

Parenteral Nutrition: Current Practices and Innovations

Presented as a Webcast
Tuesday, June 16, 2015

Planned and conducted by the American Society of Health-System Pharmacists and the
UNC Eshelman School of Pharmacy.



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Beverly J. Holcombe, Pharm.D., BCNSP, FASHP, is Clinical Practice Specialist with the American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.).

She received her Bachelor of Science degree from the University of North Carolina (UNC) – Chapel Hill School of Pharmacy and her Doctor of Pharmacy degree from the University of Tennessee Health Sciences Center in Memphis. Dr. Holcombe then completed an ASHP Research and Education Foundation Pharmacy Nutrition Support Services Fellowship at the University of Tennessee in Memphis.

Prior to joining A.S.P.E.N. Dr. Holcombe was a Clinical Specialist in the Pharmacy Department at UNC Health Care and Clinical Professor, UNC Eshelman School of Pharmacy. Dr. Holcombe's specialty practice at UNC Health Care was in nutrition support and she was a member of the adult nutrition support service for more than 25 years. During her tenure at UNC she participated in both didactic and experiential education for pharmacy students and post-graduate trainees. She continues to facilitate classroom education experiences for UNC pharmacy students.

Dr. Holcombe has held leadership roles in ASHP including serving on the Executive Committee of the Section of Clinical Specialists and Scientists. She has held leadership positions with the Board of Pharmacy Specialties and was chair of the first Specialty Council on Nutrition Support Pharmacy Practice. Throughout her career Dr. Holcombe has been a leader in A.S.P.E.N. Her leadership roles include serving as Secretary and a member of the Board of Directors. Dr. Holcombe has also served on numerous A.S.P.E.N. committees and task forces. Most recently she served as chair of the A.S.P.E.N. Nutrition Product Shortage Subcommittee and was a member of the Parenteral Nutrition Safety Task Force. The work of this task force culminated in the publication of the A.S.P.E.N. Parenteral Nutrition Consensus Safety Recommendations.

Dr. Holcombe has authored numerous publications on various enteral and parenteral nutrition therapies, the role of the pharmacist in providing nutrition support, parenteral nutrition safety and strategies for managing shortages of parenteral nutrition components. She served as a co-editor for the A.S.P.E.N. Parenteral Nutrition Handbook, 2nd edition published in 2014 and an associate editor for the A.S.P.E.N. Nutrition Support Practice Manual, 2nd edition and the first edition of A.S.P.E.N.'s The Science and Practice of Nutrition Support: A Case-based Core Curriculum.

Dr. Holcombe is recognized locally, nationally and internationally for her expertise in nutrition support. She has provided presentations at ASHP Midyear Clinical meetings, ASHP state affiliate conferences, A.S.P.E.N. Clinical Nutrition Week, local chapters of A.S.P.E.N. and international congresses on parenteral and enteral nutrition.

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Objectives

- Describe system-based strategies to improve the safety of parenteral nutrition therapy.
- Describe management strategies for conserving and rationing parenteral nutrition components during shortages.
- Design a parenteral nutrition formulation for an adult to include appropriate dosing of macro-and micronutrients.
- Compare the composition and dosing regimens for intravenous fat emulsion products approved for use in the United States.
- Compare the advantages and disadvantages of compounded and commercially-available parenteral nutrition admixtures.

Introduction

- Parenteral nutrition (PN) is a complex therapy
- Pharmacists with no specialty training responsible for PN
- Challenges for pharmacists
 - Who wants this order "PN per pharmacy"?
 - Can I add this medication to the PN?
 - We're getting a new CPOE system what components are required for the PN order?
 - Can we use adult trace elements for neonates?



Parenteral Nutrition:

Improving Safety



Case Study: Preterm infant requiring PN

Prescribe	<ul style="list-style-type: none"> PN with zinc X mcg/100 mL
Order Review & Data Entry	<ul style="list-style-type: none"> Zinc dose correctly converted to mcg/kg to match compounder template Zinc dose erroneously entered in compounder as mg, not mcg—1000-fold error
Data Entry Check	<ul style="list-style-type: none"> Error not noted during work check and PN label check
Compound	<ul style="list-style-type: none"> PN prepared with dozens of vials of zinc sulfate; replenished syringe on compounder 10 times Error not noted during manual syringe check
Administration	<ul style="list-style-type: none"> Numbers, not units, reported at label check
Error Identified	<ul style="list-style-type: none"> Unusual PN preparation reported
Patient Outcome	<ul style="list-style-type: none"> Treated for zinc overdose Death

PN-Associated Errors

- Complex therapy
 - May contain more than 20 ingredients
 - Classified as high-alert medication
 - Complications may occur as result of the therapy or the process
- Only 58% of organizations have precautions in place to prevent errors and patient harm.¹
- 44% of survey respondents did not track PN errors.²

1. ISMP. ISMP Medication Safety Alert. 2012; 7:1-4.
2. Boullata JI et al. *JPEN*. 2013; 73:212-232.

PN Safety Consensus Recommendations

- Standardized PN order format and template.
- Standardized electronic orders (CPOE) with direct interface to automated compounding device (ACD).
- Standardized label format and template.

Ayers P et al. *JPEN*. 2014; 38:296-333.

Parenteral Nutrition Order Template: Adult Patient.

Patient Information Patient name _____ Medical record number _____ Birth date/age _____ _____ Patient location _____ Allergies _____ Height and doing weight (M) _____ (in) Doing Wt _____ (kg) Diagnoses (Indications) for PN: _____ Vascular access device/location CVC type _____ Location _____ Administration schedule _____	
Base Formula Amino acids _____ g Dextrose _____ g IV Fat emulsion _____ g	Amount/Day g g g
Electrolytes Sodium phosphate _____ mmol Sodium chloride _____ mEq Sodium acetate _____ mEq Potassium phosphate _____ mmol Potassium chloride _____ mEq Potassium acetate _____ mEq Magnesium sulfate _____ mEq Calcium gluconate _____ mEq	mmol mEq mEq mmol mEq mEq mEq
Vitamins, Trace Elements, Additives Multi-component vitamins _____ mL Multi-component Trace elements _____ mL Other Additives (eg, individual vitamins or trace elements, cyclones, regular insulin) as clinically appropriate and compatible	mL mL
PN Instructions Total volume _____ mL, Infusion rate _____ mL/hr, start and stop times _____ Cycle information _____ Prescriber and contact information _____	

Printed with permission. Ayers P et al. *JPEN*. 2013; 38:296-333.

PN Safety Recommendations

- Criteria to identify and evaluate pharmacists competent to review and evaluate orders and preparation of PN.
- Implement soft and hard limits on ACD.
- Develop and implement weight-based limits on ACD.
- Monitor and review ACD alert overrides.

Ayers P et al. *JPEN*. 2014; 38:296-333.

PN Safety Recommendations

- Increased training and competency assessment regarding <797> and compounding sterile products.
- Procedures and protocols to decrease of catheter-associated bloodstream infections.
- Use checklists and sign off sheets for critical aspects of the PN process

Ayers P et al. *JPEN*. 2014; 38:296-333.

Parenteral Nutrition:

Managing Shortages



Do you feel like Old Mother Hubbard? Is your PN cupboard bare?



<http://inkspiredmusings.blogspot.com/2012/05/old-mother-hubbard-nursery-rhyme-time.html>

- Are you currently experiencing a shortage of one or more PN components?
- In the last 5 years have you had to reduce the dose of a component from a patient's PN?
- Have you observed patient harm or suboptimal patient outcome as a result of PN component shortage?

PN Shortage Management Strategies

http://www.nutritioncare.org/Guidelines_and_Clinical_Resources/Product_Shortage_s/Product_Shortage_Management/

Nutrient Deficiencies Associated with Trace Element Shortages

- Zinc
 - 3 premature infants with dermatitis (2012)
 - 4 infants- 3 with dermatitis, 1 death (2013)
 - 1 adult with biochemical deficiency (2014)
 - 1 adult with impaired wound healing (2014)
- Selenium
 - 5 pediatric patients with biochemical deficiency (2012)
- Copper
 - 1 adult with anemia and leukopenia (2013)
 - 1 adult with anemia (2014)

When is my cupboard full? (When is a shortage resolved?)

- Product available through normal supply channels
- No allocations, direct orders or drop shipments
- Able to procure sufficient product to prescribe and administer full dose daily
- FDA considers shortage resolved



PN Component Dosing Strategies After Shortages Resolve

- Rationing and conservation strategies are intended to be used only during shortages.
- Resume prescribing and administering the normal/usual/full dose daily of components to patients that require them.
- The lack of observed adverse events/deficiencies and the potential cost savings associated with "partial" dosing should not be the impetus to continue less than optimal dosing.

Parenteral Nutrition:

Adult Dosing Guidelines



PN Macronutrient Adult Dosing Guidelines: Amino Acids

Patient Population	Dose
Stable Patients	0.8-1 g/kg/d
Critically Ill	1.5-2 g/kg/d
Severe malnutrition, acute or chronic kidney injury-with or without renal replacement therapies, hepatic disease, trauma, obese, burns, etc.	See Clinical Guidelines/ Scientific literature

Adapted from Ayers P, ed. A.S.P.E.N. Parenteral Nutrition Handbook, 2nd ed. A.S.P.E.N., Silver Spring, MD, 2014.
Adapted from Mueller CM, ed. A.S.P.E.N. Adult Nutrition Support Core Curriculum, 2nd ed. A.S.P.E.N., Silver Spring, MD, 2012.

PN Macronutrient Adult Dosing Guidelines: Energy

Patient Population	Usual Dose
Stable patient	20-35 kcal/kg/d
Critically ill	25- 30 kcal/kg/d
Critically ill obese	<25 kcal/kg/d

Ayers P, ed. A.S.P.E.N. Parenteral Nutrition Handbook, 2nd ed. A.S.P.E.N., Silver Spring, MD, 2014.
Mueller CM, ed. A.S.P.E.N. Adult Nutrition Support Core Curriculum, 2nd ed. A.S.P.E.N., Silver Spring, MD, 2012.

PN Macronutrient Adult Dosing Guidelines: Dextrose

Patient Population	Usual Dose
All patients	70-85% non-protein energy Maximum 7 g/kg/d (4-5 mg/kg/min) Minimum 50 g/d
Stable patient	4-5 mg/kg/min
Critically ill	≤4 mg/kg/min

Adapted from Ayers P, ed. A.S.P.E.N. Parenteral Nutrition Handbook, 2nd ed. A.S.P.E.N., Silver Spring, MD, 2014.
Adapted from Mueller CM, ed. A.S.P.E.N. Adult Nutrition Support Core Curriculum, 2nd ed. A.S.P.E.N., Silver Spring, MD, 2012.

PN Macronutrient Adult Dosing Guidelines: Fat Emulsion

Patient Population	Usual Dose
All patients	15-30% non-protein energy Maximum 2.5 g/kg/d Prevent essential fatty acid deficiency 1-2% energy as linoleic acid and 0.5% as α-linolenic acid (Soybean oil emulsion 100 g/week)
Stable patients	1 g/kg/d
Critically ill	<1 g/kg/d

Adapted from Ayers P, ed. A.S.P.E.N. Parenteral Nutrition Handbook, 2nd ed. A.S.P.E.N., Silver Spring, MD, 2014.
Adapted from Mueller CM, ed. A.S.P.E.N. Adult Nutrition Support Core Curriculum, 2nd ed. A.S.P.E.N., Silver Spring, MD, 2012.

Daily Electrolyte Guidelines for Adults

Nutrient	Requirement	Salts Used in PN
Calcium	10-15 mEq	Gluconate*, chloride
Magnesium	8-20 mEq	Sulfate*, chloride
Phosphorus	20-40 mmol	Sodium, potassium, glycerophosphate***
Sodium	1-2 mEq/kg**	Chloride, acetate, phosphate
Potassium	1-2 mEq/kg**	Chloride, acetate, phosphate
Acetate	As needed to maintain acid-base balance	Sodium, potassium
Chloride	As needed to maintain acid-base balance	Sodium, potassium

* Preferred salt for use in PN admixtures.
** Multiple salts of these may be used to provide total of 1-2 mEq/kg
*** Imported product, not FDA approved.

Adapted from Ayers P, ed. A.S.P.E.N. Parenteral Nutrition Handbook, 2nd ed. A.S.P.E.N., Silver Spring, MD, 2014.

U.S. IV Adult Multivitamins Recommended Daily Dose

Component	Dose per 10 mL
A (retinol)	1 mg
D (ergocalciferol)	5 mcg
E (dl-alpha tocopheryl acetate)	10 mg
K (phyloquinone)*	150 mcg
C (ascorbic acid)	200 mg
B-1 (thiamin)	6 mg
B-2 (riboflavin)	3.6 mg
Niacinamide	40 mg
Dexpanthenol	15 mg
B-6 (pyridoxine)	6 mg
B-12 (cyanocobalamin)	5 mcg
Biotin	60 mcg
Folic Acid	600 mcg

* One manufacturer provides product that is phyloquinone-free.

Adult IV Multi-Trace Element Products

Trace Elements	A.S.P.E.N. Recommended Daily Adult Requirements*	Multitrace** 4&5 (per mL)	Multitrace** 4&5 Concentrate (per mL)	Addamel N*** (per mL)
Zinc	2.5-5 mg	1 mg	5 mg	0.65 mg
Copper	0.3-0.5 mg	0.4 mg	1 mg	0.13 mg
Manganese	0.06-0.1 mg	0.1 mg	0.5 mg	0.027 mg
Chromium	10-15 mcg	4 mcg	10 mcg	1 mcg
Selenium	20-60 mcg	20 mcg	60 mcg	3.2 mcg
Iron	Not routinely	-	-	0.11 mg
Molybdenum	added	-	-	1.9 mcg
Iodine	in the	-	-	0.013 mg
Fluorine	U.S.	-	-	0.095 mg

*Printed with permission from A.S.P.E.N. Vanek V, et al. *Nutr Clin Pract.* 2012; 27:440-491.
 ** American Regent. US products
 ***Available under temporary importation; not FDA approved.

A non-critically ill adult patient with normal hepatic and renal function requires PN for a prolonged post-op ileus. The order is "pharmacy to manage PN".

Using the scale below assess your knowledge and confidence to order an initial PN for this patient.

1
2
3
4
5

I have no clue
I'll try but need help
I can do this

Parenteral Nutrition:

Fat Emulsions on the Horizon



Intravenous Fat Emulsions: Functions

- Source of essential fatty acids
- Alternative to carbohydrates as a source of non-protein energy
- Standard soy-based oil (SO) IV fat emulsions (IVFE) meet the requirement to prevent EFAD in patients receiving PN



Courtesy of Kathy Gura, PharmD, BCNSP, FASHP, FPPAG, FASPEN

Alternative Oil-based Emulsions

- Used outside the U.S. for many years
- Alternative oils
 - Olive
 - Medium chain
 - Fish
 - Combinations
- Products approved in U.S.
 - Mixture of olive oil and soybean oil emulsion (4:1)
 - Clinolipid (Clinoleic outside U.S.)

What's Different

- Phytosterol content
- Vitamin E content
- Inflammatory characteristics due to oil source

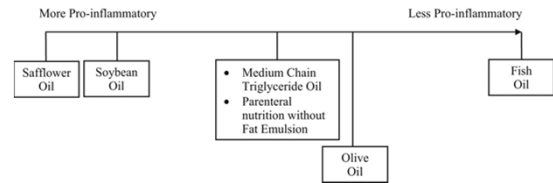
Courtesy of Kathy Gura, PharmD, BCNSP, FASHP, FPPAG, FASPEN

Comparison of IV Fat Emulsions

OIL	Intralipid	Omegaven	Clinoleic/ Clinolipid	SMOFlipid
Soybean	100%		20%	30%
MCT				30%
Olive			80%	25%
Fish		100%		15%
Glycerol (%)	2.25	2.5	2.5	2.5
Egg Phospholipid (%)	1.2	1.2	1.2	1.2
Phytosterols (mg/L)	439 ± 5.7	3.66	274 ± 2.6	207
Vitamin E (mg/L)	38 mg	150-296 mg	32 mg	163-225 mg

Courtesy of Kathy Gura, PharmD, BCNSP, FASHP, FPPAG, FASPEN

Inflammatory Characteristics of Oils



Reprinted with permission from A.S.P.E.N. Vanek V et al. *Nutr Clin Pract.* 2012;27:150-192.

A.S.P.E.N. Position Statement

Based on substantial biochemical and clinical evidence, alternative oil-based IVFEs may have the following effects when compared to standard SO IVFEs:

- Less pro inflammatory effects
- Less immune suppression
- More antioxidant effects
- May potentially be a better alternative energy source

Vanek V et al. *Nutr Clin Pract.* 2012;27:150-192.

Clinical Use of Alternative Oil IVFE

- Original IVFE use/approval energy and essential fatty acids; safety
- Challenging to get new products approved in U.S.
- Difficult to demonstrate specific therapeutic indication for alternative oil IVFE

Status of Alternative Oil IVFE in U.S.

- Soy-oil based IVFEs continue to be the standard of care
- Mixture of olive and soybean oils emulsion (4:1) approved but not on market
 - Approved for use in adults
 - Not for pediatric patients and neonates
- Fish oil-based IVFE on compassionate use for parenteral nutrition-associated liver disease (PNALD)

Parenteral Nutrition:

Commercially-available products vs. Compounded admixtures



Commercially-Available PN Products

- Industry-manufactured
- Fixed combination of amino acids and dextrose
 - May include IVFE
 - May include fixed amount of electrolytes
- Components separated by internal membrane (multi-chamber bag)
- Membrane must be broken and components mixed prior to administration
- NOT complete, ready-to-hang; NOT “premixed”

Commercially-Available PN Products



Dextrose/Amino Acids



Dextrose/Amino acids/fat

Considerations: Cost

- Multiple analyses
- Different variables
 - Salaries
 - Equipment and supplies
 - Need for additional electrolytes
- Individual institution must conduct cost analysis considering the many factors associated with PN therapy
 - Small institutions
 - Low PN volume

Considerations: Safety

- Potential to reduce errors
 - Simplified compounding
 - Potential to reduce catheter-associated bloodstream infections
- Safety concerns
 - Additive quantity and compatibility questions
 - Not complete-must add vitamins and trace elements
 - Membrane must be broken and mixed
 - Labelling in % concentration and ions

Considerations: Clinical Use

- Useful during PN component shortages
- Fixed ratio of macronutrients not appropriate for all adult patients
 - Obesity
 - Critical care
- Fixed electrolyte content not optimal for all patients

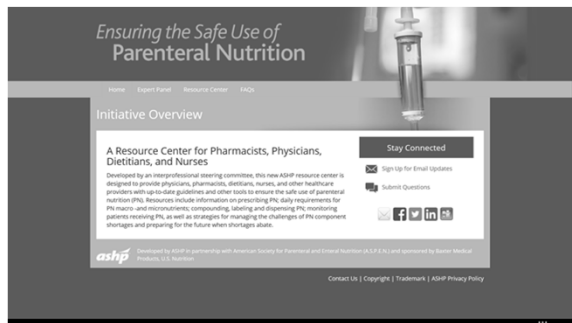
Commercially-Available PN: Bottom Line

- Offer advantages with regard to compounding
- May reduce costs –institution specific analysis
- May reduce catheter-associated bloodstream infections
- Useful during shortages
- Fixed macronutrients and electrolytes may not meet needs of adult patients

Take Home Messages

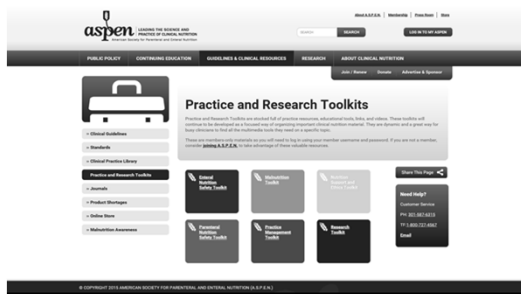
- Pharmacists with no specialty training are responsible for various aspects of the PN process.
- The safety of PN therapy can be improved by evaluating the system and implementing a standardized process.
- Providing PN during shortages requires vigilance and continuous assessment of the entire process to optimize patient care and avoid patient harm.
- The decision to use commercially-available or traditional compounded PN requires a thorough and detailed analysis of all aspects of the PN process and system.

ASHP PN Resource Center



<http://www.pnsafeuse.org/home>

American Society for Parenteral and Enteral Nutrition



http://www.nutritioncare.org/guidelines_and_clinical_resources/

Stay tuned for Q&A!

- Email questions to pgr@unc.edu
- Complete the evaluation and process your CPE online at elearning.ashp.org/my-activities
- Next webcast: Tuesday, July 14, Noon ET
 - Cytomegalovirus Infection in Solid Organ Transplant
 - Presented by Ruth-Ann Lee, Pharm.D., CPP

SELF – ASSESSMENT QUESTIONS

The presentation self-assessment questions are listed here for your convenience. Note the correct answers for future reference.

1. Parenteral nutrition-associated medication errors
 - a. Can be eliminated by using an automated compounder.
 - b. Rarely result in patient harm or suboptimal patient outcomes.
 - c. Can occur at any point in the process from prescribing to monitoring.
 - d. Are routinely documented in medication error reporting systems.

2. Measures to improve the safety of parenteral nutrition therapy include
 - a. Implementing an electronic standardized order format.
 - b. Eliminating weight-based dose warnings on the automated compounder.
 - c. Developing institution-specific compatibility and stability guidelines.
 - d. Eliminating credentialing of providers who prescribe PN.

3. Strategies to safely manage a shortage of parenteral nutrition component include
 - a. Purchasing as much product as possible.
 - b. Administering neonatal-specific products to adults.
 - c. Compounding in a single, central location.
 - d. Extending beyond-use-dating for PN components.

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