PARENTERAL NUTRITION

Parenteral Nutrition (PN) is a form of artificial nutrition and hydration given through a central or peripheral vein for patients whose GI tracts cannot be accessed, are not functioning/are functioning inadequately, or whose nutrition needs cannot be met with oral diets or enteral nutrition support. It is an intravenous mixture containing crystalline amino acids, fat emulsion, sterile water, electrolytes, vitamins, and minerals. Parenteral nutrition can be a standardized commercially available product, or an individually customized/compounded formula. It may come as a 2-in1 (amino acids + dextrose) or 3-in-1 product (amino acids + dextrose + intravenous fat emulsion, sometimes called a total nutrient admixture or TNA).

Indications:

- Nonfunctioning gastrointestinal tract due to major gastrointestinal surgeries or conditions such as GI fistulas, Crohn's disease, short bowel syndrome, severe acute necrotizing pancreatitis, severe liver failure, and intractable diarrhea or vomiting
- When EN is contraindicated or the GI tract has severely decreased functional ability to conditions such as small bowel obstruction, paralytic ileus, mesenteric ischemia, GI fistula (except when EN access is possible distal to the fistula, or output is small (<200ml/d) supporting a trial of EN)
- Critical illness with poor enteral tolerance or access
- Perioperative nutrition support of patients with moderate to severe malnutrition

Routes of PN:

The routes of parenteral nutrition administration are dependant on length of therapy needed, nutrient requirements, available intravenous access, and fluid requirements.

- **Total Parenteral Nutrition (TPN):** May be referred to as Central Parenteral Nutrition (CPN) as it is infused to a central vein. TPN/CPN is given through a port in a large central vein such as the subclavian or jugular vein or by using a PICC line that originates in the arm and extends to one of the central veins. It is imperative that TPN is infused into a central (and not peripheral) line. This method is chosen if the patient has high nutritional needs or long-term use needs. TPN can contain all the protein, fats, carbohydrates, and nutrients needed for survival. Technically only "Total" if patient is receiving all their nutrition needs, and has no intake via other routes, though most still refer to CPN as "TPN," even if it doesn't exactly fit the definition.

- **Peripheral Parenteral Nutrition (PPN**): This form of parenteral nutrition is given through a smaller vein, usually in the hand or forearm. PPN is intended for short-term use, usually less than two weeks, and usually meets only partial amounts of patient needs. The patient must be able to tolerate a larger fluid volume, due to the formula needing to be lower osmolality when infusing into a smaller vein. PPN use has been more scrutinized in recent years as the risks do not always outweigh the benefits of the partial nutrition support.

Parenteral Nutrition Contents:

When calculating kcals in a volume of a given concentration, remember

Volume x concentration = grams

Example: 250 ml of 70% dextrose = 250 x 0.70 = 175 grams dextrose

Amino acids – contain 4 kcal/g. Concentrations vary, usually 8.5% to 15%

Dextrose – contain 3.4 kcal/g. Concentrations vary, 70% is most common

IVFE (intravenous fat emulsion; preferable term to "lipids") – contain 10 kcal/kg. May be made from soy or olive/soy mix; other products being developed. Usually 10-30% solution. Emulsion uses egg ingredients, so ensure patient does not have a true egg allergy. Some IVFE are soy-based; check for true soy allergy. Hang time of separate IVFE is 12 hours (when given as a piggyback to 2-in-1 TPN). Hang time in a 3-in-1 is 24 hours. Dosing: generally not more than 1g/kg/day; approx. 15-30% non-protein kcals. The primary role of IVFE is to prevent essential fatty acid deficiency, and provide energy (kcals).

Maintenance fluids – added sterile water to meet patient's hydration needs. Can adjust based on patient needs. Monitor urine output, GI losses, insensible losses

Micronutrients – Electrolytes, trace elements (copper, manganese, zinc, selenium; iron usually not added esp. with 3-in-1 mixes as it can destabilize the fat emulsion), multivitamin, other additives

Electrolytes: Consider electrolyte composition of body fluids being lost; you may need to communicate this information to the pharmacist to help better estimate the patient's electrolyte needs.

Electrolyte Requirements:

Electrolytes	Standard requirement
Na+	1-2 mEq/kg
K+	1-2 mEq/kg
Ca++	10-15 mEq
Mg	8-20 mEq
PO4	20-40 mmol

*Based on generally healthy people with normal losses. From "Safe Practices for Parenteral Nutrition" *JPEN* 2004;28(suppl):S39-70, A.S.P.E.N.

Volume and Average Electrolyte Content of Gastrointestinal Secretions

Source/ Type of Secretion	*Avg. Volume (mL/24 h)*	*Electrolyte Concentration (mEq/L)*			
		Na+	*K+*	*Cl-*	*HCO3-*
Saliva	1500 (500-2000)	10 (2-10)	26 (20-30)	10 (8-18)	30
Stomach	1500 (100-4000)	60 (9-116)	10 (0-32)	130 (8-154)	0
Duodenum	Variable (100-2000)	140	5	80	0
Illeum	3000 (100-9000)	140 (80-150)	5 (2-8)	104 (43-137)	30
Colon	Variable	60	30	40	0
Pancreas	Variable (100-800)	140 (113-185)	5 (3-7)	75 (74-95)	115
Bile	Variable (50-800)	145 (135-164)	5 (3-12)	100 (89-180)	35

Factors that *increase* specific electrolyte needs:

Calcium – high protein intake
Magnesium – with GI losses, drugs, refeeding
Phosphorus – high dextrose intake, refeeding
Sodium – diarrhea, vomiting, NG suction, GI losses
Potassium – diarrhea, vomiting, NG suction, medications, refeeding, GI losses
Acetate – renal insufficiency, metabolic acidosis, GI losses of bicarbonate
Chloride – metabolic alkalosis, volume depletion, gastric losses

Other Important Terms:

Glucose Infusion Rate (GIR): Calculated as mg of dextrose (used interchangeably with glucose) infused per kg of Actual Body Weight per Minute. *Aim for <5 in general*; <4 for critically ill, ≤7 may be tolerated in medically stable patients.

IVFE Infusion Rate: Calculated as grams of IVFE infused per kg of Actual Body Weight per hour. Should *not exceed 0.11 g/kg/h*.

Initiating PN: (See also Prescribing PN Checklist (note CPOE=Computerized Prescriber Order Entry system).

Review the justification for PN. Is it appropriate, warranted, likely to provide a benefit? If it is for short term only (<7 days) and patient is nourished, may not be necessary. Is it desired by the patient (advance directives/living will)? Have the risks been explained/discussed? Has enteral access been evaluated and discussed? PN is a high-risk therapy and is not equivalent to EN.

Initiating PN: As the Dietitian, your first responsibility is to calculate kcal and protein needs. Use your clinical judgement, taking into account any concurrent dx, increased needs, altered absorption/excretion, etc., just as you would with a patient eating orally. For the underweight/malnourished patient, even if not at risk of frank refeeding syndrome, it is suggested to start conservatively to assess and establish tolerance. Overfeeding with PN can result in multiple metabolic derangements.

It is recommended to check labs (primarily CMP with Phos, Mg) *before* starting PN. Electrolyte disturbances should be normalized/electrolytes replaced before initiating PN therapy. The PN infusion will likely exacerbate any abnormality and may have severe consequences.

(A note on *Refeeding syndrome:* in a malnourished patient, infusing CHO via PN may induce refeeding syndrome, which is a sudden drop in serum phosphorus, magnesium, and potassium that results from the rapid intracellular shift of these electrolytes and minerals, and can be fatal. Patients at risk for refeeding syndrome should have their PN initiated more cautiously providing half of the energy requirements on day 1, and advancing slowly over the next 3-5 days as electrolytes are closely monitored and stabilized. Additional *thiamine* supplementation is recommended when initiating PN in a patient with prolonged history of poor intake or severe weight loss.)

Suggested Nutrient Intake for Adult Patients on PN

PN component	*Critically Ill Patients*	*Stable Patients*
Protein	1.5-2 g/kg/d	0.8-1 g/kg/d
Carbohydrate	≤4 mg/kg/min	≤7 mg/kg/min, ≤7g/kg/d
IV fat emulsion	≤1 g/kg/d	1 g/kg/d
Total energy	25-30 kcal/kg/d	20-30 kcal/kg/d
Fluid	minimum needed to deliver adequate macronutrients	30-40 mL/kg/d

Steps:

-Estimate kcal and protein needs, then subtract the protein kcals from your total kcal goal. These are your non-protein kcals (to be made up by dextrose and IVFE).
-Consider your solution. Using a 3-in-1 TPN solution may help reduce risk of steatosis, possibly by decreasing hepatic triglyceride uptake, and promoting fatty acid oxidation. It also requires less nursing time and may be overall more cost effective. However, there may be times when a 2-in-1 with IVFE piggyback is needed (for example, 3-in-1 solutions are more sensitive to destabilization with certain electrolyte concentrations or medications). IVFE piggyback should be given slowly over at least 8-10 hours at a minimum. Note IVFE is considered safe for use in pancreatitis patients without hypertriglyceridemia.

-Consider macronutrient distribution: try starting with 15-30% of non-protein kcal from IVFE, with the remaining 70-85% of non-protein kcal from dextrose. Consider patient's ability to tolerate dextrose (diabetes management; see below notes on Day One).

-Check your math: calculate GIR with your dextrose target and patient's actual body weight. Calculate IVFE infusion rate. Within recommended guidelines?

-Determine estimated fluid needs (consider disease states that impact: renal, heart failure; consider extra fluids they are getting with other meds, oral/enteral; consider any losses – GI, drains, diarrhea, etc.) and suggest total PN bag volume to meet fluid needs. Pharmacy will determine actual amounts of sterile water, electrolytes, and other additives that need to be added to achieve the total volume desired.

Initiating: Focus on macronutrients (grams)

Day One: protein can start at goal. Suggested to start conservatively with dextrose. The initial maximum carbohydrate given in an adult is usually 150-200 g/day; for those with DM or hyperglycemia of stress: 100-150 g dextrose initially. IVFE: the IVFE in PN can be added or increased if the patient has serum triglycerides ≤400 mg/dL. Common to start at 50% goal for dextrose and IVFE, 100% goal for protein if using a 3-in-1. (If using a 2-in-1, lipids may be run separately 2-3x a week.)

Day Two: monitor labs & tolerance; continue protein, increase IVFE and dextrose to approximately 75% of goal.

Day Three: monitor labs & tolerance; advance PN to goal amounts of energy and protein.

-All PN ingredients should be ordered in amounts per day (for adult patients), not in terms of amount per liter, concentration, or volume. I.e., ordered in terms of *grams* of macronutrients, milliequivalents/ millimoles/milligrams/micrograms of micronutrients per day.

-Electrolytes, vitamins, trace minerals will be determined by pharmacy. Electrolytes should be ordered as the complete salt form rather than the individual ion. If your patient has altered fluid or electrolyte needs, estimate losses and communicate to the pharmacist any anticipated electrolyte adjustments that may be needed so they can monitor.

-Coordinate with IV pharmacist; discuss your plan and be open to input. This improves the quality of care you are providing to this high-risk patient. Often they appreciate the phone call and may ask you to help them obtain labs done at the facility, or have other questions such as the patient's most recent weight. They will still need to wait to get the doctor's order to proceed; there may be times you need to help coordinate between the nursing staff/MD at your building and the pharmacist to provide smooth and efficient care. Remember that all PN recommendations should be processed promptly, as PN bags are often compounded several days ahead, which unfortunately can compound any delays as well.

-Recommend other routine monitoring if not already in place, such as daily weights, I & O's, labs per pharmacy's protocol, capillary blood glucose concentrations every 6 hours (or more frequently if hyperglycemic).

-Assess if any oral or enteral intake is possible. Even very small amounts of intake via the GI tract can be beneficial in promoting enterohepatic circulation of bile acids, and reduce risk of PN-associated hepatobiliary complications. It can also support the microvilli in the GI tract and reduce risk of gut atrophy and subsequent bacterial translocation. Low fistula output (<200ml/day) warrants a trial of oral/enteral intake, and changes in output should be monitored.

Cyclic PN:

Cyclic TPN has multiple benefits including decreased liver burden; compared to continuous PN infusion, cyclic PN infusion has been shown to reduce concentrations of serum liver enzymes and conjugated bilirubin. A break from PN also may improve quality of life & mobility for the patient to participate with therapies, and also result in better likelihood of infusing goal volumes due to fewer interruptions. Typically, cyclic PN is run at goal rate for a number of hours, with it being run at half the goal rate for the first and last hour (***ramp-up & ramp-down***). It is important to slowly adjust the rate at start & stop to support blood glucose levels, which should be monitored at least every 6 hours during infusion, and 30-60 minutes after PN stop. *Rebound hypoglycemia* can occur with abrupt discontinuation of PN. Typically, pharmacy will recommend the specific rate, since they will know the final compounded PN volume.

*Glucose Infusion Rate (GIR) and IVFE Infusion Rate: When recommending a change to cyclic PN, remember to check the glucose infusion rate (GIR; should be <5 in general; <4 for critically ill, <7 for medically stable) and IVFE infusion rate (should not exceed 0.11 g/kg/h) to see if the higher rate is still acceptable for the patient. To calculate GIR: mg dextrose ÷ actual body wt of pt in kg ÷ minutes of proposed infusion time. Providing CHO at a rate that is too high increases risk of hyperglycemia, lipogenesis (increased triglyceridemia).

A 12-hour cyclic regimen is most common, but it's important to look at the individual patient. For example, a patient with advanced COPD may have increased CO2 production & respiratory stress with shortened infusion of the same amount of dextrose. Renal or lung disease may impact acid/base buffering and ability to tolerate electrolyte shifts. Elderly and low body weight patients may have a harder time with volume tolerance with the faster infusion rate.

Monitoring:

Monitoring of PN therapy is a compilation of best practices, rather than evidence-based guidelines. Residents on PN need frequent monitoring by the Registered Dietitian including weights, labs, and hydration status, as well as GI function. The following table outlines suggested monitoring for residents receiving PN. *The pharmacy that provides the facility's PN bags may/often have their own guidelines for lab monitoring.*

PARAMETER	INITIAL	DAILY	WEEKLY
Na, K, CO2, BUN, Cr	X	X*	X
Ca, PO4, Mg	X	X*	X
CBC	X	X*	X
CBGs	X	X*	X
PT/PTT	X		X
Triglyceride	X		X
Liver Function Tests	X		X
Prealbumin	X		X
Weight	X	X	X
Intake/output	X	X	As Needed

*Daily until stable, then once or twice weekly

-*Physical exam* is especially important in assessing fluid status. With electrolyte additives being adjusted regularly in the TPN, the BMP may not always give you the full story, esp. on hydration. Be sure to assess weight changes, I&O's, urine output (amount, color, etc.), skin turgor, mucous membranes, presence of edema (sacral edema may be better to check than pedal edema for a patient that is primarily in bed). For the long-term PN patient, periodic nutrition-focused physical assessment may help detect micronutrient deficiencies or excess.

-Be aware of *medication changes* that can affect TPN and electrolytes/electrolyte needs.

-When *assessing labs*, remember that there are other systems at work that are shifting labs also; for example, the lungs and kidneys are important buffering systems for acid/base balance and can compensate for some shifts. Don't micro-manage; the clinician's role is to course-tune and let the body fine-tune. *Monitor trends*. Your job is to monitor any ongoing losses or trends that the body won't be able to keep up with, and coordinate with MD & pharmacist to support the individual's needs.

-Periodically *check in with IV pharmacist* to coordinate if recommending any changes or as needed. Check that they are getting their labs and any other necessary paperwork/orders as planned.

-*Weight monitoring* – a quick (confirmed) gain or loss in weight is likely reflective of a change in fluid balance. Weight changes over time are more consistent with inadequate/excess kcals, or could reflect more gradual changes in fluid balance.

-Monitor/review/optimize any *oral or enteral intake* that is feasible.

Assessing a New Admit on PN:

Many of the checks you go through will be similar to those you would use if you were initiating PN or monitoring a current PN patient.

Points to Consider:

-Did the PN orders get carried over accurately from the hospital? Review any hospital RD notes if available.

-Justification for PN? What are the goals of PN for this patient?

-What is hanging in the patient's room (or in nursing med fridge)? (check that the label matches the pharmacy PN order form; check that the orders in the chart match the pharmacy PN order form, which is often found in the Medication Administration Record/MAR)

-Physical observation/assessment of the patient & interview. Obtain nutrition/diet/weight history.

-Have orders been initiated for appropriate monitoring? Daily weights, I's & O's, blood glucose checks, labs per pharmacy?

-Do the PN provisions make sense/appropriate for the patient's current condition? (acute issues/illness, changes in fluid/electrolyte needs, change in activity, medication changes, changes in any other intake oral or enteral?) Or, do you need to recommend changes to better meet the patient's nutrition needs?

-Any current labs available? It may be too early to assess any trends unless you have extensive H&P data available.

-Anticipated length of PN? Would a change to cyclic infusion be appropriate, to support participation with therapies (PT, OT, etc.) and long-term PN tolerance? Is any trophic oral/enteral intake feasible to support gut integrity and liver health, minimize risk of hepatobiliary complications?

-Coordinate care with IV pharmacist. Are they getting their labs/any info they need? Discuss any changes you may be considering/recommending.

-Complete your assessment. Any changes/recommendations? Courteously call nursing attention/MD attention to them as priority to avoid an undue delay in changes. Remember, pharmacy can't act on RD recommendations, they need MD orders.

Complications of PN & Trouble-Shooting:

PN Component Shortages: various components have gone through periods of shortage. Sources for information on current shortages include the A.S.P.E.N. website drug shortage webpage (found at nutritioncare.org) and the U.S. Food and Drug Administration drug shortage web page. A.S.P.E.N. has published guidelines to aid clinicians in managing shortages of various components and can be accessed at http://www.nutritioncare.org/Professional_Resources/Drug_Shortages_Update/. When components become readily available again, dosing of the PN component should return to regimens used prior to the shortage.

Hepatobiliary Complications: PN-Associated Liver Disease (PNALD) is a common complication especially in those dependent on long-term support. Overfeeding with PN can contribute to liver complications, though other altered processes that occur with PN put the liver at risk. Three types of hepatobiliary complications associated with PN: *steatosis, cholestasis, and gallbladder sludge/stones.*

Steatosis is usually benign and may present as a modest increase in serum aminotransferase (AST & ALT) that occurs within the first two weeks of PN and often normalizes, even with continued PN.

PN-associated cholestasis is a more serious complication because it may progress to liver cirrhosis and failure. It involves impaired or obstructed biliary secretion. It typically presents as an increase in alkaline phosphatase (ALP), GGT, and conjugated bilirubin; conjugated bilirubin >2mg/dL is considered the prime indicator of cholestasis.

Gallbladder sludge/stones may occur during PN therapy as a result of gallbladder stasis, which is related to the lack of enteral stimulation.

Strategies to manage PN-Associated Liver Complications (rising LFTs):

-Consider non-PN factors, rule out: hepatotoxic meds; herbal supplements; biliary obstruction; hepatitis; sepsis

-Consider PN modifications: decease dextrose; decrease IVFE (should be <1g/kg/d); provide a balance of IVFE and dextrose/try a 3-in-1 mixture; cyclic PN infusion for liver rest

-Maximize enteral intake: encourage/advocate for oral intake or tube feeding, even at a very slow rate/trophic feed

-Prevent/treat bacterial overgrowth: consider enteral antibiotics (such as Metronidazole, Neomycin, Doxycycline, Ciprofloxacin, Rifaximin); in Chronic Intestinal Psuedo-Obstruction patients, consider motility agents (such as Metoclopramide, Erythromycin, Tegaserod, Ocreotide)

-Pharmacotherapy: consider aggressive treatment of infection; consider use of Ursodeoxycholic acid (ursodiol)

-Intestinal transplantation: consider for patients with PN failure

Metabolic Bone Disease: Osteoporosis and osteomalacia associated with long-term PN use. Complex mechanism; strategies to prevent: PN formulation to minimize hypercacliuria (avoid high doses of protein); provide adequate calcium, phosphorus, and magnesium; avoid metabolic acidosis; provide vitamins and trace elements; minimize aluminum contamination. IV bisphosphonate therapy is available. Encourage weight-bearing exercise as able; ensure safety and minimize fall/injury risk. Smoking cessation.

Micronutrient Deficiencies/Excess:

-*Vitamins:* an adult on PN should receive a daily dose of a standard PN multivitamin. Supplementation of additional micronutrients may be warranted at times; for example, extra thiamin may be appropriate for a patient with a history of alcohol abuse. Several vitamins are known to undergo substantial degradation after addition to the PN admixture; for this reason, the multivitamin is usually added daily to the PN formulation by nursing staff immediately before the infusion occurs.

-*Trace Elements:* relatively uncommon in PN patients but can occur. Increased zinc needs with high intestinal losses or draining wounds; zinc is important to replete slowly and cautiously. Levels of trace elements are difficult to monitor, as serum levels do not accurately measure total body balance; often stored in tissues. Excess manganese and copper can occur in patients with hepatobiliary disease secondary to decreased excretion.

Hypertriglyceridemia: Acceptable triglyceride levels for patient on PN is <400mg/dL. Hypertriglyceridemia can occur with rapid IVFE infusion (>110mg/kg/h) or overfeeding dextrose. Increases risk of pancreatitis, impairs immune response, and can alter pulmonary hemodynamics. If levels rise above 400mg/dL, IVFE should be held from the PN regimen, and labs followed.

Essential Fatty Acid Deficiency: determined by a triene to tetraene ratio of >0.2. Can occur within 1-3 weeks in adults receiving PN without IVFE. To prevent EFAD, provide approximately 250mL of 20% IVFE (50 grams) twice a week, or 100 grams once a week. For patients who are intolerant to IVFE, a topical application or oral ingestion of safflower or sunflower seed oils can alleviate biochemical deficiency of EFAD.

Discontinuing PN:

When the resident is ready to begin the transition to enteral or oral intake, ideally, it should be accomplished by monitoring oral/enteral intake and concomitantly decreasing the parenteral nutrition to maintain a stable nutrient intake until about 65-75% of estimated nutrient needs can be met by the oral/enteral route. Included in assessing adequacy of intake, an assessment should include discussion of gastrointestinal symptoms during the discontinuation process.

References:

Mueller, C. M. (2012). *The A.S.P.E.N. Adult Nutrition Support Core Curriculum, 2nd edition.* Silver Spring, MD: American Society for Parenteral and Enteral Nutrition.

Phil Ayers, B. H. (2014). *Parenteral Nutrition Handbook, second edition.* Silver Spring, MD: American Society for Enteral and Parenteral Nutrition.

Task Force for the Revision of Safe Practies for Parenteral Nutrition. (2004). Safe Practices for Parenteral Nutrition. *JPEN*, S39-70.

The A.S.P.E.N. website also has many free resources and references available at nutritioncare.org.