TPN BASICS FOR THE HOSPITAL PHARMACIST

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MALNUTRITION IN HOSPITALS

- 45% of patients in Canada are malnourished at admission
- Independently associated with increased costs and length of stay
- Nutrition care can reduce malnutrition and the associated morbidity and mortality
- The Canadian Nutrition Screening Tool is a quick tool to identify patients at risk – 2 questions on admission
- Early intervention ideal - PN is just one type of nutrition support
- At KHSC, ~500 bed hospital approximately 5-15 patients may receive (PN) at any given time
- Major guidelines ESPEN and ASPEN
- No specific “C”SPEN, however some work in critical care nutrition
Special Report

Safe Practices for Parenteral Nutrition

Task Force for the Revision of Safe Practices for Parenteral Nutrition: Jay Mirtallo, MS, RPh, BCNSP, Chair, Todd Canada, PharmD, BCNSP, Deborah Johnson, MS, RN, Vanessa Kumpf, PharmD, BCNSP, Craig Petersen, RD, CNSD, Gordon Sacks, PharmD, BCNSP, David Seres, MD, CNSP, and Peggi Guenter, PhD, RN, CNSN

APPROVED BY A.S.P.E.N. BOARD OF DIRECTORS JULY 21, 2004

Clinical Guidelines


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**BACKGROUND**

- 1665 Sir Christopher Wren
  - administered IV wine/ale to dogs
- 1712 trial of olive oil infusion in dogs
- 1896 high dextrose in central vein in dogs
- 1904 PN SC - abandoned as too painful
- 1937 trials of olive oil infusion, spirits
- 1964 lipid emulsions banned 2nd AE
- 1975 purified soybean formulations
- 1978 Micronutrients needs identified
- olive oil has made a comeback
- Containers from glass to PVC
- 2 in 1 to 3 in 1
CliniCare Pharmacy
DISCLAIMER

Presenter is **NOT** an expert in this subject area

Presenter is interested in sharing knowledge regarding total parenteral nutrition

No conflicts of interest to disclose
SCOPE OF PRESENTATION

- Adult patients only
- Recognition of many different hospital practices
- Specific compounding/stability issues will not be addressed
- Complex issues will not be presented
LEARNING OBJECTIVES

- Describe components and administration requirements for PN in adult patients
- Develop pharmacist clinical role in PN management
OUTLINE

- Overview of PN
  - Goals and Indications
  - Composition and Formulation
  - Delivery and monitoring
  - Complications
- Pharmacists’ roles related to PN
- Case presentation and discussion
“You're not allowed to use the sprinkler system to keep your audience awake.”
“WHAT'S INTRAVENOUS FEEDING? MY MOM SAYS IF I DON'T EAT MY VEGETABLES, SHE'D DO THAT TO ME!”
THE GOALS OF PN

- Maintain adequate nutrition
- Support anabolism and nitrogen balance
- Prevent abnormalities or deficiencies with:
  - Fluids
  - Electrolytes
  - Vitamins and trace elements
"I'd like to be fed intravenously. I've heard about your hospital food!"
Micronutrients: Vitamins, Minerals, and Electrolytes
# Table 5. Suggested Intravenous Electrolyte Doses for Adults\(^5,25\)

<table>
<thead>
<tr>
<th>Electrolyte</th>
<th>Maintenance Range(^a)</th>
<th>Intake Maximums(^b,c)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium</td>
<td>1–2 mEq/kg/d</td>
<td>150 mEq/L</td>
</tr>
<tr>
<td>Potassium</td>
<td>1–2 mEq/kg/d</td>
<td>240 mEq/d</td>
</tr>
<tr>
<td>Calcium</td>
<td>10–15 mEq/d</td>
<td>25 mEq/d</td>
</tr>
<tr>
<td>Magnesium</td>
<td>8–20 mEq/d</td>
<td>48 mEq/d</td>
</tr>
<tr>
<td>Phosphate</td>
<td>20–40 mmol/d</td>
<td>60 mmol/d</td>
</tr>
<tr>
<td>Chloride/acetate</td>
<td>Change to maintain acid base balance</td>
<td></td>
</tr>
</tbody>
</table>

\(^a\)These requirements are based on healthy people with normal losses.

\(^b\)Suggested maximums may vary depending on facility policies. Compounding limitations may not allow for additions at maximum threshold.

\(^c\)Intake maximums are to be used as a guide to help the practitioner with safe electrolyte dosing and avoid potential error but should not supersede clinical judgment.
STANDARD MULTIVITAMINS

- Adult: (based on RDA)
- Multi – 12
  - Multi-12 with vitamin K in the USA only
  - Vitamin K 150 mcg per day required
    - can be given daily or weekly
- Pediatric Multivitamins contain vitamin K
- Not contained or inadequate amounts in PN (vitamin D, iron)

Fat soluble vitamins:
- Vitamin A (retinol) 3300 units
- Vitamin D (ergocalciferol) 200 units
- Vitamin E 10 units

Water Soluble Vitamins
- Vitamin C (ascorbic acid) 100 mg
- Niacinamide 40 mg
- Vitamin B2 3.6 mg
- Vitamin B1 (thiamine) 3 mg
- Vitamin B6 (pyridoxine HCl) 4 mg
- Dexpanthenol 15 mg
- Biotin 60 mcg
- Folic acid 400 mcg
- Vitamin B12 (cyanocobalamin) 5 mcg
## TRACE ELEMENTS

<table>
<thead>
<tr>
<th></th>
<th>Micro+4 conc® per mL</th>
<th>Micro+6 conc® per mL</th>
<th>RDA 2009 (ASPEN)</th>
<th>RDA 2019 (ASPEN)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zinc</td>
<td>5 mg</td>
<td>5 mg</td>
<td>2-5 mg</td>
<td>3-5 mg</td>
</tr>
<tr>
<td>Selenium</td>
<td>-</td>
<td>60 mcg</td>
<td>20-60 mcg</td>
<td>60-100 mcg</td>
</tr>
<tr>
<td>Copper</td>
<td>1 mg</td>
<td>1 mg</td>
<td>0.3-0.5 mg</td>
<td>0.3-0.5 mg</td>
</tr>
<tr>
<td>Chromium</td>
<td>10 mcg</td>
<td>10 mcg</td>
<td>10-15 mcg</td>
<td>&lt; 1000 mcg</td>
</tr>
<tr>
<td>Manganese</td>
<td>0.5 mg (500 mcg)</td>
<td>0.5 mg (500 mcg)</td>
<td>60-100 mcg</td>
<td>55 mcg</td>
</tr>
<tr>
<td>Iodine</td>
<td>-</td>
<td>75 mcg</td>
<td>n/a</td>
<td>n/a</td>
</tr>
</tbody>
</table>

Available products do not match the recommended daily allowances (RDA) for adults. One dose daily is recommended; one dose is usually 1 mL.
FORMULATION

- Multi-chamber bags versus compounded
- 2-in-one and 3-in-one
- Fat emulsion differences
TRUE or FALSE?

ALL CENTRAL LINE TIPS END UP IN THE SAME ANATOMICAL LOCATION?
Central lines (most common)
- PICC, Hickman, central line(IJ), port-a-cath

Peripheral (rare)
- Can only infuse up to 10% dextrose or 900mOsm/L

Filters
- 0.22 micron for amino acid and dextrose solution (2 in 1)
- 1.2 micron required when infusing lipids or 3 in 1

Timing of lipid infusion administration

Protect from light?
<table>
<thead>
<tr>
<th>Parameter</th>
<th>Initial</th>
<th>Daily</th>
<th>Weekly</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anthropometric</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Height</td>
<td>x</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Physical examination</td>
<td>x</td>
<td>x</td>
<td></td>
</tr>
<tr>
<td>Intake and output</td>
<td>x</td>
<td>x</td>
<td></td>
</tr>
<tr>
<td>Metabolic assessment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Na, K, Cl, CO₂</td>
<td>x</td>
<td>x&lt;sup&gt;a&lt;/sup&gt;</td>
<td>x</td>
</tr>
<tr>
<td>Ca, Phos, Mg</td>
<td>x</td>
<td>x&lt;sup&gt;a&lt;/sup&gt;</td>
<td>x</td>
</tr>
<tr>
<td>Glucose</td>
<td>x</td>
<td>x&lt;sup&gt;a&lt;/sup&gt;</td>
<td>x</td>
</tr>
<tr>
<td>BUN/Scr</td>
<td>x</td>
<td>x&lt;sup&gt;a&lt;/sup&gt;</td>
<td>x</td>
</tr>
<tr>
<td>Liver function tests</td>
<td>x</td>
<td></td>
<td>x</td>
</tr>
<tr>
<td>Prothrombin time</td>
<td>x</td>
<td></td>
<td>x</td>
</tr>
<tr>
<td>Prealbumin</td>
<td>x</td>
<td></td>
<td>x</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>x&lt;sup&gt;b&lt;/sup&gt;</td>
<td>x&lt;sup&gt;a&lt;/sup&gt;</td>
<td>x</td>
</tr>
<tr>
<td>Complete blood count</td>
<td>x</td>
<td>x&lt;sup&gt;a&lt;/sup&gt;</td>
<td>x</td>
</tr>
<tr>
<td>Nitrogen balance</td>
<td>As needed</td>
<td>As needed</td>
<td>As needed</td>
</tr>
<tr>
<td>Indirect calorimetry</td>
<td>As needed</td>
<td>As needed</td>
<td>As needed</td>
</tr>
</tbody>
</table>

BUN, blood urea nitrogen; Phos, phosphate; Scr, serum creatinine.

<sup>a</sup>Daily until stable, then once or twice weekly.

<sup>b</sup>Initially and before each advancement of intravenous fat emulsions, then once weekly. If septic, more frequent monitoring is prudent.
**KHSC ORDER SET PARENTERAL NUTRITION MONITORING**

<table>
<thead>
<tr>
<th>Vitals</th>
</tr>
</thead>
<tbody>
<tr>
<td>☑ Baseline height and weight before starting PN</td>
</tr>
<tr>
<td>☑ Weigh weekly every Monday. Discontinue when PN discontinued</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Lines</th>
</tr>
</thead>
<tbody>
<tr>
<td>☑ PICC line (double lumen) or central line insertion</td>
</tr>
<tr>
<td>☑ Change amino acid/dextrose and fat emulsion infusion set every 24 hours</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Lab Investigations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before starting PN (if not already done):</td>
</tr>
<tr>
<td>☑ CBC, PTT, PT/INR, Na, K, Cl, creatinine, glucose, calcium, magnesium, phosphate, ALT, ALP, total bilirubin, albumin, triglycerides</td>
</tr>
<tr>
<td>THEN daily for 5 days. Discontinue when PN discontinued:</td>
</tr>
<tr>
<td>☑ Na, K, Cl, creatinine, glucose, calcium, magnesium, phosphate</td>
</tr>
<tr>
<td>THEN every Monday. Discontinue when PN discontinued:</td>
</tr>
<tr>
<td>☑ CBC for 1 month, then reassess</td>
</tr>
<tr>
<td>☑ Na, K, Cl, creatinine, glucose, calcium, magnesium, phosphate</td>
</tr>
<tr>
<td>☑ ALP, total bilirubin, albumin, triglycerides, ALT</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Additional Lab Investigations</th>
</tr>
</thead>
<tbody>
<tr>
<td>☑ Capillary blood glucose q6 h until target rate achieved, then physician to reassess frequency</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>PN solution</th>
</tr>
</thead>
<tbody>
<tr>
<td>☑ Change amino acid/dextrose solution every 24 hours (maximum hang time 24 hours)</td>
</tr>
</tbody>
</table>
MRS. T.

- 89 female
- 45 kg (recent wt loss)
- DM2 (no meds)
- HTN
- AFIB, CHADS 5-6
- CrCl 0.63 mL/sec (37 mL/min)
- Home medications:
  - Apixaban 5 mg po bid
  - Metoprolol 25 mg po bid
  - Valsartan 40 mg po daily
  - Furosemide 40 mg po daily
  - Potassium 16 mmol po daily
  - Magnesium oxide 420 mg po bid
  - Vitamin D, calcium, iron

Course in hospital:
- Day 0 admission with Bowel obstruction – NPO - NG tube
- Day 10 - TPN to start
TPN INITIATION

- Amino acid and dextrose via PICC @ 25 mL/h x 24 hours, then increase by 10 mL/h every 24 hours until goal rate 70 mL/h
- Lipid infusion 20% at 15mL/h x 12 hours daily
- Standard electrolytes
SAFE PRESCRIBING

- High alert medication
- Standardized orders (solution and monitoring)
- Hospital policies
- Pharmacy procedures
- RN/MD education
### SAMPLE ASPEN ORDER TEMPLATE

#### Patient Information
- **Patient name:**
- **Medical record number:**
- **Birthday/age:**
- **Patient location:**
- **Allergies:**

- **Height and dosing weight:**
  - **Ht:** _____cm
  - **Dosing Wt:** _____kg

- **Diagnosis/Indication(s) for PN:**
- **Vascular access device/Location:**
  - **CVC type:**__________
  - **Location:**__________
- **Administration date/time:**

#### Base Formula

<table>
<thead>
<tr>
<th>Base Formula</th>
<th>Amount/day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amino acids</td>
<td>g</td>
</tr>
<tr>
<td>Dextrose</td>
<td>g</td>
</tr>
<tr>
<td>IV Fat emulsion</td>
<td>g</td>
</tr>
</tbody>
</table>

#### Electrolytes

<table>
<thead>
<tr>
<th>Electrolyte</th>
<th>Amount/mmol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium phosphate</td>
<td>mmol</td>
</tr>
<tr>
<td>Sodium chloride</td>
<td>mEq</td>
</tr>
<tr>
<td>Sodium acetate</td>
<td>mEq</td>
</tr>
<tr>
<td>Potassium phosphate</td>
<td>mmol</td>
</tr>
<tr>
<td>Potassium chloride</td>
<td>mEq</td>
</tr>
<tr>
<td>Potassium acetate</td>
<td>mEq</td>
</tr>
<tr>
<td>Magnesium sulfate</td>
<td>mEq</td>
</tr>
<tr>
<td>Calcium gluconate</td>
<td>mEq</td>
</tr>
</tbody>
</table>

#### Vitamins, Trace Elements, Additives

<table>
<thead>
<tr>
<th>Additive Type</th>
<th>Amount/mL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multi-component vitamins</td>
<td>mL</td>
</tr>
<tr>
<td>Multi-component Trace elements</td>
<td>mL</td>
</tr>
<tr>
<td>Other Additives (eg, individual vitamins or trace elements, cystine, regular insulin) as clinically appropriate and compatible</td>
<td></td>
</tr>
</tbody>
</table>

#### PN Instructions

- **Total volume:**______mL
- **Infusion rate:**______mL/hr
- **Start and stop times:**________

#### Cycle Information

- **Prescriber and contact information:**________

---

*Figure 1. Parenteral Nutrition Order Template: Adult Patient.*
### Amino Acid and Dextrose Solution (Choose one)
- [ ] Amino acid 5% and dextrose 16.6%
- [ ] Amino acid 5% and dextrose 10%
- [ ] Other: ____________________________

### Micronutrient Additives

#### Micronutrient Additives Continued...

**Infusion Rate**
- [ ] Initiate amino acid and dextrose infusion IV at 25 mL/h for 6 hours, then increase by 25 mL/h every 6 hours if capillary blood glucose is less than 10 mmol/L until target rate of ______ mEq/h is reached
- [ ] Initiate amino acid and dextrose infusion IV at ______ mEq/h for ______ hours, then increase by ______ mEq/h every ______ hours if capillary blood glucose is less than 10 mmol/L, until target rate of ______ mEq/h is reached
- [ ] Cyclic PN regimen: ____________________________
- [ ] If rate is not increased on schedule due to increased blood glucose THEN contact physician to obtain insulin orders

#### Fat Emulsion
- [ ] No fat emulsion
- [ ] 20% fat emulsion (choose one)
  - [ ] ClinOleic® *(Contraindicated with egg, soy or olive oil allergy)*
    - Infuse with 1.2 micron in-line filter
  - [ ] SMOF® *(Contraindicated with egg, soy, olive oil and fish oil allergy)*
  - [ ] Intralipid® *(Contraindicated with egg or soy allergy)*

**Infusion Rate**
- [ ] ______ mEq/h for 12 hours daily. Discard remaining solution when complete
- [ ] __________ mEq/h for ______ hours ________ (indicate specific days). Discard remaining solution when complete

#### Additional Supplementation
- [ ] Phytonadione (Vitamin K1) 10 mg IV/Subcutaneous weekly on Friday while receiving PN (if patient is not on Warfarin)

### PN Interruptions
- [ ] If PN solution is unavailable, run 10% dextrose (O10W) at the prescribed amino acid and dextrose infusion rate and re-start PN infusion as soon as possible
- [ ] If PN interruption is greater than 72 hours new orders are required
- [ ] If PN is interrupted for less than 72 hours resume at previous target rate
- [ ] If PN interruption is anticipated to be greater than 24 hours, notify Pharmacy
PATIENT CASE

Hyperglycemia
You follow up on the patient 36 hours later and notice rate is still at 25 mL/h and serum glucose is consistently above 10 mmol/L.

- How will you manage the hyperglycemia?
HOW WILL YOU MANAGE HYPERGLYCEMIA?

- Call the doctor/dietitian/diabetes expert
- Reduce dextrose in PN solution
- Initiate a subcutaneous insulin sliding scale
- Initiate a titratable intravenous insulin infusion
- Initiate long acting insulin
- Add insulin to the PN bag
HYPERGLYCEMIA DISCUSSION

- No single ideal recommendation
- Institution specific, may depend on location and monitoring available
  - E.g. ease of running IV insulin infusion (critical care) versus nursing unit
- Insulin sliding scales not effective alone
- Action may depend on whether patient is on continuous or cyclic regimen
- May depend on if insulin dependent or DM2
- Addition directly to bag may be possible if policies support
- Safety of giving long acting insulin and possible PN interruptions
- Order “while on TPN”
COMPLICATIONS OF PN

Mechanical:
- Problems with the catheter, air or fat embolism, thrombophlebitis and thrombosis, infusion pump issues

Infectious:
- Frequent complication
- Predisposed due to
  - compromised immunity, cancer, age
  - use of broad spectrum antibiotics
  - poor nutrition
  - solution contamination
  - hyperglycemia
  - indwelling catheter
COMPLICATIONS OF PN

Metabolic/nutritional:
- Electrolyte abnormalities
- Fluid overload/dehydration
- Hyper/hypoglycemia
- Hyperlipidemia
- Hepatic dysfunction
- Acid-base disorders
- Metabolic bone disease
- Vitamin/trace element deficiencies/toxicities
COMPLICATIONS OF PN

- Metabolic/nutritional
  - Electrolyte abnormalities
  - Fluid overload/dehydration
  - Hyper/hypoglycemia
  - Hyperlipidemia
  - Hepatic dysfunction
  - Acid-base disorders
  - Metabolic bone disease
  - Vitamin/trace element deficiencies
ROLE OF HCP’S WITH PN?
HOSPITAL PHARMACISTS AND PN

Roles will vary by site (presence of NST or not)

- Distribution role:
  - Compounding solutions
  - Calculations for additives
  - Verifying for compatibility (e.g. calcium/phosphate)
  - Adding medications
  - Backorders!

- Clinical role:
  - Daily monitoring at initiation of therapy until goal rate achieved
  - Weekly monitoring during therapy
  - Correction of abnormalities
  - Managing complications
  - Collaborating for long-term patients (nutritional deficiencies/home PN)

- Other roles?
REFEEDING SYNDROME (RFS)

- Serious complication of nutrition support (PN and EN)
  - Metabolic disturbances occurring when nutrition support is initiated in malnourished individuals
  - Hypophosphatemia is the hallmark of RFS.

- Risks:
  - Underweight or recent unintentional weight loss, malnourished or poor nutritional intake 1-2 weeks, starvation, alcoholism, malabsorption

- Preventable
  - Identify patients at risk
  - Slow titration over 3-5 days
  - Baseline blood work and replacements prior to initiation (especially K, Phos, Mg)
    - May require more than daily serum levels in some cases
  - Consider empiric thiamine replacement
  - Monitor until stable at goal rate
MRS. T.

- 89 female
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Course in hospital:
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PATIENT CASE
Refeeding
BASELINE BLOOD WORK

- Potassium 3.1 mmol/L (normal ~ 3.5-5.5)
- Magnesium 0.54 mmol/L (normal ~ 0.67-1.07)
- Phosphate 0.74 mmol/L (normal ~ 0.78 to 1.48)

- Is Mrs. T at risk for refeeding?
- How will you supplement the electrolytes?
PT’S RISK FACTORS FOR REFEEDING

- Low electrolytes at baseline
- 10 days NPO
- Low weight (? Preexisting malnutrition)
- Malabsorption 2\textsuperscript{nd} BO
HOW DO YOU REPLACE THE ELECTROLYTES?

- Increase in PN solution
- IV replacement
- Oral replacement
RFS DISCUSSION - PREVENTION

- Identify patients at risk
- Baseline blood work and replacements prior to initiation (especially K, Phos, Mg)
  - May require more than daily serum levels in some cases
- Slow titration of carbohydrate over 3-5 days
- Consider empiric thiamine replacement
- Monitor until stable at goal rate
SHOULD WE HAVE GIVEN THIAMINE?

YES  NO  MAYBE  I DON'T KNOW
PATIENT CASE

Hepatic complications
Patient at goal rate

Hyperglycemia under control with insulin glargine

Electrolytes stable within normal limits with PN solution

This morning’s bloodwork shows abnormal liver panel with increases in transaminases, alkaline phosphatase and bilirubin.

The team asks you how to manage PN associated abnormal liver panel.

Assuming there are no other reasons for the changes, what options can you propose to the team?
HEPATIC COMPLICATIONS DISCUSSION

- Less common complication in the short term patient
- Usually around 30 days of therapy (between 1 and 4 weeks)
- Mild elevations in serum liver enzymes, usually less than three times the upper limit of normal rarely leading to development of liver disease
- Can be caused by “overfeeding” causing steatosis
- In patients NPO – bypassing the GI tract not ideal
**HEPATIC COMPLICATIONS**

**OPTIONS FOR PN MODIFICATION**

- PNALD – PN associated liver disease includes cholestasis, cholelithiasis and hepatic steatosis.
- Consider reductions in carbohydrate
- Reduce amount of fat emulsion
- Change to a different fat emulsion with less soy content
- Cycling TPN - limited evidence but thought to reduce prolonged hyperinsulinemia
- Allow PO intake if possible or EN
OPTIMAL HOSPITAL PHARMACIST ROLE?

- Centre specific
- Depends on staffing and number of PN patients
- Identify roles within the team to avoid duplication
PN is nutrition support, not meant to be medication delivery or electrolyte replacement (can optimize to a certain extent only)

Ideally Nutrition Support Teams exist for collaborative practice

Need regular monitoring, especially at initiation and with nutrition transitions

Most common abnormalities are refeeding, and glycemic control

Long term patients may require additional monitoring if longer than 1 month of PN

Peripheral PN less desired, however formulations do exist with 3-in-1 products

Look for trends in lab values – frequent errors with blood draws if line contaminated

Should start slow and taper off

Check volume – e.g. dehydration if PN only source and ongoing losses may need hydration

Other future topics – optimal vitamin K, choice of lipids, adjusting micronutrients, compatibilities/stabilities…. 
REFERENCES

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- Gervasio J. Total Nutrient Admixtures (3-in-1) Pros vs Cons for Adults. 2015/ Digital Commons @ Butler University
- Websites/links:
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  - https://www.criticalcarenutrition.com/