosphatemia in the first 2 – 3 DOL, in at risk neonates. After the first DOL Ca:P ratios should be 2.6 – 3 mEq Ca: 1 mmol P.[45,46]

c. Magnesium (Mg) - Hypermagnesemia may occur in premature neonates whose mothers received Mg therapy. However, once serum Mg normalizes, Mg supplementation is required.

H. *Contaminants in PN*

a. Chromium (Cr), Manganese (Mn) and minute amounts of copper (Cu) and selenium (Se) are present in PN among other trace elements as contaminants. (See section I for details)

b. Aluminum - In contrast to minerals that have been found to have a role in an enzymatic metalloproteins, only aluminum has not been found to have any biological role. When normal physical barriers are bypassed, aluminum has been associated with toxicity, both neurological and to bone health. Aluminum is present in all ingredients of PN as well as some other IV solutions with additives, with the highest levels being found in calcium gluconate, inorganic phosphates (substantially higher in K phosphate than Na phosphate), and cysteine hydrochloride.

Aluminum accumulates in bone and ~ 45% of total body aluminum found is deposited in bone. Bishop et al performed a randomized study of 182 preterm neonates. They compared neonates randomly assigned to receive standard PN or aluminum depleted PN. At 18 months post-conceptual age (PCA), a subgroup of the patients had the Bayley Scales of Infant Development Mental Developmental Index performed. The study revealed a loss of 1 index point for each day patients received the standard aluminum-containing PN.[48] A follow up study at 13 – 15 years of age of the same patients showed decreased bone density and higher fracture rate in patients that received standard PN compared to aluminum depleted PN.[49]

The FDA requires warnings stating that in patients with impaired renal function, which is common in preterm neonates, infusion of solutions with more than 5 µg/kg per day of aluminum may result in central nervous system and bone toxicity. When aluminum has been measured in studies, the solutions have lower aluminum concentrations than the components' labels projected, but none of the compounded neonatal or pediatric PN have an aluminum concentration below the FDA recommended 5 µg/kg per day.

Neonates on long term PN have been shown to have up to 8-fold aluminum concentrations compared to those who do not require long term PN. The greatest risk of aluminum exposure occurs in IV preparations for micronutrients. Aluminum exposure via PN has been shown to have long-term effects in preterm neonates. Every effort should be made to minimize the aluminum content, although with the currently available products, the concentration will still be above the recommended amount.[36] Thus avoiding prolonged PN if possible and advancement of enteral feedings is critical to minimize accumulated aluminum exposure. It is recommended to optimize PN despite aluminum content, with goal of exposing neonates to PN for the shortest amount of time while providing adequate nutritional care.

I. Vitamins and Trace Elements

a. Vitamins are a group of substances that the body cannot produce, that are needed for normal cell function, growth, and development. Multivitamins are added to PN solutions. At JHACH, Infuvite Pediatric is used. With the amount added to PN, neonates will not receive recommended minimal daily dose of vitamin A or D until they are > 2.5 kg and may receive excessive amounts of some of the water-soluble vitamins.

b. Zinc (Zn) is a cofactor for over 300 metalloenzymes and is essential for growth, cell differentiation, and metabolism of macronutrients. Zn is important for GI development, immune function, and growth. Accumulation of Zn stores occurs primarily during the last trimester of pregnancy therefore premature neonates are at high risk for deficiency if intake is inadequate. This is compounded by increased GI tract and urinary losses. Zn deficiency manifests after 3 months with symptoms including poor growth, periorificial dermatitis, glossitis, and increased risk for infections. Neonates with GI surgeries and high GI output have higher Zn needs.

c. Cu is a cofactor for metalloenzymes including superoxide dismutase which function as free radical scavengers and play an important role in preventing oxidative stress. Cu is transported by ceruloplasmin, a protein that is also needed for iron (Fe) release from hepatic stores to bind to transferrin. Neonatal stores accumulate during the third trimester of pregnancy therefore premature neonates have low reserves. Cu needs are higher in premature neonates compared to term and deficiency is described in those with insufficient intake. Parenteral Cu is excreted in bile therefore in premature neonates with PNAC the historical practice was to decrease the dose of Cu in PN solutions. Thus, placing the neonate at risk for deficiency.

   Cu status is assessed by measuring Cu and ceruloplasmin levels. Ceruloplasmin is an acute phase reactant and therefore levels may measure high during the inflammatory states. Deficiency manifests as hypochromic anemia, pancytopenia, poor wound healing, neutropenia, osteopenia, and fractures.

d. Se a cofactor for the selenoenzymes which include glutathione peroxidase which acts as an antioxidant and scavenges free radicals to help protect against oxidative stress. Complications of prematurity including BPD, retinopathy of prematurity (ROP), IVH, and necrotizing enterocolitis (NEC) result due to free radical damage. Se is also important in the function of thyroid hormones. Similar to other nutrients, Se accretion occurs during the last trimester of pregnancy, therefore premature neonates are born with insufficient stores. It is recommended that all neonates have Se added to PN.

e. Cr functions as a potentiator of insulin, specifically for glucose tolerance factor. Cr is a contaminant of PN solutions and therefore short term PN does not require additional CR. However, those who will be PN dependent for more than a month may require the addition. Neonates with renal failure should have Cr held from PN due to reliance on urinary excretion.

f. Mn is a cofactor for multiple enzymes. It is found to accumulate in body tissues including the liver and brain. Mn is a contaminant in PN and there is growing concern of toxicity when additional Mn is added.

g. Fe - The body requires Fe for the synthesis of oxygen transport proteins (e.g., hemoglobin and myoglobin) and for the formation of heme and other iron-containing enzymes involved in electron transfer and oxidation-reductions.[37] Due to concerns of Fe overload, radical formation, and possible increased risk of sepsis with parenteral Fe supplementation, it is not recommended to add Fe for neonates requiring short term PN. The decision to add IV Fe to neonates on PN can be made on individual basis after 4 weeks of PN.

The current recommended doses of trace elements in PN are noted as follows:

BW	Zn	Se	Cu	Mn	Cr
≤ 2.5 kg	400 mcg/kg/day	2 mcg/kg/day	20 mcg/kg/day	0	0
> 2.5 kg	250 mcg/kg/day	2 mcg/kg/day	10 mcg/kg/day	0	0

J. *Carnitine*

Carnitine facilitates the transport of long-chain fatty acids across the mitochondrial membrane, and thus makes them available for beta-oxidation. Premature neonates have limited stores of carnitine and synthesis is limited. Studies done by Eberhard Schmidt-Sommerfeld et al and Bonner et al demonstrated that premature neonates requiring total PN develop carnitine deficiency with impaired fatty oxidation and ketogenesis and supplementation improves this metabolic disturbance.[31,32]

Carnitine is routinely added to PN at 15 mg/kg/day in VLBW neonates with a weight < 1,500 grams. For neonates > 1,500 grams with prolonged periods without enteral nutrition, carnitine may be added, although the exact time at which carnitine is needed is not well defined. The practice at JHACH is to add carnitine in neonates > 1,500 grams after 2 weeks of PN and continued minimal enteral feedings.

K. *Discontinuation of PN*

PN should be continued until adequate nutritional intake from enteral feeding is tolerated, ideally until ~ 75% of nutritional requirement (120 mL/kg/day in preterm neonates) is reached.[33] The weaning of PN as enteral feeds advance is a critical window during which deficits in nutritional intake may occur particularly when subjects reach 1/3

enteral feeds until full enteral feeds.[34] This research supports a standardized approach to weaning PN to prevent nutritional deficits.

TPN Clinical Management/Pathway:

FLUIDS				
Weight	**1st 24 Hours**	**Advance By**	**Goal**	**Comments**
< 750 g	100 mL/kg/day	Increase by 20 mL/kg/day	150 mL/kg/day	• Fluid intake during the initiation and advancement phase must promote postnatal diuresis • Premature neonates may lose up to 15 – 20% of BW with the goal to regain to BW by DOL 10 – 14 • Neonates with an open patent ductus arteriosus (PDA) may be fluid restricted during the growth phase to reduce risk for CLD
750 – 1,000 g	80 mL/kg/day			
> 1,000 g	60 mL/kg/day			

MACRONUTRIENTS **if utilizing starter PN, skip 1st custom PN column and move to advance by column**					
	Starter PN	**1st Custom PN**	**Advance By**	**Goal**	**Comments**
Energy		40 – 50 kcal/kg/day		• ELBW: 105 - 115 kcal/kg/day • VLBW: 90 – 100 kcal/kg/day	May need up to 160 kcal/kg/day but should not exceed that
Protein	• Min: **50 mL/kg/day** (2 g/kg/day) • Max**: 88 mL/kg/day** (3.5 g/kg/day)	3 g/kg/day	0.5 g/kg/day	• ELBW: 3.5 g/kg/day • VLBW: 3.5 g/kg/day • Newborn Nursery (NBN): 3 g/kg/day	Max 4 g/kg/day in special circumstances (discuss with Dietician); **Add cysteine 40 mg/g AA, MUST be exact for appropriate Ca-P solubility graph**
Lipids	• ELBW: 1 g/kg/day • VLBW: 2 g/kg/day	• ELBW: 1 g/kg/day • VLBW: 2 g/kg/day	1 – 2 g/kg/day	3 g/kg/day	
Dextrose	• Min: **50 mL/kg/day** (GIR: 3 mg/kg/min) • Max**: 88 mL/kg/day** (GIR: 6.2 mg/kg/min)	GIR 4 – 6 mg/kg/min	Advance GIR by 1 – 2 mg/kg/min for glucose < 150 mg/dL	GIR 8 – 10 mg/kg/min	Recommend max GIR 12 mg/kg/min unless strong clinical indication

ELECTROLYTES					
	Starter PN	**1st Custom PN**	**Advance By**	**Goal**	**Comments**
K		As needed	1 – 2 mEq/kg/day	2 – 4 mEq/kg/day	• **Adding K early is essential to decrease risk of refeeding syndrome, especially for IUGR/SGA infants** • Avoid addition of Na in the first 48 hours of life unless clinically indicated (preferably Na phosphate or acetate) • Consider adding K as acetate in the absence of significant renal dysfunction
Na			2 – 3 mEq/kg/day after 48 hours of life, then advance by 1 – 2 mEq/kg/day	4 – 6 mEq/kg/day	
Chloride			As needed		
Acetate		As needed			

MINERALS					
	Starter PN	**1st Custom PN**	**Advance By**	**Goal**	**Comments**
Ca	• Min: **50 mL/kg/day** (0.8 mEq/kg/day) • Max**: 88 mL/kg/day** (1.3 mEq/kg/day)	Maximize Ca:P	Maximize Ca: P	3.2 – 7 mEq/kg/day	• **2 – 3 mEq Ca: 1 mmol P (1 – 1.5 mEq: 1 molar ratio)** • Decreases in bone mineral content are not detected until there is a 30% to 40% loss of bone mineral
P		0 – 1 mmol/kg/day	Based on serum level, up to a daily dose of 1.3 – 2 mmol/kg/day	1.6 – 2.6 mmol/kg/day	**Premature infants are at risk for hypophosphatemia if no P in early PN**
Mg		0.3 mg/kg/day if mother did not receive Mg and neonate's Mg level is not normal	Based on serum level, up to a daily dose of 0.3 – 0.5 mg/kg/day	0.2 – 0.5 mg/kg/day	

Adjusting Lipids for TG > 200 mg/dL

Serum TG Levels (mg/dL)	Lipid Adjustments
200 – 249	Continue lipids and do not advance that evening
250 – 299	Decrease lipids by 0.5 – 1 g/kg/day that evening
300 – 350	• Hold lipids and decrease by 50% that evening ○ Maintain lipids at 0.5 – 1 g/kg/day to prevent EFAD • Decrease GIR if > 10 mg/kg/min
> 350	• Hold lipids; no lipids that evening • Decrease GIR if > 10 mg/kg/min
If lipid dose is being lowered due to abnormal TG, this should be done during morning rounds and does not need to wait until the new bag is delivered. Recheck TG 24 – 48 hours after adjustments to PN. If TG has decreased, recheck TG levels in 24 hours.	

Adjusting Trace Elements

Vitamins/Trace Elements/Carnitine				
Weight	**Vitamins**	**Zn**	**Se**	**Cu**
< 1.5 kg	2 mL/kg/day (max: 5 mL)	400 mcg/kg/day	2 mcg/kg/day	20 mcg/kg/day
1.5 to < 5 kg		250 mcg/kg/day		
Liver dysfunction (direct bilirubin > 2 mg/dL) • Increase Zn mcg/kg/day by 200 mcg/kg/day • Assess Cu status in PN and if elevated, decrease Cu to 10 mcg/kg/day **Renal dysfunction (creatinine > 1 mg/dL)** • Omit Se (if not on dialysis) • Can add Zn 400 mcg/kg/day and Cu 20 mcg/kg/day				
Carnitine	If weight > 1.5 kg and no enteral nutrition > 14 days, add 15 mg/kg/day			

Monitoring

Lab	Initiation	Advancement	Stable
Glucose	At initiation	Daily	Daily
Electrolytes	At initiation	ELBW/VLBW: daily until stable > 15 kg: 2 times a week	Weekly
Liver function tests (LFTs), direct bilirubin	At initiation	Weekly	Weekly while on PN
Ca, P, Mg	At initiation	24 – 48 hours	Weekly while at goal or weaning
TG	1 – 2 days after initiation	2 – 3 times a week	Weekly while at goal; if PN adjustment due to increased TG, recheck no later than 48 hours after dose change
Trace elements	Not indicated	Not indicated	Zn, Cu, ceruloplasmin, Mn, Se and Cr levels after 30 days of PN dependence
Vitamin levels	Not indicated	Not indicated	After 30 days of PN dependence

Summary:

PN is a critical component of care for premature and critically ill term neonates. Despite best effort and optimization components, PN is not able to provide optimal nutrition for neonates and should be used for the shortest time possible.

References:

1. Robinson, D. T., Calkins, K. L., Chen, Y., Cober, M. P., Falciglia, G. H., Church, D. D., Mey, J., McKeever, L., & Sentongo, T. (2023). Guidelines for parenteral nutrition in preterm infants: The American Society for parenteral and enteral nutrition. *Journal of Parenteral and Enteral Nutrition*, *47*(7), 830-858.
2. Koletzko, B., Cheah, F., Domellöf, M., Poindexter, B., Vain, N., & Goudoever, J. V. (2021). *Nutritional care of preterm infants: Scientific basis and practical guidelines*. Karger Medical and Scientific Publishers.
3. Oh, W., Poindexter, B. B., Perritt, R., Lemons, J. A., Bauer, C. R., Ehrenkranz, R. A., Stoll, B. J., Poole, K., & Wright, L. L. (2005). Association between fluid intake and weight loss during the first ten days of life and risk of Bronchopulmonary dysplasia in extremely low birth weight infants. *The Journal of Pediatrics*, *147*(6), 786-790.
4. Trivedi, A., & Sinn, J. K. (2013). Early versus late administration of amino acids in preterm infants receiving parenteral nutrition. *Cochrane Database of Systematic Reviews*. https://doi.org/10.1002/14651858.cd008771.pub2.
5. Moyses, H. E., Johnson, M. J., Leaf, A. A., & Cornelius, V. R. (2013). Early parenteral nutrition and growth outcomes in preterm infants: A systematic review and meta-analysis. *The American Journal of Clinical Nutrition*, *97*(4), 816-826.
6. Kotsopoulos, K., Benadiba-Torch, A., Cuddy, A., & Shah, P. S. (2006). Safety and efficacy of early amino acids in preterm <28 weeks gestation: Prospective observational comparison. *Journal of Perinatology*, *26*(12), 749-754.
7. Balakrishnan, M., Tucker, R., Stephens, B. E., & Bliss, J. M. (2011). Blood urea nitrogen and serum bicarbonate in extremely low birth weight infants receiving higher protein intake in the first week after birth. *Journal of Perinatology*, *31*(8), 535-539.
8. Jadhav, P., Parimi, P. S., & Kalhan, S. C. (2007). Parenteral amino acid and metabolic acidosis in premature infants. *Journal of Parenteral and Enteral Nutrition*, *31*(4), 278-283.
9. Bonsante, F., Gouyon, J., Robillard, P., Gouyon, B., & Iacobelli, S. (2017). Early optimal parenteral nutrition and metabolic acidosis in very preterm infants. *PLOS ONE*, *12*(11), e0186936. https://doi.org/10.1371/journal.pone.0186936
10. Adamkin, D. H. (2017). Neonatal hypoglycemia. *Seminars in Fetal and Neonatal Medicine*, *22*(1), 36-41. https://doi.org/10.1016/j.siny.2016.08.007.
11. Arsenault, D., Brenn, M., Kim, S., Gura, K., Compher, C., Simpser, E., & Puder, M. (2011). A.S.P.E.N. Clinical guidelines. *Journal of Parenteral and Enteral Nutrition*, *36*(1), 81-95.
12. Poindexter, B.B. and Ehrenkranz R.A. (2015). Nutrient requirements and provision of nutritional support in the premature neonate. In: Martin RJ, Fanaroff AA, Walsh MC, editors. Fanaroff and Martin's Neonatal-Perinatal Medicine, 10th edition. Philadelphia(PA):Saunders, an imprint of Elsevier Inc. 43:592-612.

13. Mesotten, D., Joosten, K., Van Kempen, A., Verbruggen, S., Braegger, C., Bronsky, J., Cai, W., Campoy, C., Carnielli, V., Darmaun, D., Decsi, T., Domellöf, M., Embleton, N., Fewtrell, M., Fidler Mis, N., Franz, A., Goulet, O., Hartman, C., Hill, S., … Yan, W. (2018). Espghan/Espen/Espr/Cspen guidelines on pediatric parenteral nutrition: Carbohydrates. *Clinical Nutrition*, *37*(6), 2337-2343
14. Embleton, N. D., & Van Den Akker, C. H. (2017). Early parenteral amino acid intakes in preterm babies: Does NEON light the way? *Archives of Disease in Childhood - Fetal and Neonatal Edition*, *103*(2), F92-F94. https://doi.org/10.1136/archdischild-2017-313406.
15. Leenders, E. K., De Waard, M., & van Goudoever, J. B. (2017). Low- versus high-dose and early versus late parenteral amino-acid administration in very-low-Birth-Weight infants: A systematic review and meta-analysis. *Neonatology*, *113*(3), 187-205.
16. Stephens, B. E., Walden, R. V., Gargus, R. A., Tucker, R., McKinley, L., Mance, M., Nye, J., & Vohr, B. R. (2009). First-week protein and energy intakes are associated with 18-Month developmental outcomes in extremely low birth weight infants. *Pediatrics*, *123*(5), 1337-1343.
17. Vlaardingerbroek, H., Vermeulen, M. J., Rook, D., Van den Akker, C. H., Dorst, K., Wattimena, J. L., Vermes, A., Schierbeek, H., & Van Goudoever, J. B. (2013). Safety and efficacy of early parenteral lipid and high-dose amino acid administration to very low birth weight infants. *The Journal of Pediatrics*, *163*(3), 638-644.e5.
18. Hemachandra, A. H., & Cowett, R. M. (1999). Neonatal hyperglycemia. *Pediatrics In Review*, *20*(7), e16-e24.
19. Lim, M. S., Choi, C. W., Kim, B. I., & Yang, H. R. (2013). Clinical factors affecting lipid metabolism and optimal dose of heparin in preterm infants on parenteral nutrition. *Pediatric Gastroenterology, Hepatology & Nutrition*, *16*(2), 116.
20. Balint, J., & American Society for Parenteral and Enteral Nutrition. (2015). *The A. S. P. E. N. Pediatric nutrition support core curriculum* (2nd ed.).
21. Drenckpohl, D., McConnell, C., Gaffney, S., Niehaus, M., & Macwan, K. S. (2008). Randomized trial of very low birth weight infants receiving higher rates of infusion of intravenous fat emulsions during the first week of life. *Pediatrics*, *122*(4), 743-751.
22. Morgensen K. Essential Fatty Acid Deficiency. (2017). Practical Gastroenterology,164:37-44.
23. Burrin, D. G., Ng, K., Stoll, B., & De Pipaón, M. S. (2014). Impact of new-generation lipid emulsions on cellular mechanisms of parenteral nutrition–associated liver disease. *Advances in Nutrition*, *5*(1), 82-91. https://doi.org/10.3945/an.113.004796.
24. Repa, A., Binder, C., Thanhaeuser, M., Kreissl, A., Pablik, E., Huber-Dangl, M., Berger, A., & Haiden, N. (2018). A mixed lipid emulsion for prevention of parenteral nutrition associated Cholestasis in extremely low birth weight infants: A randomized clinical trial. *The Journal of Pediatrics*, *194*, 87-93.e1.
25. Uthaya, S., Liu, X., Babalis, D., Doré, C. J., Warwick, J., Bell, J., Thomas, L., Ashby, D., Durighel, G., Ederies, A., Yanez-Lopez, M., & Modi, N. (2016). Nutritional evaluation and optimization in neonates: A randomized, double-blind controlled trial of amino acid regimen and intravenous lipid composition in preterm parenteral nutrition. *The American Journal of Clinical Nutrition*, *103*(6), 1443-1452.

26. Lapillonne A, Fidler Mis N, Goulet O, van den Akker CHP, Wu J, Koletzko B,al. ESPGHAN/ESPEN/ESPR/CSPEN guidelines on pediatric parenteral nutrition: lipids. Clin Nutr. 2018;37:2324–36
27. Bischoff, A. R., Tomlinson, C., & Belik, J. (2016). Sodium intake requirements for preterm neonates: Review and recommendations. *Journal of Pediatric Gastroenterology & Nutrition*, *63*(6), e123-e129.
28. Crews, J., Rueda-de-Leon, E., Remus, D., Sayles, R., Mateus, J., & Shakeel, F. (2018). Total parenteral nutrition standardization and electronic ordering to reduce errors: A quality improvement initiative. *Pediatric Quality & Safety*, *3*(4), e093.
29. Brener Dik, P. H., Galletti, M. F., Fernández Jonusas, S. A., Alonso, G., Mariani, G. L., & Fustiñana, C. A. (2015). Early hypophosphatemia in preterm infants receiving aggressive parenteral nutrition. *Journal of Perinatology*, *35*(9), 712-715.
30. Ross, J. R., Finch, C., Ebeling, M., & Taylor, S. N. (2013). Refeeding syndrome in very-low-birth-weight intrauterine growth-restricted neonates. *Journal of Perinatology*, *33*(9), 717-720.
31. Schmidt-Sommerfeld, E., Penn, D., & Wolf, H. (1983). Carnitine deficiency in premature infants receiving total parenteral nutrition: Effect of L-carnitine supplementation. *The Journal of Pediatrics*, *102*(6), 931-935.
32. Bonner, C. M., DeBrie, K. L., Hug, G., Landrigan, E., & Taylor, B. J. (1995). Effects of parenteral L-carnitine supplementation on fat metabolism and nutrition in premature neonates. *The Journal of Pediatrics*, *126*(2), 287-292.
33. Miller, M., Vaidya, R., Rastogi, D., Bhutada, A., & Rastogi, S. (2013). From parenteral to enteral nutrition. *Journal of Parenteral and Enteral Nutrition*, *38*(4), 489-497.
34. Falciglia, G. H., Murthy, K., Holl, J. L., Palac, H. L., Oumarbaeva, Y., Woods, D. M., & Robinson, D. T. (2018). Energy and protein intake during the transition from parenteral to enteral nutrition in infants of very low birth weight. *The Journal of Pediatrics*, *202*, 38-43.e1
35. Fessler, A. G., & Rejrat, C. E. (2021). Re-evaluating safe Osmolarity for peripheral parenteral nutrition in neonatal intensive care patients. *The Journal of Pediatric Pharmacology and Therapeutics*, *26*(6), 632-637. https://doi.org/10.5863/1551-6776-26.6.632
36. Corkins, M. R., Abrams, S. A., Fuchs, G. J., Goday, P. S., Hannon, T. S., Kim, J. H., Lindsey, C. W., & Rome, E. S. (2019). Aluminum effects in infants and children. *Pediatrics*, *144*(6).
37. Abbaspour N., Hurrell R., Kelishadi R. (2014). Review on iron and its importance for human health. *Journal of Research in Medical Sciences,* 19,164-74.
38. Nigrovic, L. E., Kimia, A. A., Shah, S. S., & Neuman, M. I. (2012). Relationship between cerebrospinal fluid glucose and serum glucose. *New England Journal of Medicine*, *366*(6), 576-578
39. Fell, G. L., Nandivada, P., Gura, K. M., & Puder, M. (2015). Intravenous lipid emulsions in parenteral nutrition. *Advances in Nutrition*, *6*(5), 600-610.
40. 40. Blanco, C. L., McGill-Vargas, L. L., Gastaldelli, A., Seidner, S. R., McCurnin, D. C., Leland, M. M., Anzueto, D. G., Johnson, M. C., Liang, H., DeFronzo, R. A., & Musi, N. (2015). Peripheral insulin resistance and impaired insulin signaling contribute to abnormal glucose metabolism in preterm baboons. *Endocrinology*, *156*(3), 813-823

41. Van Goudoever, J. B., Carnielli, V., Darmaun, D., Sainz de Pipaon, M., Braegger, C., Bronsky, J., Cai, W., Campoy, C., Carnielli, V., Darmaun, D., Decsi, T., Domellöf, M., Embleton, N., Fewtrell, M., Fidler Mis, N., Franz, A., Goulet, O., Hartman, C., Hill, S., … Yan, W. (2018). Espghan/Espen/Espr/Cspen guidelines on pediatric parenteral nutrition: Amino acids. *Clinical Nutrition*, *37*(6), 2315-2323.
42. Soghier LM, Brion LP.Cysteine, cystine or N-acetylcysteine supplementation in parenterally fed neonates. *Cochrane Database of Systematic Reviews* 2006, Issue 4. Art. No.: CD004869.
43. Brigelius-Flohé, R. (2006). Bioactivity of vitamin E. *Nutrition Research Reviews*, *19*(2), 174-186.
44. Nandivada, P., Fell, G. L., Mitchell, P. D., Potemkin, A. K., O'Loughlin, A. A., Gura, K. M., & Puder, M. (2016). Long-term fish oil lipid emulsion use in children with intestinal failure–associated liver disease. *Journal of Parenteral and Enteral Nutrition*, *41*(6), 930- 937
45. Da Silva, J. S., Seres, D. S., Sabino, K., Adams, S. C., Berdahl, G. J., Citty, S. W., Cober, M. P., Evans, D. C., Greaves, J. R., Gura, K. M., Michalski, A., Plogsted, S., Sacks, G. S., Tucker, A. M., Worthington, P., Walker, R. N., & Ayers, P. (2020). ASPEN consensus recommendations for Refeeding syndrome. *Nutrition in Clinical Practice*, *35*(2), 178-195.
46. Mihatsch, W., Fewtrell, M., Goulet, O., Molgaard, C., Picaud, J., Senterre, T., Braegger, C., Bronsky, J., Cai, W., Campoy, C., Carnielli, V., Darmaun, D., Decsi, T., Domellöf, M., Embleton, N., Fewtrell, M., Fidler Mis, N., Franz, A., Goulet, O., … Yan, W. (2018). Espghan/Espen/Espr/Cspen guidelines on pediatric parenteral nutrition: Calcium, phosphorus and magnesium. *Clinical Nutrition*, *37*(6), 2360-2365
47. Greer, F. R. (2016). Calcium and phosphorus and the preterm infant. *NeoReviews*, *17*(4), e195-e202.
48. Bishop, N. J., Morley, R., Day, J. P., & Lucas, A. (1997). Aluminum neurotoxicity in preterm infants receiving intravenous-feeding solutions. *New England Journal of Medicine*, *336*(22), 1557-1562.
49. Fewtrell, M. S., Bishop, N. J., Edmonds, C. J., Isaacs, E. B., & Lucas, A. (2009). Aluminum exposure from parenteral nutrition in preterm infants: Bone health at 15-Year follow-up. *Pediatrics*, *124*(5), 1372-1379.
50. Hay WW Jr. Nutritional Support Strategies for the Preterm Infant in the Neonatal Intensive Care Unit. Pediatr Gastroenterol Hepatol Nutr. 2018 Oct;21(4):234-247.
51. World Review of Nutrition and Dietetics. Nutritional care of Preterm Infants Scientific Basis and Practical Guidelines 2nd Edition Volume 122 Page 68
52. Zozaya, C.; Aziz, K.;Singhal, N.; Ye, X.Y.; Drolet, C.;Emberley, J.; Lee, K.-S.; Shah, V.S.; on behalf of the Canadian Neonatal Network (CNN) Investigators. Association of Weight Changes by Three Days after Birth and Mortality and/or Severe Neurological Injury in Preterm Infants < 29Weeks Gestational Age: A Multicenter Cohort Study. Children 2022, 9, 276

Outcome Measures:

1. Time to regain BW
    a. To evaluate the number of days it takes for an infant to regain their BW when PN is used as a nutritional intervention. This will assess the effectiveness of PN in promoting weight recovery and overall growth in neonates with feeding difficulties or medical conditions requiring parenteral nutrition.
    b. Primary endpoint:
        i. Time (in days) to reach BW following the initiation of PN
    c. Secondary endpoints:
        i. Time to start oral/enteral feeding
        ii. Incidence of PN-related complications
        iii. Rate of weight gain per day during PN use
    d. Outcome classification:
        i. Short regain time: ≤ 14 days to regain BW
        ii. Moderate regain time: 15 – 21 days to regain BW
        iii. Delayed regain time: > 21 days to regain BW
2. Time to goal lipids
    a. To assess the time required for a patient to reach the goal lipid dose while receiving PN. This outcome measure is particularly important in the management of neonates, premature infants, or patients with feeding difficulties who require PN to ensure adequate energy and essential fatty acid intake.
    b. Primary endpoint:
        i. Time (in days) to reach the goal lipid dose for each patient
    c. Secondary endpoints:
        i. Incidence of hypertriglyceridemia (e.g., triglycerides > 250 mg/dL)
        ii. Frequency of lipid dose adjustments (e.g., how often the infusion rate is altered)
        iii. Growth progress and weight gain during the PN regimen
        iv. Liver function changes or complications during the lipid infusion
    d. Outcome Classification:
        i. Rapid: Goal lipid dose reached in < 3 days
        ii. Moderate: Goal lipid dose reached within 3 – 5 days
        iii. Delayed: Goal lipid dose reached after > 5 days
3. Time to goal protein
    a. To evaluate the time, it takes for a patient to reach the target protein levels (goal protein dose) while receiving PN. This measure is critical for ensuring that patients, particularly neonates, preterm infants, or patients with gastrointestinal or metabolic issues, receive the necessary amount of protein to support growth, development, and recovery.
    b. Primary endpoint:
        i. Time (in days) to reach the goal protein dose (measured in g/kg/day) for each patient
    c. Secondary endpoints:
        i. Incidence of hyperammonemia or other protein-related complications
        ii. Frequency of protein dose adjustments during PN administration

iii. Growth progress and weight gain during the period of receiving goal protein levels

d. Outcome classification:
    i. Rapid: Goal protein dose reached in < 3 days
    ii. Moderate: Goal protein dose reached within 3 – 5 days
    iii. Delayed: Goal protein dose reached after > 5 days

4. Time to goal GIR
    a. To assess the time, it takes for a patient receiving TPN to reach the target GIR, which is an essential parameter for managing glucose metabolism and energy provision, particularly in neonates, preterm infants, or patients with metabolic challenges. The goal is to ensure appropriate glucose provision while avoiding hyperglycemia or hypoglycemia.
    b. Primary endpoint:
        i. Time (in days) to reach the goal GIR (measured in mg/kg/min)
    c. Secondary endpoints:
        i. Incidence of hyperglycemia (e.g., blood glucose > 180 mg/dL)
        ii. Frequency of GIR adjustments (e.g., how often the infusion rate is altered)
        iii. Blood glucose variability during PN administration
        iv. Growth progress and weight gain during the period of receiving goal GIR levels
    d. Outcome Classification:
        i. Rapid: Goal GIR dose reached in < 3 days
        ii. Moderate: Goal GIR dose reached within 3 – 5 days
        iii. Delayed: Goal GIR dose reached after > 5 days
5. Time to goal calories
    a. To assess the time required for a patient to reach the target caloric intake (goal calories) while receiving PN. This outcome measure is particularly important for patients who require PN support, such as neonates, preterm infants, or those with gastrointestinal or metabolic conditions, to ensure that they receive adequate caloric provision for growth, development, and recovery.
    b. Primary endpoint:
        i. Time (in days) to reach the goal caloric intake (measured in kcal/kg/day) for each patient
    c. Secondary endpoints:
        i. Incidence of hyperglycemia or hypoglycemia during the caloric titration process
        ii. Frequency of caloric adjustments and the reason for adjustments
        iii. Weight gain during PN administration and comparison to age-appropriate growth standards.
        iv. Changes in clinical markers, including liver function and electrolytes
    d. Outcome Classification:
        i. Rapid: Goal calories dose reached in < 3 days
        ii. Moderate: Goal calories dose reached within 3 – 5 days
        iii. Delayed: Goal calories dose reached after > 5 days

Clinical Pathway Team

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Date Approved by Hospital Wide JHACH Clinical Practice Council (if applicable):

Date Available on Webpage: January 7, 2025

Last Content Revised: January 7, 2025

Last Formatted: January 7, 2025

Template Last Revised. Any changes to this template must be approved by the Clinical Pathways Program Director.

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