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The Hitchhiker's Guide to Parenteral Nutrition Management for Adult Patients

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While parenteral nutrition is a life-saving modality for people with intestinal failure, it is not without significant risk. In the hospital setting, under certain clinical circumstances, patients will also benefit from the use of parenteral nutrition. The purpose of this article is to aid the clinician in the safe provision of parenteral nutrition support, including development of the prescription, appropriate monitoring, and awareness of the issues involved in the preparation and stability of commonly used additives. Frequently asked questions and challenges that arise with the use of parenteral nutrition are also addressed.

INTRODUCTION

Feeding nutritionally compromised patients has never been as easy, or as hard, as it is today. We are able to provide nutrients parenterally and enterally to patients who once would have been considered "unfeedable." Today's inpatient population is sicker than patients in the past; the same may be said for patients needing specialized nutrition support. This results in challenges to clinicians caring for these patients. Our goal in writing this article is to provide a succinct and easy to follow guide for practicing clinicians ordering parenteral nutrition.

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INDICATIONS

The guiding principle of nutrition support is to use the least invasive and most physiologic method of feeding. Infusing chemicals directly into the bloodstream is the least preferred method of providing nutrition support (1). Yet, for a select subset of the population, intravenous infusion of central parenteral nutrition (PN) or peripheral parenteral nutrition (PPN) is the only viable means to provide substrates for metabolism. PN carries with it inherent risks associated with the placement of a central venous catheter. Due to the increased risk of complications with PN therapy, including thrombosis and infection, a careful assessment of PN appropriate-

Table 1
Indications, Relative Indications and Contraindications for Parenteral Nutrition

Parenteral nutrition is usually indicated in the following situations

- Documented inability to absorb adequate nutrients via the GI tract such as:
  - Massive small-bowel resection/short bowel syndrome (at least initially)
  - Radiation enteritis
  - Severe diarrhea
  - Untreatable steatorrhea/malabsorption (i.e., **not** pancreatic insufficiency, small bowel bacterial overgrowth, or celiac disease)
- Complete bowel obstruction, or intestinal pseudo-obstruction
- Severe catabolism with or without malnutrition when GI tract is not usable within 5–7 days
- Inability to obtain enteral access
- Inability to provide sufficient nutrients/fluids enterally
- Pancreatitis accompanied by abdominal pain with jejunal delivery of nutrients
- Persistent GI hemorrhage
- Acute abdomen/ileus
- Lengthy GI work-up requiring NPO status for several days in a malnourished patient
- High output enterocutaneous fistula (>500 mL) and inability to gain enteral access distal to the fistula site
- Trauma requiring repeat surgical procedures

Parenteral nutrition* may *be indicated in the following situations

- Enterocutaneous fistula
- Inflammatory bowel disease not responding to medical therapy
- Hyperemesis gravidarum when nausea and vomiting persist longer than 5–7 days and enteral nutrition is not possible
- Partial small bowel obstruction
- Intensive chemotherapy/severe mucositis
- Major surgery/stress when enteral nutrition not expected to resume within 7–10 days
- Intractable vomiting when jejunal feeding is not possible
- Chylous ascites or chylothorax when low fat/fat free EN does not adequately decrease output

Contraindications for Parenteral Nutrition

- Functioning gastrointestinal tract
- Treatment anticipated for less than 5 days in patients without severe malnutrition
- Inability to obtain venous access
- A prognosis that does not warrant aggressive nutrition support
- When the risks of PN are judged to exceed the potential benefits

Used with permission from the University of Virginia Health System Nutrition Support Traineeship Syllabus (Parrish CR, Krenitsky J, McCray S). Parenteral Module. University of Virginia Health System Nutrition Support Traineeship Syllabus, 2003.

Table 2
Important Factors to Consider when Assessing a Patient for Parenteral Nutrition

- Anthropometric Data – include:
  - Recent weight changes
  - Current height and weight
- Lab values – including:
  - Comprehensive metabolic panel
  - Serum magnesium level
  - Serum phosphorus level
  - Serum triglycerides as indicated (Table 18)
- Medical/Surgical History
  - Anatomy (resections)/ostomies
  - Pre-existing conditions such as diabetes, renal failure, liver disease, etc.
- Diet/Medication History – include:
  - Food/drug allergies
  - Diet intake prior to admission
  - Special diets
  - Herbal/supplement use
  - Home and current medications

ness should precede placement of a central venous catheter (1,2). Table 1 lists indications and contraindications for PN.

PATIENT ASSESSMENT

Prior to initiating PN, a nutrition assessment is necessary to determine nutrient needs and to anticipate any metabolic changes that may occur due to the patient's underlying condition, medications or concurrent therapies, etc. Table 2 provides a list of factors to consider when assessing a patient's nutritional status. Determining energy and protein needs in the severely malnourished patient under physical stress, often ventilator-dependent with little mobility, can be difficult. Critical illness brings further challenges in determining the appropriate calorie level, as matching caloric expenditure to caloric provision may be detrimental—providing lower calorie levels initially has been advocated (3,4). Calorie requirements often increase in relation to stress, fever, and seizures, while a decrease in needs may be seen in the setting of sedation or reduced mobility. While indirect calorimetry is considered the "gold standard" to determine caloric expenditure, formulas and calculations are frequently used. Unfortunately, no studies to date have demonstrated

Table 3
Daily Energy and Substrate Guidelines for Adult PN (5–8)

Nutrient	*Acute Care*	*Critical Care*
Energy	25–30 total kcals/kg/d	25 total kcals/kg/d
• Refeeding	15–25 kcal/kg/d	15–25 kcal/kg/d
• Obesity (≥130% IBW)	15–20 kcal/kg/d adjusted weight *	15–20 kcal/kg/d adjusted weight *
Protein	0.8–1.0 g/kg/d maintenance 1.2–2.0 g/kg/d catabolism	1.5–2.2 g/kg/d
Dextrose	<7 g/kg/d	<5 g/kg/d
Lipid**	<2.5 g/kg/d	0.4–0.75 g/kg/d

*Adjusted weight based on a 50% correction factor ([usual weight – ideal body weight] × 0.50)
**If a patient is to be on PN for greater than 3 weeks, a minimum of 2%–4% of total calories should come from IV fat emulsion (IVFE) including linoleic acid to prevent essential fatty acid deficiency (EFAD) (9)

benefit by comparing the use of metabolic cart results with various formulas in terms of clinical outcomes. Regardless of which calculation is used to estimate nutrient requirements, it is important to note that there is a lack of evidence correlating a given calorie and protein level to clinical outcomes, and the controversy over which formula is "best" is ongoing. Guidelines for designing PN formulations have been developed by various organizations and experts in the field of specialized nutrition support, some of which are listed on Table 3.

VENOUS ACCESS

Line type, nutrition formulation and other medication needs are inter-related and need to be approached in a unified manner. Table 4 describes the advantages and disadvantages of intravenous access typically used for parenteral nutrition support. Nutritional limitations associated with those lines are also provided. Further details on these topics have been included in the following paragraphs.

PERIPHERAL NUTRITION SUPPORT (PPN)

Peripheral access is sometimes used for patients who need short-term (<2 weeks) nutrition support. Because of the high volume of fluid needed, patients requiring fluid restriction are not candidates for this type of therapy. In order to meet a patient's nutritional needs using PPN, infusion rates greater than 150 mL/hr may be required; this limits the use of PPN to patients with normal renal, cardiac, hepatic, and pulmonary function. Due to the risk of thrombophlebitis, these solutions are generally limited to an osmolarity of <600–900 mOsm/L (12,14). See Table 5 and Table 6 for calculation of mOsm in parenteral solutions. Even at 600–900 mOsm, these solutions are hypertonic, hence any patient with poor peripheral access should not receive PPN. Instead, alternatives should be considered, based on the individual patient's circumstances. These include the use of Central PN or provision of peripheral protein-sparing IV fluids containing 5% dextrose. The anticipated duration of parenteral support and how soon the patient may be transitioned to enteral nutrition will factor into this decision. Patients with rapid or frequent loss of peripheral access with IV fluids (D_5, etc.) are poor candidates for PPN. As a rule of thumb, if the patient's peripheral access has been changed 2–3 times within the first 48 hours following admission on *standard* IV fluids, PPN should not be attempted. Combinations of heparin and hydrocortisone added to the PPN formulation, with or without the use of a nitroglycerin patch placed proximal, and as close as possible to the catheter site, have been used to extend the viability of peripheral catheters (16–18) (Table 7).

Peripheral lines should be changed every 48–72 hours to minimize the risk of infection and thrombophlebitis (13). PPN avoids the inherent risks associated with central venous access, but is not suitable unless the patient meets the criteria in Table 8. Patients not meeting these criteria and needing intravenous

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Table 4

Review of Access Devices Used for Nutritional Support (10–13)

Line Type	*Advantages*	*Disadvantages*
Peripheral Lines		
Peripheral – Short	• Least expensive • Easily placed and removed • Lowest risk for catheter related infections • Beneficial for patients needing short term nutrition support (<1 week) • Need to change frequently (48–72 hours)	• Loss of line is common. High levels of phlebitis and vein damage with nutrition support • Kcals usually limited due to volume restriction • Limited to one lumen • Limits infusion osmolality to 600–900 mOsm/L and infusion pH between 5 and 9 (lower limit of mOsm represents INS standards)
Peripheral – Midline	• May be used for a longer duration than peripheral catheters • Ease of placement compared to central lines • Allows access to larger vessel	• Must maintain guidelines for peripheral lines when looking at concentration and pH • Not a central line
Central Lines		
Peripherally Inserted Central Catheters or (PICC) lines	• Able to infuse solutions >900 mOsm/L • May be placed by trained RN • Decreased rate of infection when compared to other central lines in home care patients • Able to place lines with multiple lumens • Many PICC lines can be used for CT contrast injection	• Not as long term as other centrally placed catheters—length of stay ~ a year • More difficult self care if located in anticubital position (should not be painful) • Blood sampling not always possible • More frequent flushing and maintenance required • More pain is associated
Hickman®, and Broviac®	• Able to give solutions >900 mOsm/L • Provide full nutritional support via IV route • Able to place lines with multiple lumens • Able to remain in place for extended time periods (1–3 years usual)	• Surgical procedure, more difficult to place involving increased cost and monitoring as well as risk to patient. Adds additional time and complexity in placement • Removal also more involved than PICC removal, due to tunnel • Catheter protruding from chest may affect some people's self image
Groshong® Catheters	• Able to give solutions >900 mOsm/L • Provide full nutritional support via IV route • Able to place lines with multiple lumens. • Able to remain in place for extended time periods • May be "locked" with normal saline	• Surgical procedure, more difficult to place involving increased cost and monitoring and risk to patient • Adds additional time and complexity in placement • Removal also more involved than PICC removal, due to tunnel • Catheter protruding from chest may affect some people's self image
Femoral Lines	• Gives IV access to patients with no other option	• Increased infection risk
Multiple Lumen acute care catheters	• Economical, can be removed by trained RN • May be placed at bedside or in radiology by a physician	• Increased infection rate compared to single lumen and tunneled catheters. Usually not repairable if damaged • Should not be used in home care, for acute care only • Short dwell time, 1–2 weeks
Port	• Long term use with lowest infection risk of all options (dwell time may be years) • Site care only when accessed • Body image intact • Ideal for intermittent access	• Placement and removal are surgical procedures performed in the operating room or interventional suite • Requires "stick" to access port with Huber needle. If needle is in place, risk of infection increases

Table 5
One Method to Calculate Osmolarity of IV Admixtures

1. First, multiply the gm, mEq or mL by the mOsm/unit listed in Table 6
2. Add all the multiplied values to determine the total mOsm for the mixture
3. Add each volume in the formulation to give a total in liters
4. Divide the total mOsm by the total volume in liters to determine the mOsm/L of the formulation

Table 6
Milliosmoles of Selected Additives (15)

Additive	*mOsm/Unit*
Sterile Water	0.00
Dextrose Options (3.4 cal/g)	
Dextrose 5, 10, 30, 50, 70%	~5 mOsm/g
Amino Acid Options (4 cal/g)	
Amino Acid 8.5, 10, 15%	~10 mOsm/g
Intravenous Fat Emulsion (IVFE) Options	
10% (1.1 cal/mL) 20% (2.0 cal/mL) 30% (3.0 cal/mL)	~0.280 mOsm/mL
Micronutrients	
Calcium Gluconate	0.662 mOsm/mEq
Magnesium Sulfate	1 mOsm/mEq
Multi-trace Elements (MTE-5)	0.36 mOsm/ml
MVI infusion Concentrate (MVI-12)	41.1 mOsm/dose
Potassium Acetate	2 mOsm/mEq
Potassium Chloride	2 mOsm/mEq
Potassium Phosphate	2.47 mOsm/mM
Sodium Acetate	2 mOsm/mEq
Sodium Chloride	2 mOsm/mEq
Sodium Phosphate	4.0 mOsm/mM

nutrition are candidates for *central* PN.

Several conveniently packaged, "fixed concentration" PPN products are available commercially and are suitable for peripheral administration. These formulations contain dextrose ranging from final concentrations of 5%–10% or 3% glycerol in addition to amino acids in final concentrations of 3% to 4.25%. Some of these products are available with or without a standard amount of electrolytes. PPN formulations can also be compounded on an individual basis (customized) allowing the flexibility to add intravenous fat emulsions (IVFE) or manipulate electrolytes. IVFE are not included in commercial premixed formulations, but 10% or 20% concentrations of IVFE may be given as a piggyback. All IVFE are isotonic and lower the overall osmolarity of the infusate. Some clinicians will provide up to 60% of the total caloric requirements as lipid, while others limit the lipid to less than 1 gm/kg/day due to the possibility of altered immune function associated with infusion of long chain triglycerides (19). Patients on IVFE should be monitored for Fat Overload Syndrome; a syndrome characterized by hypertriglyceridemia, fever, clotting disorders, hepatosplenomegaly, and variable end organ dysfunction. This syndrome has been reported in the setting of excessive IVFE administration to children and critically ill adult patients (20,21). This is particularly important in the critical care setting where the sedative, propofol (Diprivan© and two generic versions), a medication in a 10% IVFE base, is frequently used.

Table 7
Peripheral Parenteral Nutrition "Vein Protector" (16)

- Hydrocortisone, 15 mg
- Heparin, 1500 units
- Plus: transdermal nitroglycerin (NTG) patch, 0.1 mg/hour

Table 8
Criteria for use of Peripheral Parenteral Nutrition

- Nutritional needs <1800 kcals per day
- Patient requires less than 10 to 14 days of intravenous nutrition
- Peripheral venous access is available (good peripheral veins)
- Requires only one intravenous line with intravenous fat emulsion (IVFE) administration via piggyback infusion
- Fluid restriction is not an issue

CENTRAL NUTRITIONAL SUPPORT

Central venous catheters provide temporary or long-term access to large diameter veins with blood flows in the range of 2–6 L/min. This rapid blood flow allows infusion of formulations with osmolarities in excess of 900 mOsm/L (central solutions range from ~1500–2800 mOsm/L). Central venous access devices include

Table 9
Commercially Available Crystalline Amino Acid Solutions

Brand Name	*Type/Indication*	*Stock Concentrations*
Aminosyn II™	Standard	3.5%, 4.25%, 5%, 7%, 8.5%, 10%
Travasol™	Standard	3.5%, 4.25%, 5.5%, 8.5%, 10%
Aminosyn II™	Standard/fluid restriction	15%
Clinisol™	Standard/fluid restriction	15%
Novamine™	Standard/fluid restriction	15%
Prosol™	Standard/fluid restrictions	20%
Hepatamine™	Hepatic failure	8%
Hepatasol™	Hepatic failure	8%
Aminosyn HBC™	Metabolic stress	7%
Freamine HBC™	Metabolic stress	6.9%
Branchamin™ (Contains only leucine, isoleucine and valine use to supplement standard amino acid base)	Metabolic stress	4%
Amino PF™	Pediatric	7%, 10%
Trophamine™	Pediatric	6%, 10%
Aminess™ (Essential amino acids plus histidine)	Renal	5.2%
Aminosyn RF™ (Essential amino acids plus arginine)	Renal	5.2%
Nephramine™ (Essential amino acids plus histidine)	Renal	5.4%
Renamin™ (Essential and some non-essential amino acids)	Renal	6.5%

Adapted from Barber JR, Miller SJ, Sacks GS. Parenteral feeding formulations. In: Gottschlich MM, Ed. *The Science and Practice of Nutrition Support: A Case-Based Core Curriculum.* Dubuque, IA: Kendall/Hunt Publishing Co.;2001: 251–268 with permission from the American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.).

Groshong®, Hickman®, Hohn®, multiple lumen catheters, peripherally inserted central catheter (PICC) lines, and implanted intravenous port devices. Many central catheters provide multiple lumens; if multiple lumens exist, a single lumen should be designated for PN use only (22). The distal lumen is usually the largest diameter and can be reserved for blood transfusions and blood sampling. Central catheters are the route of choice for patients with fluid management issues, such as congestive heart failure (CHF) or renal failure, patients with poor peripheral venous access and those requiring PN >10–14 days, assuming they meet criteria for PN use.

DESIGNING THE FORMULATION

Macronutrients

Carbohydrate

Carbohydrate is generally provided in amounts up to 60% of total kcals/day. In the hospitalized patient, initial dextrose in PN solutions should not exceed 7.2 g/kg/day (5 mg/kg/minute) to minimize the occurrence of fatty liver and hyperglycemia (23). However, in stable, hospitalized or home patients receiving cycled PN, the glucose infusion rate may exceed 5 mg/kg/minute when the patient might require additional calories for weight maintenance or gain.

Protein

Protein (amino acids) is typically supplied in the range of 1.5 g protein/kg/day depending on the amount of stress and catabolism present. Critical care, post-surgical, burn, dialysis and many other types of hospitalized patients often require protein administration in the range of 1.2–2 g/kg/day. In severe catabolic states, protein needs may be as high as 2–2.5 g/kg/day (24). Acute renal failure often demands high protein supplementation, from 1.5–1.6 g/kg/day due to protein losses through the glomeruli, dialysis or catabolism (25). Alternatively, in times of renal insufficiency or failure when a patient is *not yet dialyzed* and has rising blood urea nitrogen concentrations, a decrease in protein to 0.8

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Table 10
Energy and Vitamin K Content of Commonly Used IVFE (32–35)

Lipid Emulsion	*Kcals/mL**	*Soybean Oil g/L*	*Safflower Oil g/L*	*Vitamin K mcg/dL*
Intralipid 10%	1.1	100	0	30.8
Intralipid 20%	2	200	0	67.5
Intralipid 30%	3	300	0	93
Liposyn II 10%	1.1	50	50	13.2
Liposyn II 20%	2	100	100	26
Liposyn III 10%	1.1	100	0	31
Liposyn III 20%	2	200	0	62
Liposyn III 30%	2.9	300	0	93

*Kcals/mL differ according to lipid and glycerol content of IVFE

gm/kg may avoid uremic complications (26). *However*, if total kcals are inadequate to support protein utilization or glucose is poorly controlled, catabolism of endogenous protein (lean body mass) will render this intervention useless. Of note, dietary protein only comprises 25% of the nitrogen pool that is turned over each day. Hence, a change in protein from 1.3 down to 1 g/kg/day in a 75 kg patient represents a mere decrease of 22 g protein/day. GI bleeding, hyperglycemia and the obligatory catabolism of trauma/sepsis would generate appreciably more urea than this "additional" 22 grams of protein/day. In the past, restricting protein in patients with liver failure was the standard practice; however, it is now accepted that this may worsen the underlying liver disease, and does not aid hepatic encephalopathic episodes. For very nice reviews of protein in liver and renal disease, see references 27 and 28. Table 9 describes the commonly available amino acid products and their characteristics.

To Count, or Not to Count Protein as Calories?

Total calories are used to characterize oral diets and tube feeding products. Characterizing the PN prescription as protein and non-protein calories does not make physiological sense (29,30). The use of non-protein calories for calculations presumes that one can direct protein utilization. Consider: When you provide amino acids to a catabolic patient, oxidation rates may equal or exceed amino acid infusion rates. There are multiple pathways taken by amino acids; utilization of substrate at the cellular level is not limited to a single pathway. Mixed fuel utilization will always take place, although the relative amounts of each substrate may change.

Fat

Intravenous fat emulsions (IVFE), (formerly called lipid emulsions), are generally used to provide 20%–30% of daily kcals unless conditions exist which prohibit or complicate lipid administration of this amount, i.e. hypertriglyceridemia or propofol infusions. Note that the vehicle for propofol is 10% IVFE and it provides essential fatty acids, calories (1.1 cal/mL infused) and vitamin K (31). See Table 10 for commercial lipid emulsions available in the U.S and their vitamin K content. The content of vitamin K varies depending on the manufacturer and concentration, with safflower oil containing less vitamin K than soybean oil. Vitamin K typically increases proportionally with increasing lipid concentrations (example, viatmin K content doubles

Table 11
Normal Serum Electrolyte Values and Parenteral and Enteral Ranges (36–38)

Electrolyte	*Normal Serum Range**	*Parenteral Intake Range*	*Adult Enteral Requirements*
Sodium	135–145 mM/L	0–200 mEq/L	100–150 mEq/day
Chloride	As needed to maintain acid-base balance		
Potassium	3.5–5.1 mM/L	0–240 mEq/day	60–120 mEq/day
Acetate**	As needed to maintain acid-base balance		
Phosphate	2.3–4.7 mg/dl	0–60 mM/day	15–30 mM/day
Magnesium	1.7–2.5 mEq/L	0–48 mEq/day	8–24 mEq/day
Calcium	9.2–11.0 mg/dl (ionized calcium 0.8–1.2 mEq/L)	0–25 mEq/day	9–22 mEq/day

*Note: Normal lab values vary between institutions and the populations they serve.

**Acetate is converted to bicarbonate in the liver.

Table 12
Approximate Electrolyte Composition of Various Body Fluids (36)

		Electrolytes (mEq/L)			
Source	*Volume (mL/d)*	*Na*	*K*	*HCO_3*	*Cl*
Saliva	500–2000	2–10	20–30	30	8–18
Gastric	2000–2500				
	pH<4	60	10	—	90
	pH>4	100	10	—	100
Pancreatic	1000	140	5	90	75
Bile	1500	140	5	35	100
Small Bowel	3500	100	15	25	100
Colonic	—	60	30	—	75
Diarrhea	1000–4000	60	30	45	45
Urine	1500	40	0	—	20
Sweat	1500	50	5	—	55

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with an increase from 10% to 20%) (32–34).

Micronutrients

Electrolytes in PN formulations are added according to anticipated patient requirements, metabolic response to medications, and recommended daily intakes. Table 11 provides typical ranges for parenteral electrolyte content. Excessive electrolyte losses from wounds, GI suction, surgical drains, fever (sweat loss), emesis, and diarrhea need to be replaced in the PN formulation or other IV solutions. Table 12 provides the approximate electrolyte composition and volume of many body fluids.

Vitamins and trace elements are usually added as commercially prepared multivitamin and trace metal "cocktails," which may meet daily requirements and prevent toxicity. Table 13 reviews the current recommendations for parenteral multivitamin injections by the Food and Drug Administration (FDA) (39).

The short term (<1 week) PN patient rarely needs supplementation of Vitamin K, while the long-term patient requiring PN for weeks to months will likely require 2–4 mg/week of parenteral vitamin K (40,41). The newest commercial vitamin products, Infuvite® (Baxter Healthcare Inc, Deerfield, IL), and MVI-Adult® (Mayne Pharma (USA), Paramus, NJ) were formulated to meet the latest FDA standards and include Vitamin K. Mayne Pharma manufactures a product that does not contain vitamin K (MVI-Adult without vitamin K®), but use of this product is not necessary, as even patients on coumadin need some vitamin K. It is important to remember, however, that wide fluctuations in vitamin K intake have significant impact on the effects of coumadin, and thus, intake should remain consistent when patients are placed on this anticoagulant (42). As previously discussed, IVFEs also contain vitamin K and may contribute significant amounts depending on the oil used, rate of infusion and concentration of lipid (Table 10).

General trace element dosing guidelines are listed in Table 14. There is some concern that the recommended manganese dose may be excessive for long-term PN patients. Periodic monitoring is recommended to ensure whole blood manganese levels remain within safe limits for patients receiving PN (44). When considering the dosing of multivitamins and trace elements, adjustments may need to be made in certain set-

Table 13
Recommended Daily Intake of Intravenous Vitamins (39)

Vitamin	*FDA/AMA/NAG* Recommended amounts/day*
Thiamin (B1)	6 mg
Riboflavin (B2)	3.6 mg
Pyridoxine (B6)	6 mg
Cyanocobalamin (B12)	5 mcg
Niacin	40 mg
Folic Acid	600 mcg
Pantothenic acid	15 mg
Biotin	60 mcg
Ascorbic acid (C)	200 mg
Vitamin A	3300 IU
Vitamin D	5 mg
Vitamin E	10 IU
Vitamin K	150 mcg

*National Advisory Group on Standards and Practice Guidelines for PN (ASPEN)

Table 14
Recommended Adult Daily Intake of Intravenous Trace Minerals (43)

Trace element	*Amount*
Chromium	10–15 mcg
Copper	0.3–0.5 mg
Manganese	60–100 mcg
Selenium	20-60 mcg
Zinc*	2.5–5.0 mg

*Note: Recommended zinc requirement per liter of ostomy or stool output lost:

- 12.2mg/L small bowel fluid
- 17.1mg/kg stool / ileostomy

Adapted from Mirtallo J, Canada T, Johnson D, Kumpf V, Petersen C, Sacks G, Seres D, Guenter P; Task Force for the Revision of Safe Practices for Parenteral Nutrition. Safe practices for parenteral nutrition. J Parenter Enteral Nutr, 2004; 28:S39–S70 with permission from the American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.). A.S.P.E.N. does not endorse the use of this material in any form other than its entirety.

tings. For example, in the presence of cholestatic liver disease, reductions in manganese and copper are often necessary (45,47).

Medications

A variety of medications may be added to PN solutions, however, only insulin and H_2-antagonists will be considered here. A recent review is available elsewhere (48).

Insulin

Hyperglycemia is the most common complication of PN. Regular human insulin is commonly added to PN to aid in blood glucose control. For a patient previously requiring insulin, addition of 1 unit of regular insulin per 10 g dextrose to the PN admixture is a safe, conservative starting point. If fasting blood glucose concentrations prior to PN initiation are running consistently >200 mg/dL, then a greater ratio of insulin to carbohydrate may be appropriate (e.g., 1.5–2 units per 10 g dextrose). Sliding scale coverage with regular or one of the more rapid acting insulin analogs such as insulin lispro (Humalog®) or insulin aspart (Novolog®) should be added to the medication regimen of the PN patient to provide additional coverage where needed. However, these insulin analogs are not compatible with PN formulations and thus only regular human insulin can be added into the PN admixture. The monitoring interval for blood glucose should be based on the duration of action of the insulin product. Elevated blood glucose levels can generally be controlled within a few days of PN by adding 70%–100% of the sliding scale insulin given during the time of the previous PN formulation. When following this method, success of the sliding scale ultimately depends upon changes in patient condition, medications, and initiation of an oral diet or enteral nutrition.

Patients need to be closely monitored for blood glucose variations after insulin has been adjusted in a PN formulation. Some clinicians limit the dose of regular human insulin in PN to less than 2 units per 10 g dextrose; however, changing attitudes regarding glycemic control have prompted modification of this position depending on the monitoring capability of the facility. Due to improved patient outcomes associated with better glycemic control in the intensive care unit, it is common practice in our institution to target blood glucose concentrations between 80–130 mg/dL for most patients (49). The use of an insulin drip or tighter sliding scale insulin regimen may be more appropriate in some environments to reduce the risk of hypoglycemia, as well as the frustration, personnel time and costs needed to reformulate PN admixtures if blood glucose drops too low. When using an insulin drip, the amount of insulin to be added to the future PN bag can be calculated as two-thirds of the total insulin infused during the previous PN administration. This takes into

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Table 15
Common Medications which may Effect Blood Glucose Levels (51,52)

Hyperglycemia	*Hypoglycemia*
Corticosteroids	Flouroquinolones
Diuretics	• In particular: Gatifloxacin
Adrenergic agents	Insulin
Cyclosporin	Alcohol
Tacrolimus	Sulfonylureas
Sandostatin	Methandrostenolone
Phenytoin	Clofibrate
Phenobarbital	Cypionate
Lithium	B-blockers
Calcitonin	Monoamine Oxidase Inhibitors (MAOI)
Rifampin	

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account the improved bioavailability of insulin when added to the PN.

Adjusting dextrose concentration in intravenous nutrition and monitoring for medication effects can further aid the practicing clinician in blood glucose control. Lowering dextrose concentrations is one way to improve glycemic control where needed. IVFE may be used to provide a greater percentage of the caloric intake. In the refractory hyperglycemic patient, sometimes PN just needs to be discontinued until euglycemia is achieved (50). Anticipating drug effects on blood glucose levels helps maintain control. Table 15 lists some medications, which are known to affect blood glucose levels. Illness, stress, and activity of the patient may also play a role and must be considered when adjusting glucose management. Table 16 provides additional suggestions to aid in blood glucose control.

H_2-antagonists

H_2 antagonists are often added to the PN admixture in patients requiring gastrointestinal stress ulcer prophylaxis. Famotidine is a common additive and has been shown to be stable in 3-in-1 admixtures of various compositions for at least 72 hours (53). The adult recommended dose of famotidine is 20 mg dosed every 12 hours, which can be added to PN as 40 mg per 24-hour bag. Famotidine is renally excreted, therefore, a 50% dose reduction is recommended when a patient's creatinine clearance is <50 mg/min. Ranitidine may also be added to PN formulations. It is stable in 3-in-1 solutions for 24 hours, however more than 10% of the drug may be lost at 48 hours (54). The adult recommended dose is 200–300 mg daily, generally not to exceed 400 mg per day. Doses should be reduced to 50 mg daily if the creatinine clearance is <50 mg/min (55). Patients receiving an intravenous or oral proton pump inhibitor usually do not need a H_2-antagonist.

Table16
Suggested Strategies for Improving Glucose Control

- Do not overfeed the patient
- Limit dextrose in TPN to 150 g/day initially
- Review other sources of IV dextrose (including CVVHD, peritoneal dialysis, antibiotic drips, etc.—PN may need to be adjusted accordingly).
- Increase units of insulin given at each step for sliding scale coverage
- Increase frequency of glucose checks if necessary (every 4–6 hours)
- Add insulin drip
- Stop TPN for 24 hours and get glucose under control

Iron

Iron supplementation may be needed for chronic home PN patients. Although body stores should last for up to 6 months, deficiencies have been reported after 2 months on PN without supplementation (56). Iron dextran has been used in 2-in-1 PN formulations in doses of 10–75 mg/day with no apparent side effects (57,58). However, the addition of iron to 3-in-1 PN admixtures has not been well studied and reports of incompatibilities exist (58). Anaphylaxis and destabilization of lipid formulations are both problems associated with this form of iron, and many clinicians prefer to supplement iron separately from PN solutions. Some of the newer iron products such as Ferrlecit® (Na ferric gluconate complex) by Schein and Venofer® (iron sucrose or iron saccharate complex) by American Regent may be considered for use separate from PN. Due to the complexity of PN formulations and the small market share of the PN population, compatibility studies of these new iron compounds in PN are unlikely to ever be performed by the manufacturers.

FREQUENTLY ASKED QUESTIONS IN THE CLINICAL SETTING

How Should PN Be Initiated?

Although PN infusion rates are often gradually advanced, there is no real reason to do this. Patients with diabetes, at a high risk for refeeding, or patients starting PN at home might benefit from this approach; however, in the acute care setting, this is not necessary. Hospitalized patients requiring PN can be started at the goal rate for the volume to be provided; assuming measures have been taken to minimize metabolic response (i.e., patient not overfed).

Hyperglycemia puts the patient at risk for infection and thwarts utilization of nutrients that the parenteral formulation provides. Overfeeding should be

avoided with any form of nutrition support; dextrose is usually the macronutrient of most concern with PN; therefore, if calorie requirements are the reason for a slow escalation, then the dextrose can be provided at a fractional amount of the goal and increased as the patient tolerates. If the PN carbohydrate content has been limited in anticipation of refeeding, or for the presence of hyperglycemia, there is no need to also limit the PN rate or "titrate the rate up" as this would be "doubly cautious" and unnecessary. Daily reformulations as necessary are based on current lab values and the response to any changes made previously.

When Should PN Be Discontinued?

PN should be discontinued with transition to PO or enteral nutrition as soon as feasible. Many patients may benefit from a trophic enteral feeding while on PN. Once enteral feedings or PO intake has advanced to >50% of estimated kcals, and the patient is tolerating this well, the PN formula can be weaned or discontinued. PN can be restarted in 2–3 days if the patient does not continue to tolerate enteral or PO nutrition or if intake is less than 50% of estimated requirements. Attention to glycemic control post-PN is crucial in those patients who have not previously been diagnosed as having diabetes mellitus, yet required insulin with the PN and became hyperglycemic again once PN stopped. PN therapy may act as a very expensive surrogate glucose tolerance test.

How Should PN Be Tapered?

There is a general belief that PN formulations require tapering. Rebound hypoglycemia is rarely seen but is often discussed in the clinical setting (59–61). The risk is very low, even in patients with diabetes mellitus, as they are somewhat "protected" by inherent insulin deficiency. Stopping PN with insulin is the same as stopping an independent insulin drip; remember, the half-life of regular insulin is only 5 minutes (although, somewhat longer if the patient is in renal failure). A taper down of PN is not needed, especially if the patient is receiving another dependable source of carbohydrate. If a particular patient is prone to hypoglycemia, tapering PN over 1–2 hours before discontinuation is justified and can avoid this problem.

When Should I Be on the Lookout for Refeeding?

Many hospitalized patients are malnourished due to the nature of their disease and/or treatment effects. When initiating nutrition support, it is important to monitor these patients closely to avoid refeeding. Refeeding syndrome is characterized by an abrupt decrease in serum potassium, magnesium and/or phosphorus. This results from pancreatic stimulation and insulin secretion (the driving force behind refeeding) after the introduction of a consistent nutrient source, primarily carbohydrate. The clinical presentation of refeeding syndrome can also include sodium and fluid retention causing edema, which may result in stress to the cardiac and respiratory systems. In these patients, PN should be started at partial, or "refeeding" calories, especially carbohydrate, with an appropriate supplementation of electrolytes and vitamins as appropriate. Once the patient is stable, PN can then be advanced to target as tolerated. A thorough discussion of this topic is available elsewhere (62).

What Happens If the Patient is Overfed?

While it is natural to want to provide "hyperalimentation" via the parenteral route for malnourished and catabolic patients, overfeeding, especially in cases of previously undernourished patients can cause more harm than good (see refeeding above). Critically ill and post-surgical patients often have an "obligatory hypercatabolism" not correctible by feeding (63). Overfeeding these patients may increase stress on vital organs including the heart, liver, and kidneys (64,65). All PN patients should be monitored closely and calories rarely need to exceed 30–35 kcal/kg. Indirect calorimetry may be helpful in some patients to help determine calorie needs and avoid under, or overfeeding (66).

Which is Best? 3-in-1 Versus 2-in-1

Many institutions have switched from the traditional 2-in-1 PN admixtures to a 3-in-1 admixture combining IVFE into the amino acid/dextrose mix rather than hanging the IVFE separately. Both systems are available to the practicing clinician and each has advantages as well as disadvantages. These are reviewed in

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Table 17
Advantages and Disadvantages of the Total Nutrient Admixture (3-in-1) System

Advantages
- All components aseptically compounded by the pharmacy
- Preparation is more efficient for pharmacy personnel, especially if automated
- Less manipulation of the system during administration
- Less risk of contamination during administration
- Less nursing time needed for 1 bag/d and no piggyback to administer
- Less supply and equipment expense for only 1 pump and IV tubing
- More convenient storage, fewer supplies, easier administration in home care settings
- Glucose and venous access tolerance may be better in some situations
- Possible applications in fluid-restricted patients
- May be more cost-effective overall in certain settings

Disadvantages
- Larger particle size of admixed lipid emulsion precludes use of 0.22-micron (bacteria-eliminating) filter, and requires larger pore size filter of 1.2 micron
- Admixed lipid emulsion less stable, more prone to separation of lipid components
- Admixtures are more sensitive to destabilization with certain electrolyte concentrations or the addition of iron
- Difficult to visualize precipitate or particulate material in the opaque admixture
- Certain medications are incompatible with lipid emulsion portion of admixture
- Catheter occlusion more common with daily lipid administration
- Less attractive in pediatric settings due to pH and compatibility considerations

Table 17.

Intravenous Fat Emulsion Hang Time

The CDC has recommended that due to the potential for bacterial contamination, 3-in-1 solutions should not hang for longer than 24 hours. If lipid is hung separately from the PN formulation such as in 2-in-1 solutions, each container of IVFE should not hang longer than 12 hours.

Series Editor's Note: The Centers for Disease Control and Prevention issued recommendations in 1982, that "infusions of lipid emulsions should be completed within 12 hours of starting" (1). This was based on reports of microbial growth in containers of lipid emulsion that were **deliberately-contaminated with microorganisms** (2). In 1996 the CDC modified their recommendations to allow lipids in 3-in-1 PN to hang for 24 hours, but restated the recommendation for IV lipid emulsions alone to be completed within 12 hours (3). The only adult study that has compared the 24 hour infusion of IV lipid emulsions with 3-in-1 PN did not show a significant difference in infectious complications between groups (4).

In short, the CDC recommendations are based on in-vitro studies after containers were purposefully contaminated. There is absolutely no outcome information in adult patients that a 24-hr hang-time increases infections. If a 12-hr hang-time policy means that a nurse manipulates the line more often, a 12-hr hang-time policy may actually increase patient infections. The hang-time concern (myth) may be real for pediatric patients where daily lipid is dispensed from a large volume container and there is greater potential for contamination, but the best data we have points to no more infections with 24-hr hang time than there is with 3-in-1 in adults.

1. Anonymous. CDC Guideline for Prevention of Intravenous Therapy-related Infections. *Infection Control,* 1982; 3: 52-72.
2. Melly MA, Meng HC, Schaffer W. Microbial growth in lipid emulsions used in parenteral nutrition. *Arch Surg,* 1975; 110: 314-318.
3. Pearson ML. Hospital Infection Control Practices Advisory Committee: Guideline for prevention of intravascular device-related infections. *Infection Control Hosp. Epidemiology*, 1996; 17: 438-473.
4. Vasilakis A, Apelgren KN. Answering the fat emulsion contamination question: three in one admixture vs conventional total parenteral nutrition in a clinical setting. *J Parenter Enteral Nutr*, 1988;12(4):356-359.

What is the Best Way to Manage Serum Electrolyte Abnormalities?

Experience may be the best instructor for adjusting electrolytes in parenteral formulations. Adjustments must take into account patient losses, organ function,

Table 18
Suggested Monitoring for Parenteral Nutrition (In-patient)

Parameter	*Baseline*	*Initiation*	*Critically Ill*	*Stable Patients*
CBC with differential	Yes		Weekly	Weekly
PT, PTT	Yes		Weekly	Weekly
Basic chemistry—Na, K, Cl, CO_2, BUN, creatinine	Yes	Daily ×3	Daily	1–2 times per week
Magnesium, calcium, phosphorus	Yes	Day 1	As needed	Weekly
Serum triglycerides	Yes	Day 1	As needed	As needed
Serum glucose	Yes	Daily	Daily	1–2 times per week
Capillary glucose	Q 6 hrs × 48 hrs; stop if WNL	As needed	3 x day until consistently <150 mg/dl*	As needed
Weight	Yes	Daily	Daily	2–3 times per week
Intake and output	Yes	Daily	Daily	As needed
ALT, AST, ALP, total bilirubin	Yes	Day 1	Weekly	Monthly
Nitrogen balance	As needed		As needed	As needed

CBC = complete blood cell count; BUN = blood urea nitrogen; PT = prothrombin time; PTT = partial thromboplastin time; ALT = alanine aminotransferase; AST = aspartate aminotransferase; ALP = alkaline phosphatase.

*More tightly controlled blood glucose levels of 80-130 may be sought (49).

Adapted from Mirtallo JM. Introduction to parenteral nutrition. In: Gottschlich MM, Ed. *The Science and Practice of Nutrition Support: A Case-Based Core Curriculum.* Dubuque, IA: Kendall/Hunt Publishing Co.;2001: 211–223, with permission from the American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.). A.S.P.E.N. does not endorse the use of this material in any form other than its entirety.

oral/enteral intake and the impact of medications. Experience allows anticipation of trends and impact on electrolyte manipulations. This is particularly helpful when monitoring intervals are extended as they are for home PN patients. Trends in serum electrolyte levels are far more meaningful than looking at a single value. Serum electrolyte levels fluctuate under natural physiologic control and variance in lab equipment. Minute adjustments in PN electrolytes are rarely beneficial and often only warranted if the patient has been on PN for a long enough time period that response is well known. For a nice review/guidelines for electrolyte replacement, see references 44,67,68.

How Often Should Labs Be Checked?

Daily labs are needed when initiating PN. This frequent level of monitoring may be warranted for several days to >2 weeks while electrolytes are being adjusted and the impact of PN initiation and advancement takes place. Guidelines for appropriate lab monitoring are addressed in Table 18.

Long-term Complications

Long-term complications of PN can include fatty liver, cholestasis, metabolic bone disease, and electrolyte/vitamin/mineral depletion or toxicity (46). In the long-term PN patient, it is important to be aware of, and monitor for, these adverse effects. This topic is beyond the scope of this article, however, a nice review of long-term complications is readily available (47). See Table 19 for gastrointestinal complications of long term PN.

What Should You Do When the Labs on Your PN Patient Look Like This?!!

Lab	*Result @ 4:00 A.M.*
Sodium	125
Potassium	6.7
Chloride	101
CO_2	17
BUN	12
Creatinine	0.7
Glucose	896
Triglycerides	684
Magnesium	3.5

Table 19
Complications of Long Term PN (9,36)

Problem	*Possible Causes*	*Symptoms*	*Treatment/Prevention*
Fatty Liver	Exact etiology unknown. Theories include: Overfeeding of dextrose &/or total calories; overfeeding of fat; EFAD; carnitine deficiency,choline deficiency	Elevation of LFTs	• Avoid overfeeding • Do not exceed recommended dosages of macronutrients (Table 3) • Enteral nutrition as soon as possible (even if trophic) • Enteric antibiotics if blind loops/ bacterial overgrowth possible • Add Taurine to PN
Cholestasis	Exact etiology unknown. Theories include: lack of nutrition in the bowel leading to decreased bile stimulation and impaired bile flow; overfeeding of glucose, lipid and/or amino acids; toxic tryptophan metabolites, choline deficiency	Elevated alkaline phosphatase; progressive increase in total bilirubin	• Avoid overfeeding • Do not exceed recommended dosages of macronutrients (Table 3) • Enteral nutrition as soon as possible • Enteric antibiotics if blind loops/ bacterial overgrowth possible
Gastrointestinal Atrophy	Atrophy of villi in the GI tract due to lack of enteral nutrients	Observed *in vitro*; *in vivo* only symptom may be enteric bacteremia and sepsis without clear source	• Enteral/oral nutrition concurrent or as soon as possible

Gottschlich MM, Ed. Nutrition Support Dietetics Core Curriculum. 2nd edition. American Society of Parenteral and Enteral Nutrition. Silver Spring, MD: 1993.

A. Order insulin (20 units SQ) and sodium polystyrene resin (Kayexalate®) 30 mL enema STAT
B. Call the endocrine fellow
C. Check fingerstick glucose at the bedside NOW for quick verification of chemistry result *before giving insulin*

Note: This patient's fingerstick glucose at 1800 and 2400 during PN infusion were 141 and 103 respectively.

The above situation demonstrates spurious lab results after PN contamination of a blood sample drawn from a central line without following proper flushing procedure. The procedure includes turning off the PN, flushing the line, discarding the initial aspirate, then drawing up the sample amount needed for the lab and then resuming the PN. If the PN admixture is not turned off and/or if the flush is inadequate prior to the draw, the lab results will reflect the extraordinarily high glucose, potassium and triglyceride levels in the sample secondary to contamination with the PN solution. Other electrolyte imbalances may also be seen. Although the PN may be held upon reviewing these results, a quick check of a bedside finger stick blood sugar and subsequent lab redraw is the most appropriate response.

CONCLUSION

PN is a valuable and necessary medical treatment for many patients providing both nutritional sustenance and life extension at a time when it is not possible to sustain them any other way. By focusing on the essential elements of PN management, this form of nutrition support can be applied successfully with minimal complications, thus providing great benefit to those who at one time would have been deemed "unfeedable." See Table 20 for summary guidelines. ■

Table 20
Summary Guidelines

1. Determine if PN is truly indicated
2. Assess the patient (medical/surgical history, review drug/medication profile, anthropometric data and lab values)
3. Determine need for long-term vs. short term <7–10 days IV access
4. Determine estimated kcal, protein and lipid needs
   - 20–30 kcal/kg
   - Protein 0.8–1.5 gm/kg
     - Higher levels may be needed in severe catabolic states
   - Lipid to provide ≤30% of kcals
5. Determine initial electrolyte, vitamin and trace element requirements; consider ongoing losses
6. Consider any additional additives to PN formulation including insulin and H_2-antagonists
7. Monitor for:
   - Risk of refeeding syndrome
   - Glucose intolerance
     - If so initiate feeding at a low dextrose level and advance cautiously as lab values are stable. If not then attempt to advance to goal within the first 24-48 hours
8. Initiate trophic feedings or convert patient to PO or enteral feeding when feasible

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