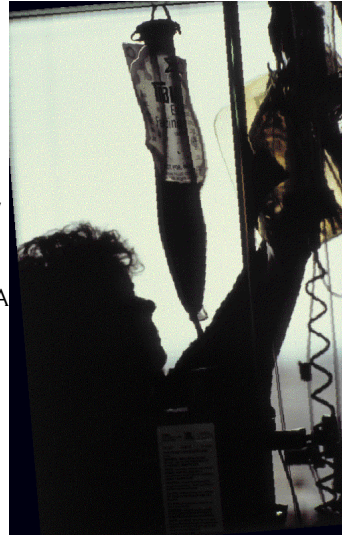


PERIPHERAL PARENTERAL NUTRITION

CAROL J. ROLLINS, MS, RD, PHARM.D.,
BCNSP COORDINATOR, NUTRITION SUPPORT SERVICE/
CLINICAL PHARMACIST FOR HOME INFUSION,
ARIZONA HEALTH SCIENCES CENTER TUCSON, ARIZONA

Parenteral nutrition (PN) is an appropriate route of nutrition support when patients with identified malnutrition or significant risk of malnutrition cannot meet their nutritional requirements through the gastrointestinal (GI) tract.¹ Although typically referred to as TPN, an acronym for *total* parenteral nutrition, patients who tolerate some oral intake or tube feeding require delivery of only part of their nutrients via the parenteral route. Use of the GI tract is encouraged to the extent possible. Septic complications may be reduced and gut villi better preserved with administration of at least some nutrients into the GI tract.^{2,3}



ACCESS SITES FOR PARENTERAL NUTRITION

Access for parenteral nutrition is generally obtained by placement of a central venous catheter. Cannulation of the subclavian, internal jugular, or femoral veins with advancement of the catheter tip into the

superior or inferior vena cava achieves central venous access. Catheter tip placement elsewhere than the vena cava is considered peripheral access. Based on catheter tip location, the Intravenous Nursing Society (INS) recognizes peripheral catheters as midclavicular, midline, and short peripheral.^{4,5} Acceptable dwell time differs for these 3 categories;

continued pg 2

however, risk of vascular irritation or damage and thrombosis requires that guidelines for peripheral administration be imposed for all classes of peripheral catheters. Guidelines include limiting dextrose concentrations and hypertonicity of substances administered, since dilution by blood flow is less than with central venous administration. Parenteral nutrition administered via the peripheral venous route, known as *peripheral* parenteral nutrition or PPN, must be formulated with these limitations in mind. Typical indications for PPN include short-term use, modest needs, and contraindications to central access (subclavian or jugular catheters) placement, such as radical neck dissection.

CAUSES OF INFUSION-SITE FAILURE

Several factors related to the cannula, patient, and infusate influence the ability to provide PPN successfully. Acquiring and maintaining access for an appropriate period of time is essential. Infusion site failure is manifested by phlebitis, thrombosis, or infiltration/extravasation.

- Phlebitis is inflammation of a vein, and is characterized by erythema with or without pain. It may include a visual streak along the vein, edema, and hardening of the vein (cord formation).⁴
- Thrombosis is formation of a blood clot within the vessel.
- Thrombophlebitis is a combination of phlebitis and thrombosis.
- Infiltration is leakage of a non-vesicant product into tissue.
- Extravasation is the proper term when the product is a vesicant.⁴

The reported incidence of phlebitis or thrombophlebitis ranges from 2.3% up to approximately 80%,^{4,6-9} and an incidence of up to 45% is reported for infiltration/extravasation.⁶

SITES OF CANNULATION

The site of cannulation, cannula size and dwell time, insertion technique, and catheter care affect development of complications that may result in infusion site failure.

Larger veins, such as the median, cephalic, or basilic veins in the forearm, are preferred for hypertonic or irritating substances, for larger volume infusions, and for therapies administered using a pump.¹⁰ PPN fits all these criteria. Midclavicular lines are generally inserted through the basilic or cephalic veins of the upper arm or at the antecubital fossa and extend at least to the proximal axillary vein, where vein size and blood flow are relatively large.

Midline catheters are inserted through veins in the antecubital fossa and extend 5 to 7 inches into the vessel, where vein diameter is still about 5 to 6 millimeters.^{5,11} Short peripheral catheters generally extend less than 3 inches into a superficial vein.⁴ Vein diameter here is smaller, and dwell time is generally limited to a few days. Site rotation and peripheral catheter replacement every 48 to 72 hours is common.¹¹⁻¹⁴ The cumulative risk of complications increases each day that a catheter is in place. The risk remains at 10% to 15% per day from day 2 until day 4.^{6,15}

Use of superficial veins in the upper extremities allows proper assessment for complications.¹² Guidelines from the INS and the Centers for Disease Control strongly recommend that only veins in the upper extremities be cannulated in adults, since the risk of deep vein thrombosis is increased in the lower extremities.^{4,11,12,16} Selection of the smallest gauge and shortest catheter acceptable for administration of

therapy may help limit complications. The catheter must be in a vein of adequate diameter to allow blood flow around the catheter and hemodilution of the infusate.^{4,13}

Successful PPN therapy requires an adequate number of healthy veins for cannulation when short peripheral catheters are used. Patients with poor venous access are rarely acceptable candidates for PPN therapy, unless midline or midclavicular access can be attained. Veins tend to lose supporting tissue and become elongated and tortuous with age.¹³ Veins are generally smaller and more fragile in older patients than in younger patients. Those with a history of long-term corticosteroid use, severe malnutrition, and debilitating diseases also tend to have small fragile veins. Repeated intravenous therapies can result in venous trauma and scarring, which limit peripheral access.

INDICATIONS OF PPN

PPN is useful for supplementation of inadequate oral or tube feeding intake, hypocaloric support with low to moderate protein provision, transitional support until central access can be obtained, and temporary support until catheter replacement following recurrent catheter-related sepsis.

Current nutritional status and underlying conditions help determine nutritional requirements,

which in turn dictates the amount of fluid and lipid emulsion necessary. In general, it is difficult to provide adequate support via PPN for a patient with severe metabolic stress or nutritional depletion requiring electrolyte replacement and high calorie or protein intake.

“It is difficult to provide adequate support via PPN for a patient with severe metabolic stress or nutritional depletion.”

Parenteral support for more than a few days, even at lower levels of calorie and protein provision, is difficult to maintain with short peripheral catheters. Midline or midclavicular catheter placement should be considered when PPN is expected to be necessary for more than 1 week. Barring any complications, midline catheters can remain in place for up to 4 weeks and midclavicular catheters for up to 3 months.^{4,5}

FORMULATIONS FOR PPN

Infusate-related factors influence venous complications and patient tolerance to PPN. Preparations of dextrose with normal saline and dextrose with amino acid solution consistently result in peripheral vein phlebitis when the osmolality exceeds 900 mOsm/L.⁶

IMPORTANCE OF LIPID EMULSION

Lipid emulsion appears to provide protection to the vein and allows tolerance to higher osmolarity infusates. Animal studies demonstrate reduced endothelial damage from amino acid solutions when fat emulsion is also infused.^{17,18} Venous patency time was improved in neonates given a high-fat formulation versus a lower-fat formulation of the same osmolarity.¹⁹ A longer patency time was also noted when the neonates received a lower osmolarity PPN formulation (547 mOsm/L vs 702 mOsm/L and 702 mOsm/L vs 784 mOsm/L) in a paired crossover study design.¹⁹

TOTAL NUTRIENT ADMIXTURE

Vein tolerance to hyposmolar formulations may be further improved by admixture of the lipid emulsion with the dextrose-amino acid solution (total nutrient admixture [TNA]). This beneficial effect may be secondary to the increase in pH of the TNA formulation and may be negated since peripheral vein TNAs are notoriously unstable admixtures compared with central TNAs.²⁰ In a randomized trial comparing co-infused lipids with admixed lipids, significantly better vein tolerance was noted with the admixed formulation.²¹ Tolerance to osmolarities of approximately 1300 mOsm/L for formulations admixed with lipid have been reported.^{22,23}

Another report noted no problems in 63% of patients receiving a PPN formulation with admixed lipids having an osmolarity of 1146 mOsm/L. Twenty-three percent of patients experienced transient pain, and 14% had the infusion stopped.²⁴ This suggests that osmolarities in the range of 1100 mOsm/L to 1300 mOsm/L are acceptable when lipid emulsion is admixed with dextrose-amino acid solutions. Caution with these higher osmolarities is advised.

REDUCING THE RISKS FOR THROMBOSIS AND PHLEBITIS

Addition of low-dose heparin and hydrocortisone to PPN formulations may increase tolerance to hyperosmolar formulations. The incidence of vein thrombosis appears to be reduced by addition of low-dose heparin (1 unit/mL) to peripherally administered fluids.^{25,26} Premature infants receiving 1 unit of heparin per milliliter of PPN had about one-third the incidence of thrombophlebitis (5.7% vs 17.2%) and nearly double the duration of catheter patency of those without heparin.²⁵ Adding 10 mg/L of hydrocortisone and 1000 units of heparin per liter to infusion solutions of 5% dextrose or 5% dextrose with 0.45% sodium chloride produced nearly the same results in phlebitis as buffering the solutions (pH 7.2 to 7.5).²⁷ Heparin should be avoided in patients with a history of heparin-induced thrombocytopenia. Significant reduction of peripheral vein thrombophlebitis has been reported in randomized placebo controlled trials with use of transdermal glyceryl trinitrate in both PPN and non-PPN patients.²⁸⁻³⁰ In normal healthy subjects, application of a topical nonsteroidal anti-inflammatory agent to the cannulation site on one arm reduced the incidence of phlebitis by nearly half in comparison with the site on the other arm, which served as a placebo.³¹

“The incidence of vein thrombosis appears to be reduced by addition of low-dose heparin (1 unit/mL) to peripherally administered fluids.”

MACRONUTRIENTS

Macronutrient concentrations are typically limited in PPN formulations because of osmolarity. The final concentration of amino acids is generally between 2.5% (25 g/L) and 5% (50 g/L) for PPN.³² Specialized amino acid solutions are rarely appropriate for PPN, since the patient populations for which such products are designed tend to be poor candidates for PPN therapy.

The generally recognized upper limit for dextrose concentrations in PPN formulations is 10% for adults (approximately 500 mOsm/L) and 12.5% for pediatric patients (625 mOsm/L). At these concentrations, dextrose provides 340 Kcal/L in adults and 425 Kcal/L in pediatric patients.

Glycerol (glycerin) has also been used as a carbohydrate source in commercially prepared PPN solutions. The neutral pH, higher caloric density (4.3 Kcal/g), and trihydroxy alcohol structure of glycerin favor its use in PPN.

Lipid emulsion provides a major source of calories in PPN formulations, since calories from carbohydrates are limited by the osmolarity. Guidelines suggest that fats be provided at no more than 60% of total calories and no more than 1.5 g/kg of body weight per day in adults.³³ The maximum recommended dose of lipids in children and adolescents is 2.0 g/kg/d to 2.5 g/kg/d. Infants may tolerate

OSMOLARITY OF THE PPN FORMULATION

The prescription for a PPN formulation has a significant influence on how well the therapy will be tolerated. As previously mentioned, osmolarity is a critical consideration. Dextrose, amino acids, and electrolytes are the major contributors to osmolarity. The osmolarity can be estimated as shown in the boxed equation that follows.

$$\text{OSMOLARITY (mOsm/L)} = (\text{GRAMS DEXTROSE/LITER}) \times 5 + (\text{GRAMS AMINO ACID/LITER}) \times 10 + (\text{mEq CATIONS/LITER}) \times 2$$

slightly more lipids. The cumulative effect of macronutrient concentrations on lipid stability must be considered when the PPN is to be provided as a TNA formulation.³²

MICRONUTRIENTS

The micronutrient components of PPN are similar to those of centrally administered TPN formulations, with a few exceptions. Vitamins should be administered daily using a product such as M.V.I.[®]-12 (Multivitamin Infusion) that meets the guidelines for parenteral vitamins set by the American Medical Association Nutritional Advisory Group. M.V.I.[®]-12 does not contain vitamin K, which should be administered separately if needed. Additional supplementation to correct any existing deficiencies is also appropriate.³⁴ Direct addition of M.V.I.-12 to intravenous fat emulsions is not recommended. Trace elements can be routinely added to all parenteral nutrition formulations, although the short duration of most PPN therapy makes this unnecessary unless the patient has preexisting deficiencies. Electrolytes such as sodium chloride, potassium, magnesium, phosphate, and calcium are essential for muscular and central nervous system functions, as well as for metabolism and maintenance of fluid status.³⁵

GUIDELINES FOR MONITORING THERAPY

Monitoring of PPN therapy is essentially the same as for parenteral nutrition administered via a central venous access device. Metabolic complications parallel those associated with central parenteral nutrition. The typical duration of PPN therapy and limitations on carbohydrate provision in PPN—with a subsequent increase in calories from lipid emulsion—may alter the incidence of hyperglycemia and hypertriglyceridemia. The frequency of monitoring should be based on the overall condition of the patient, on the presence of factors that may contribute to complications, and response to alterations in the nutrient prescription. Since PPN patients tend to be under less metabolic stress than most TPN patients, the frequency of laboratory monitoring may be less frequent.

SUMMARY

Peripheral parenteral nutrition can be a safe and effective therapy. Achieving peripheral vein access and subsequently maintaining access is critical to providing PPN therapy. Patient selection is greatly influenced by the condition of peripheral veins.

The PPN formulation is designed to minimize venous damage while providing adequate nutrition support. This is achieved by limiting dextrose, amino acid, and electrolyte concentrations in the PPN formulation, and providing a higher percentage of calories from lipid emulsions and giving more fluid than is typically used for central parenteral nutrition.

Micronutrients (vitamins and trace elements) are also provided. Peripheral parenteral nutrition support is generally considered a short-term therapy. Patients experiencing relatively low metabolic stress are most likely to achieve short-term nutritional goals with PPN therapy. In high stress patients, nutritional deterioration may be blunted until central venous access can be achieved.

“As with TPN, vitamins should be administered daily”

References: 1. Skipper A, Marian MJ. Parenteral nutrition. In: Gottschlich MM, Matarese LE, Shronts EP, eds. Nutrition Support Dietetics Core Curriculum. Silver Spring, Md: ASPEN; 1993:105-121. 2. Kudsk KA, Croce MA, Fabian TC, et al. Enteral versus parenteral feeding: effects on septic morbidity following blunt and penetrating abdominal trauma. *Ann Surg.* 1992;215:503-513. 3. Newsholme EA, Parry-Billings DP. Properties of glutamine release from muscle and its importance for the immune system. *J Parenter Enteral Nutr.* 1990;14 (Suppl):63S-67S. 4. Intravenous Nursing Society. Intravenous Nursing Standards of Practice, Revised 1998. *J Intravenous Nurs.* 1998; 21(Suppl 1). 5. Anon. Midline and midclavicular catheters. *J Intravenous Nurs.* 1997;20(4):175-178. 6. Maki DG, Ringer M. Risk factors for infusion-related phlebitis with small peripheral venous catheters: a randomized controlled trial. *Ann Int Med.* 1991;114:845-853. 7. Perucca R, Micek J. Treatment of infusion-related phlebitis. *J Intravenous Nurs.* 1993;16:282-286. 8. Feldstein A. Detect phlebitis and infiltration before they harm your patient. *Nursing* 86. 1986;16:44-47. 9. Tager IB, Ginsberg MB, Ellis SE et al. An epidemiologic study of the risks associated with peripheral intravenous catheters. *Am J Epidemiol.* 1983;118:839-851. 10. Anatomy and physiology applied to intravascular therapy. In: Weinstein SM. *Plumer's Principles and Practice of Intravenous Therapy*, 5th ed. JB. Lippincott Co, Philadelphia; Pa; 1993. 11. Pearson ML. The Hospital Infection Control Practices Advisory Committee. Guidelines for prevention of intravascular-device-related infections. *Infect Control Hosp Epidemiol.* 1995;17:438-73. 12. Russell DM, Close M, Jeejeebhoy KV. Peripheral total parenteral nutrition. In: Kaminski MV, ed. *Hyperalimentation: A Guide for Clinicians*. New York, NY: Marcel Dekker, Inc.; 1985:155-169. 13. Whitson M.

Intravenous therapy in the older adult: special needs and considerations. *J Intraven Nurs.* 1996;19:251-55. **14.** Ena J, Cercenado E, Martinez D et al. Cross-sectional epidemiology of phlebitis and catheter-related infections. *Infect Control Hosp Epidemiol.* 1992;13:15-20. **15.** Homer LD, Holmes KR. Risks associated with 72- and 96-hour peripheral intravenous catheter dwell times. *J Intraven Nurs.* 1998;21:301-305. **16.** Centers for Disease Control. Guidelines for prevention of intravascular infection. *J Natl Intraven Ther Assoc.* 1982;5:39-50. **17.** Fujiwara T, Kawarasaki H, Fonkalsrud EW. Reduction of post-infusion venous endothelial injury with Intralipid. *Surg Gynecol Obstet.* 1984;158:57-65. **18.** Enger E, Jacobsson B, Sorensen SE. Tissue toxicity of intravenous solutions. *Acta Paediatr Scand.* 1976;65:248-252. **19.** Pineault M, Chessex P, Piedboeuf B, Bisailon S. Beneficial effect of coinfecting a lipid emulsion on venous patency. *J Parenter Enteral Nutr.* 1989;13:637-640. **20.** Li LC, Sampogna TP. A factorial design study on the physical stability of 3-in-1 admixtures. *J Pharm Pharmacol.* 1993;45:985-7. **21.** Nordenstrom J, Jeppsson B, Loven L, Larsson J. Peripheral parenteral nutrition: effect of a standardized compounded mixture on infusion phlebitis. *Br J Surg.* 1991;78:1391-1394. **22.** Hoheim DF, O'Callaghan TA, Joswiak BJ, et al. Clinical experience with three-in-one admixtures administered peripherally. *Nutr Clin Pract.* 1990;5:118-122. **23.** Watson LA, Bommarito AA, Marshall JF. Total peripheral parenteral nutrition in pregnancy. *J Parenter Enteral Nutr.* 1990;14:485-489. **24.** Hoffmann E. A randomized study of central versus peripheral intravenous nutrition in the perioperative period. *Clin Nutr.* 199;8:179-180. **25.** Alpan G, Eyal F, Springer C, et al. Heparinization of alimentation solutions administered through peripheral veins in premature infants: a controlled study. *Pediatrics.* 1984;74:375-378. **26.** Daniell HW. Heparin in the prevention of infusion phlebitis: a double-blind controlled study. *JAMA.* 1973;226:1317-1321. **27.** Fonkalsrud EW, Carpenter K, Masuda Y, Beckerman JH. Prophylaxis against postinfusion phlebitis. *Surg Gynecol Obstet.* 1971;133:253-256. **28.** Khawaja HT, Williams JD, Weaver PC. Transdermal glyceryl trinitrate to allow peripheral total parenteral nutrition: a double-blind placebo controlled feasibility study. *J R Soc Med.* 1991;84:69-71. **29.** Tighe MJ, Wong C, Martin IG, McMahon MJ. Do heparin, hydrocortisone, and glyceryl trinitrate influence thrombophlebitis during full intravenous nutrition via a peripheral vein? *J Parenter Enteral Nutr.* 1995;19:507-509. **30.** Khawaja HT, O'Brien BJ, Buxton MJ. Cost minimisation study of transdermal glyceryl trinitrate in reducing failure of peripheral intravenous infusions. *Br J Med.* 1989;76:299-297. **31.** Payne-James JJ, Bray MJ, Kapadia S, et al. Topical nonsteroidal anti-inflammatory gel for the prevention of peripheral vein thrombophlebitis. *Anaesthesia.* 1992;47:324-326. **32.** Rollins CJ. Total nutrient admixtures: stability issues and their impact on nursing practice. *J Intraven Nurs.* 1997;20:299-304. **33.** Lenssen P. Management of total parenteral nutrition. In: Skipper A, ed. *Dietitian's Handbook of Enteral and Parenteral Nutrition.* 2nd ed. Gaithersburg, Md: Aspen Publ; 1998:481-513. **34.** The National Advisory Group on Standards and Practice Guidelines for Parenteral Nutrition. Safe practices for parenteral nutrition formulations. *J Parenter Enteral Nutr.* 1998;22:49-66. **35.** Silberman H, Eisenberg D. Nutritional requirements. In: *Parenteral and Enteral Nutrition for the Hospitalized Patient.* East Norwalk, Conn: Appleton-Century-Crofts; 1982:52-73. ●