Promoting the Safe and Appropriate Use of Parenteral Nutrition: Update on Nutrition Support Therapy in the Adult Critically Ill Patient

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Disclosures

• Received grant support from Fresenius Kabi for clinical research

• Serving on the A.S.P.E.N. Rhoads Research Foundation Board of Directors
Learning Objectives

After participating in this application-based educational activity, participants should be able to:

1. Review important recommendations in the new guidelines for the provision and assessment of nutrition support therapy in critically ill adult patients.

2. Explain strategies for patient assessment and management that will minimize complications and lead to improved patient outcomes.

3. Review the mechanical, gastrointestinal, and fluid/electrolyte complications associated with PN, including ways to prevent them.

4. Perform an in-depth assessment on how to best implement the guidelines into practice.
Methodology

- Updated and expanded 2009 ASPEN / SCCM guidelines
- Database of randomized controlled trials (RCTs) assembled in partnership with Canadian Clinical Guidelines group
- Included published literature through December 31, 2013
- Target patient population: Adult (> 18 years) critically ill patients with ≥ 2 days medical or surgical intensive care unit (ICU) length of stay (LOS)
- New subsets of patients addressed includes organ failure, acute pancreatitis, surgical subsets, sepsis, postoperative major surgery, obese

*JPEN* 2016;40:159-211.
Methodology

• Multidisciplinary clinicians jointly convened by both societies to conduct update
• RCTs were preferred source material, but nonrandomized trials, prospective observational studies and retrospective case studies were used to support responses
• GRADE criteria used to evaluate body of evidence for a given intervention and outcome
• Every committee member was polled anonymously for his/her agreement with each recommendation
• Consensus was arbitrarily set at 70% agreement

*JPEN* 2016;40:159-211.
**GRADE: Grading of Recommendations, Assessment, Development, Evaluation**

**Strength of Evidence**
- **High**: Randomized trial
  - Further research unlikely to change confidence of estimate of effect
- **Moderate**
  - Further research likely to impact
- **Low**: Observation trial (Cohort, Case series, Case study)
  - Further research very likely to have an important effect on confidence
- **Very low**: expert opinion
  - Any estimate of effect is uncertain

**Criteria to Increase or Decrease Grade**
- **Decrease grade if**:
  - Serious limitation to study quality
  - Important inconsistency
  - Uncertainty about directness
  - Imprecise or sparse data
  - High probability of bias
- **Increase grade if**:
  - Strong evidence of association
  - Evidence of a dose-response gradient
  - Plausible confounders accounted for

BMJ 2004;328(7454):1490-1494
Overview of Process

- Entire process occurred over a 4-year timeline
- Published page count is 52 pages
- 480 reference citations
- > 800 studies reviewed

Permission granted by SAGE on behalf of JPEN
Guideline Sections

A. Nutrition Assessment
B. Initiation of Enteral Nutrition (EN)
C. Dosing of EN
D. Monitoring Tolerance and Adequacy of EN
E. Selection of Appropriate EN Formulation
F. Adjunctive Therapy (fiber, probiotics, glutamine)
G. When to Use Parenteral Nutrition (PN)
H. When Indicated, Maximize Efficacy of PN

JPEN 2016;40:159-211.
Guideline Sections

I. Pulmonary Failure
J. Renal Failure
K. Hepatic Failure
L. Acute Pancreatitis
M. Surgical Subsets (Trauma, Traumatic Brain Injury (TBI), Open abdomen, Burns)
N. Sepsis
O. Postoperative Major Surgery
P. Chronically Critically Ill
Q. Obesity in Critical Illness
R. Nutrition Therapy End-of-Life

*JPEN* 2016;40:159-211.
Don’t Shoot the Messenger of these Guidelines!
Case Scenario #1

- AS is a 64 yo female with a gastric outlet obstruction from gastric carcinoma
- PMH significant for peptic ulcer disease/gastroesophageal reflux disease requiring subtotal gastrectomy; COPD requiring supplemental oxygen
- Due to inability to eat, she has lost 40 pounds over past 6 months
- Anthropometric measurements: weight-38 kg, height-5 feet 2 inches, BMI=15.3, severe muscle and fat wasting in upper and lower extremities
Audience Response Question

Which of the following is the MOST appropriate next step for this patient?

A. No action is needed since this patient is at low nutritional risk

B. Enteral nutrition (EN) at full goal rate should be initiated as soon as possible

C. EN trophic feeds with parenteral nutrition (PN) should be initiated due to vasopressor requirements

D. Exclusive PN without EN should be initiated as soon as possible
Case Scenario #1

A2. “Based on expert consensus, we suggest that nutrition assessment include an evaluation of comorbid conditions, function of the GI tract, and risk of aspiration. We suggest not using traditional indicators or surrogate markers, as they are not validated in critical care.”

JPEN 2016;40:159-211.
<table>
<thead>
<tr>
<th>Nutrition status impairment</th>
<th>Severity of disease</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Score 0</strong>&lt;br&gt;<strong>Absent</strong></td>
<td>Normal nutritional status</td>
</tr>
<tr>
<td><strong>Score 1</strong>&lt;br&gt;<strong>Mild</strong></td>
<td>Weight loss &gt; 5% in 3 months OR Food intake &lt; 50-75% of normal</td>
</tr>
<tr>
<td><strong>Score 2</strong>&lt;br&gt;<strong>Moderate</strong></td>
<td>Weight loss &gt; 5% in 2 months OR BMI 18.5-20.5 + impaired general condition OR Food intake 25-50% of normal</td>
</tr>
<tr>
<td><strong>Score 3</strong>&lt;br&gt;<strong>Severe</strong></td>
<td>Weight loss &gt; 5% in 1 month OR BMI &lt; 18.5 + impaired general condition OR Food intake 0-25% of normal</td>
</tr>
</tbody>
</table>

**Factors used to determine score** - A score of ≥3 identifies a patient for whom specialized nutrition therapy (EN or PN) should be considered. A score of ≥5 identifies a patient at high nutritional risk.

Case Scenario #1

- G2. Based upon expert consensus, in the patient determined to be at high nutrition risk (e.g., NRS 2002 score ≥ 5 or NUTRIC ≥ 6, with > 5 if no IL-6 value) or severely undernourished, when EN is not feasible, we suggest initiating exclusive PN as soon as possible following ICU admission.
  - Nutrition Care Plan: determined to be at high risk due to severe weight loss over 6 months (≈33% usual body weight) and evidence of severe muscle/fat wasting
  - Would have been ideal to start PN prior to surgery but the critical care team did not have this option
  - NRS 2002 = 5
  - PN initiated immediately after surgery due to poor nutritional status and predicted prolonged NPO status

*JPEN* 2016;40:159-211.
Case Scenario #1

- H2. We suggest that hypocaloric PN dosing (≤ 20 kcal/kg/day or 80% estimated energy needs) with adequate protein be considered in appropriate (high-risk or severely undernourished) patients requiring PN, initially over the first week of hospitalization
  - Prior to starting PN, electrolytes aggressively replenished due to increased risk for refeeding syndrome
  - Thiamine and folic acid were given prior to PN initiation and included in daily PN regimen
  - PN volume and sodium content were limited to ≈1000 mL/day and ≈ 0.45% normal saline due to fluid overload concerns
  - PN was initiated at 50% of estimated energy needs due to increased refeeding syndrome risk

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Thiamine Deficiency (B1)

• Thiamine: water-soluble vitamin which may be depleted within 2-3 weeks
• Involved in conversion of pyruvate to acetyl CoA, which enters Kreb’s cycle to yield adenosine triphosphate
• Increased delivery of glucose via PN accelerates consumption of thiamine stores
• Pyruvate is converted to lactic acid in the absence of thiamine

Development of Thiamine Deficiency

• Time period for development of lactic acidosis: 1-4 weeks

• Presentation forms of thiamine deficiency:
  – “Wet” beriberi (cardiovascular system)
    • Venous congestive state (Na/H₂O retention)
  – “Dry” beriberi (nervous system)
    • Wernicke’s encephalopathy (ocular palsies, ataxia)
    • Korsakoff’s syndrome (amnesia, inability to learn)
  – Subclinical deficiency

Recommendations

• Administer multivitamins daily
• During a shortage of multivitamins:
  – 3-5 mg thiamine daily for hospitalized patients
  – 50 mg thiamine 3x/week for home patients
• Response
  – “wet” beriberi: improvement within 6-24 hours
  – “dry” beriberi: nystagmus, ataxia, and confusion may improve within days to weeks; Korsakoff’s psychosis may take 1-3 months

Case Scenario #1

I3. Based upon expert consensus, we suggest that serum phosphate concentrations should be monitored closely and phosphate replaced appropriately when needed.

- The incidence of moderate to severe hypophosphatemia (≤ 1.5-2.2 mg/dL) is approximately 30% in the ICU
- Phosphorus is essential for ATP and 2,3-DPG
- Both ATP and 2,3-DPG are critical for optimal pulmonary function and diaphragmatic contractility
- Hypophosphatemia may be a cause of respiratory muscle weakness and failure to wean from the ventilator
- Specific protocols exist and have been published to replete patients with moderate to severe hypophosphatemia

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Treatment Regimen for Hypophosphatemia

• Weight-based Phosphorus dosing algorithm
  – Mild (2.3-3 mg/dL) - 0.32 mmol/kg over 4-6 hours
  – Moderate (1.6-2.2 mg/dL)- 0.64 mmol/kg over 4-6 hours
  – Severe (≤ 1.5 mg/dL) - 1 mmol/kg over 8-12 hours
    • K+ < 4 mEq/L, KPO4 given
    • K+ > 4 mEq/L, NaPO4 given
    • Doses were infused at a rate not exceeding 7.5 mmol/hr

IV Concentrated Phosphate Shortage

- Consider oral or enteral phosphate products/supplements to replete or maintain serum phosphorus concentrations.
- Consider commercially available standardized, commercial PN products that contain phosphate.
- Reserve phosphates for pediatric and neonatal patients requiring PN.
- Reserve phosphates for those patients with a therapeutic medical need for phosphorus.
- Consider using IV organic phosphate injections, if available.
- Consider provision of daily IV fat emulsion to all PN patients as clinically appropriate. Note: IV fat emulsions contain 15 mmol/L of phosphate as egg phospholipids.

ASPEN website (accessed 2016 Aug 17)
https://www.nutritioncare.org/News/General_News/Parenteral_Nutrition_Electrolyte_and_Mineral_Product_Shortage_Considerations/
Case Scenario #2

• 49 yo male presents to ED with severe abd pain, anorexia, N/V
• Unable to tolerate solid food x 2 days
• PMH: poorly controlled DM II, obese, hyperTG, negative h/o pancreatitis, EtOH
• Meds: fenofibrate 80mg/d, glipizide 5 mg/d, insulin glargine 60 units Q PM
• Anthropometrics: Height 68 in, weight 250 lb (113.6kg), BMI 38 kg/m², gained 5 lbs. in previous 1 month
• ED labs: BG – 425 mg/dL, TG – 4420 mg/dL, lipase – 11,200 U/L, lactate – 2.7 mmol/L

NCP April 12, 2016, DOI:10.177/0884533616640451
Case Scenario #2

- Abd CT: marked peripancreatic fat stranding and fluid; mild enhancement of pancreas head; moderate wall thickening of duodenum.
- Admitted to floor from the ED on IV fluids and insulin infusion
- Became somnolent with respiratory depression, sinus tachycardia, hypotensive (90/50 mm Hg).
- Lab values – significant for elevated lactate 8.6 mmol/L, serum creatinine 2.6 mg/dL

NCP April 12, 2016, DOI:10.177/0884533616640451
Case Scenario #2

- Transferred to the ICU, intubated, started on multiple vasopressor agents (norepi, vasopressin), with ongoing fluid resuscitation
- Medications initiated included: dexmedetomidine, fentanyl, and meropenem
- General Surgery determined there was no need for a surgical intervention at this time
- Is nutritional intervention necessary at this time?

NCP April 12, 2016, DOI:10.177/0884533616640451
Case Scenario #2

A1. “Based on expert consensus, we suggest a determination of nutrition risk (e.g., NRS 2002, NUTRIC score) be performed on all patients admitted to the ICU for whom volitional intake is anticipated to be insufficient. High nutrition risk identifies those patients most likely to benefit from early EN therapy”

JPEN 2016;40:159-211.
**NRS 2002: Factors used to determine score.** A score of ≥3 identifies a patient for whom specialized nutrition therapy (EN or PN) should be considered. A score of ≥5 identifies a patient at high nutritional risk.

<table>
<thead>
<tr>
<th>Impaired Nutritional Status</th>
<th>Absent</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Absent</td>
<td>Score 0</td>
<td>Score 1</td>
<td>Score 2</td>
<td>Score 3</td>
</tr>
</tbody>
</table>
| Normal nutritional status   |        | Wt loss > 5% in 3 mos  
   Or Food intake below 50-75% of normal requirement in preceding week | Wt loss > 5% in 2 mos  
   Or BMI 18.5–20.5 + impaired general condition  
   Or Food intake 25-50% of normal requirement in preceding week | Wt loss > 5% in 1 month (15% in 3 mos)  
   Or BMI <18.5 + impaired general condition  
   Or Food intake < 25% of normal requirement in preceding week |
| Normal nutritional requirements |        | Mild    | Moderate | Severe   |
| Absent                      | Score 0| Score 1 | Score 2  | Score 3  |
| Hip fracture                |        | Chronic patients in particular with acute complications: cirrhosis, COPD  
   *Chronic hemodialysis, diabetes, oncology* | Major abdominal surgery, Stroke  
   *Severe pneumonia, hematologic malignancy* | Head injury  
   Bone marrow transplantation  
   *Intensive care patients (APACHE II ≥ 10)* |

**Note:** If age ≥ 70 years, add 1 point. Disease states in italics are based on clinical judgement.

**Total score** = (Points for nutritional status) + (Points for disease severity) + (Points for age)

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**NUTRIC Score: Factors used to determine score.** A score of ≥6 identifies a patient at high nutritional risk.

<table>
<thead>
<tr>
<th>Factors</th>
<th>0</th>
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<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>&lt;50</td>
<td>50-74</td>
<td>≥ 75</td>
<td>-</td>
</tr>
<tr>
<td>APACHE II Score</td>
<td>&lt;15</td>
<td>15-19</td>
<td>20-27</td>
<td>≥ 28</td>
</tr>
<tr>
<td>Baseline SOFA Score</td>
<td>&lt;6</td>
<td>6-9</td>
<td>≥ 10</td>
<td>-</td>
</tr>
<tr>
<td># Comorbidities</td>
<td>0-1</td>
<td>≥ 2</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Days in hospital to ICU admit</td>
<td>0</td>
<td>≥ 1</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Interleukin-6 (µ/ml)</td>
<td>0-399</td>
<td>≥ 400</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

**Total Score** = (Total from six separate factors)
Case Scenario #2

Guideline Application

• L1a. Based upon expert consensus, we suggest that the initial nutrition assessment in acute pancreatitis evaluate disease severity to direct nutrition therapy.
  – Since disease severity may change quickly, we suggest frequent reassessment of feeding tolerance and the need for specialized nutrition therapy.
  – Nutrition Care Plan: Due to evidence of SIRS and organ failure → severe acute pancreatitis

• L1c. We suggest that patients with moderate to severe pancreatitis should have a naso/oroenteric feeding tube placed and EN started at a trophic rate and advanced to goal as fluid volume resuscitation is completed.

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Case Scenario #2

• Nutrition Care Plan: Once the patient was resuscitated and vasopressors were weaning, feeding was initiated at 20 mL/hr via nasoenteric FT with tip confirmed to be in the stomach.

• Since completion of these guidelines, a new multicenter, randomized controlled trial was conducted which does not support improved clinical outcomes with early EN as previous studies cited in the revised guidelines.

• In this case, EN was started early primarily because it was predicted that patient may require prolonged NPO status.

• L3b. We suggest that EN be provided to the patient with severe acute pancreatitis by either the gastric or jejunal route, as there is no difference in tolerance and clinical outcomes between the two.

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Case Scenario #2

• B5. Based upon expert consensus, we suggest that in the setting of hemodynamic compromise or instability, EN should be withheld until the patient is fully resuscitated and/or stable. Initiation or reinitiation of EN may be considered with caution in patients undergoing withdrawal of vasopressor support.
  – Nutrition Care Plan: The patient was deemed hemodynamically stable due to decreasing pressor doses and MAPs > 65 mm Hg.

• L2. We suggest using a standard polymeric EN formula upon initiation in a patient with severe pancreatitis. Although promising, there is currently insufficient data to recommend using an immune-enhancing formula in severe pancreatitis.
  – Nutrition Care Plan: A standard, non-fiber EN formula was selected for initiation and a modular protein supplement was used to increase the protein provision.
Case Scenario #2

• Q4. Based upon expert consensus, we suggest that high-protein hypocaloric feeding be implemented in the care of obese patients to preserve LBM, mobilize adipose stores, and minimize metabolic complications of overfeeding.
  – Nutrition care plan: High protein hypocaloric feeding impractical with available formulas.
  – A low calorie, high-protein formula was not available on the formulary at this institution

• Q5. Based upon expert consensus, we suggest for all classes of obesity that the goal of EN regimen should not exceed 65-70% of target energy requirements as measured by Indirect Calorimetry (IC).
  • If IC is unavailable, use 11 – 14 kcal/kg/d of ACTUAL BW for BMI 30 – 50 kg/m²
    and 22 – 25 kcal/kg/d of IBW for BMI > 50 kg/m²
• Q5. We suggest that protein should be provided in a range from 2 g/kg/d IBW for patients with BMI 30 – 39.9 kg/m² and up to 2.5 g/kg/d IBW for patients with BMI ≥ 40 kg/m²

• Nutrition Care Plan: Calculated BMI = 38 kg/m². The patients energy and protein needs were determined by a weight-based equation for the critically ill obese patient. He was prescribed approximately 1600 kcal (14 kcal/kg/d actual body weight).

• Estimated protein needs were 140 g or ~2 g/kg/day IBW

JPEN 2016;40:159-211.
Figure 1. Effect of protein intake (g/kg ideal body weight/d) on nitrogen balance in hospitalized obese patients from the combined databases of Choban et al\textsuperscript{25} and Dickerson et al\textsuperscript{26}. A significant correlative relationship was observed for each

Figure 2. Effect of protein intake on nitrogen balance in obese trauma ICU patients receiving hypocaloric enteral feeding
Case Scenario #2

• Monitoring tolerance of EN
  – D2a. We suggest that GRVs not be used as part of routine care to monitor ICU patients receiving EN.
  – D2b. For those ICUs where GRVs are still used, we suggest that holding EN for GRVs < 500 mL in the absence of other signs of intolerance should be avoided.

• Alternative strategies to be used to monitor critically ill patients receiving EN:
  – daily abdominal exams
  – review abdominal X-rays
  – evaluate clinical risk factors for aspiration
Case Scenario #2

• Nutrition Care Plan: It was suspected that the patient may not tolerate EN due to previous X-ray evidence for reactive inflammation involving the duodenum and history of intolerance to oral intake PTA.

• The critical care team followed the updated ICU EN protocol and monitored the patient without use of routine GRVs.

• On ICU day #3, EN titration failed as evidenced by abdominal distention, abdominal pain, vomiting, NGT (~800 mL).

• The NGT remained to gravity drainage and a new nasoenteric FT was placed in the distal duodenum in hopes of improving tolerance to the EN.

• A standard 1 kcal/mL EN formula was resumed and advanced to goal rate over the next 24 hrs.

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Beware of Presenter Bias for this Guideline!

- H3a. We suggest withholding or limiting soybean oil-based (SO) IVFE during the first week following initiation of PN in critically ill patients to a maximum of 100 g/week (often divided into 2 doses/week) if there is concern for EFAD.
  - The committee reached only 64% agreement (9 for and 5 against) to “withhold or limit” SO-based IVFE to 100 g/week as opposed to simply “withhold” for the 1st week.
  - The recommendation to entirely “withhold” SO-based IVFE for 1-week is based upon an old and flawed study in which the results have never been replicated.
  - Battistella study was conducted in trauma patients randomized to IVFE-free PN vs. SO-based IVFE PN for the first 10 days of hospitalization:
    - IVFE-free PN group was hypocaloric regimen (21 vs. 28 kcal/kg/d)
    - Caloric goals were based on NPC (not total calories)
    - IVFE infusion rates < 12 hr associated with immune dysfunction

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Lipid Emulsions (10 kcal/g)

- Critical component of cell membranes, carrier for fat-soluble vitamins, precursor to immunoactive mediators
- Essential fatty acids: linoleic & linolenic acids
- Administer at least 1-4% of total daily calories as fat to prevent EFAD
- Infuse < 30% of total daily calories as IV fat over 24 hr to avoid immune dysfunction
Figure 1. Generation progression of intravenous fat emulsions per the position paper of the American Society for Parenteral and Enteral Nutrition. FO, fish oil; MCT, medium-chain triglyceride; OO, olive oil; SO, soybean oil.
<table>
<thead>
<tr>
<th>Fatty acid composition</th>
<th>Commercial parenteral lipid emulsions</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Lipovance LCT 20%*</td>
</tr>
<tr>
<td></td>
<td>Lipovance MCT 20%*</td>
</tr>
<tr>
<td></td>
<td>ClinOleic 20%**</td>
</tr>
<tr>
<td></td>
<td>Omegaven 10%†</td>
</tr>
<tr>
<td></td>
<td>SMOFLipid 20%‡</td>
</tr>
<tr>
<td>Caproic</td>
<td>—</td>
</tr>
<tr>
<td>Caprylic</td>
<td>—</td>
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<tr>
<td>Capric</td>
<td>—</td>
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<tr>
<td>Lauric</td>
<td>—</td>
</tr>
<tr>
<td>Myristic</td>
<td>—</td>
</tr>
<tr>
<td>Palmitic</td>
<td>—</td>
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<td>Palmitoleic</td>
<td>—</td>
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<tr>
<td>Stearic</td>
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<td>Oleic</td>
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<tr>
<td>Linoleic</td>
<td>—</td>
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<tr>
<td>Stearidonic</td>
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<tr>
<td>Alpha-Linolenic</td>
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<tr>
<td>Elcosapentaeenic</td>
<td>—</td>
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<tr>
<td>Docosapentaeenic</td>
<td>—</td>
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<tr>
<td>Docosahexaeenic</td>
<td>—</td>
</tr>
</tbody>
</table>

Data supplied by the manufacturers of the lipid emulsions (Fresenius Kabi and Baxter).

*Values expressed in g/L for 20% lipid emulsions (oil = 200 g/L, egg phosphatide = 12 g/L, glycerol = 25 g/L, and α-tocopherol = 0.1 g/L).

**Values expressed in g/L for 20% lipid emulsions (oil = 200 g/L, egg phosphatide = 12 g/L and glycerol = 22.5 g/L).

†Omegaven is available as lipid emulsion supplement only and has to be added to a standard lipid emulsion. Values expressed in g/L for 10% lipid emulsions (oil = 100 g/L, egg phosphatide = 12 g/L, glycerol = 25 g/L and α-tocopherol = 0.2 g/L).

‡Values expressed in g/L for 20% lipid emulsions (oil = 200 g/L, egg phosphatide = 12 g/L, glycerol = 25 g/L, and α-tocopherol = 0.2 g/L).
<table>
<thead>
<tr>
<th>Product</th>
<th>Neonate</th>
<th>Infant and Preschool</th>
<th>School-Age Children</th>
<th>Adults</th>
<th>Ideal Infusion Time</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Dose, g/kg/d</td>
<td>Rate</td>
<td>Dose, g/kg/d</td>
<td>Rate</td>
<td>Dose, g/kg/d</td>
</tr>
<tr>
<td>IntraLipid 10% and 20%A</td>
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<td>—</td>
<td>—</td>
<td>Max 3 †</td>
</tr>
<tr>
<td>Nutrilipid</td>
<td>Starting 1–2</td>
<td>Max 0.75 mL/kg/h</td>
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<td>1–3</td>
<td>0.05–0.2 g/kg/h</td>
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<tr>
<td>Lipofundin 10% and 20%</td>
<td>2–4</td>
<td>0.05–0.2 g/kg/h ‡</td>
<td>1–3</td>
<td>0.05–0.2 g/kg/h</td>
<td>1–2</td>
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<tr>
<td>Lipovenoes 10% and 20%</td>
<td>—</td>
<td>—</td>
<td>—</td>
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<tr>
<td>Lipovenous MCT</td>
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<tr>
<td>Structolipid 20%</td>
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<td>NA</td>
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<tr>
<td>ClinOleic 20%</td>
<td>0.5–3 †</td>
<td>0.25 g/kg/h ‡</td>
<td>Max 4</td>
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<td>NA</td>
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<td>Lipidem or Lipoplus</td>
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<td>NA</td>
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<tr>
<td>SMOFlipid</td>
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<td>Max 0.125 g/kg/h per 24 h</td>
<td>0.5–3</td>
<td>Max 0.125 g/kg/h</td>
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</tr>
<tr>
<td>Omegaven</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>Max 3</td>
</tr>
</tbody>
</table>

MCT, medium-chain triglyceride; NA, product not indicated for pediatric use or safety and efficacy has not been established in pediatric patients; —, information not available to author.

*Dosing guidelines are based on the product package insert from the country represented and do not take into account specific clinical indications or guidelines. Practitioners’ complete assessment and judgement should be used for individual patient dosing. Manufacturer information for products notated with capital letters can be found in the reference list.

†For pediatric patients generically.
‡In older pediatric patients.
§Titration is required.
‖Small for gestational age or premature infants with impaired capacity to metabolize fat. If no monitoring can occur, max dose is 2 g/kg/d.
Max with titration.
⁎The maximum infusion rate should be strictly adhered to avoid a severe increase in the serum triglyceride concentration.
ASPEN/SCCM Guidelines

- H3b. Alternative IVFE may provide outcome benefit over SO-based IVFE, but we cannot make a recommendation at this time due to the lack of availability of these products in the United States.

- When these alternative IVFE (MCT, OO, FO, SMOF) become available in the United States, based upon expert opinion, we suggest their use be considered in the critically ill patient who is an appropriate candidate for PN.

- H5. We recommend a targeted blood glucose range of 140 to 180 mg/dL for the general ICU population; ranges for specific patient populations may differ (after CV surgery, TBI) and are not covered in these guidelines.
Do alternative ILE make a difference on outcomes in ICU patients?
Alternative IVFE Products

- Olive-oil (OO) based IVFE was approved in the U.S. in October 2013

![Graph showing the overall effect on ventilation days of ω-6-reducing strategy vs. LCT. LCT long-chain triglycerides, 95% CI 95% confidence intervals, SD standard deviation.]

Parenteral Fish Oil Lipid Emulsions in Critical Illness


- Meta-analysis and systematic review of RCTs conducted from 1980 – November 2014
- Included only studies patients admitted to ICU, defined as high baseline mortality rate ≥ 5%
- Intervention: FO LEs as part of PN or supplemented EN vs. EN/PN + SO-based LEs or saline
- 10 RCTs (n=733 subjects) in ICU patients ( > 18 yo) receiving fish oil lipid emulsions (FO LE) vs. placebo in the context of EN, PN, or both
- Study outcomes: mortality, ICU and hospital LOS, infections, mechanical ventilation (MV) days
Parenteral Fish Oil Lipid Emulsions in Critical Illness


- *A priori* planned for subgroup analysis to determine if lower quality studies vs. higher quality studies of FO-containing LEs had an effect on clinical outcomes

- Methodological quality of trials evaluated with a scoring system from 0 – 14 according to following criteria
  - Concealed randomization
  - Blinding
  - Intention-to-treat principle
  - Definition of outcomes
  - Extent of follow-up
  - Baseline comparability of groups
  - Cointerventions
  - Treatment protocol description

- Low quality study if any one criterion is not met
Mortality - RR 0.9; 95% CI 0.67 to 1.20; P=0.46
Infections - RR 0.64; 95% CI 0.44 to 0.94; P=0.02
MV days - WMD = -1.14; 95% CI -2.67 to 0.38; P=0.14

Figure 4: Effects of mechanical ventilation days of parenteral fish oil containing emulsions (n = 5). CI, Confidence interval; EN, Enteral nutrition; IV, Inverse variance; M-H, Mantel-Haenszel test; PN, Parenteral nutrition; SD, Standard deviation.
ICU LOS - WMD= -1.42; 95% CI -4.53 to 1.69; P=0.37
Parenteral Fish Oil Lipid Emulsions in Critical Illness

- Mean methodological score of all trials = 9 (range, 3 – 12)
- 5 studies considered of high quality, 5 of lower quality

Infections
- High quality studies showed a significant reduction of infections (RR 0.64; 95% CI 0.42 to 0.97; P = 0.04)
- Lower quality studies did not show a significant effect on infections (RR 0.65; 95% CI 0.31 to 1.35; P = 0.25)

Hospital LOS
- High quality studies showed significant reduction in days (WMD - 7.42; 95% CI -11.89 to -2.94; P = 0.001) while lower quality studies had no effect (P = 0.45)

MV and ICU LOS – no differences in high vs. low quality studies
Parenteral Fish Oil Lipid Emulsions in Critical Illness


Summary of outcome parameters
- No significant differences in mortality
- Significantly reduced infections
- No significant differences in days of MV
- Effect of study quality on outcomes
  - Reduced infections
  - Reduced hospital LOS
FIGURE 4. Mechanisms by which fatty acids can affect immune cell function. NF-κB, nuclear factor κB.
Key Takeaways

• Key Takeaway #1
  – Guidelines for Nutrition Support Therapy in Adult Critically Ill Patients include updated recommendations but also some recommendations that did not change due to a lack of any new evidence.

• Key Takeaway #2
  – There are still areas of controversy and disagreement, such as the issue of withholding SO-based IVFE for the first week of hospitalization.

• Key Takeaway #3
  – Refeeding syndrome is a preventable complication that may occur during reinstitution of nutrition in undernourished people.

• Key Takeaway #4
  – A.S.P.E.N. and ASHP websites should be consulted for parenteral nutrition (PN) shortage considerations in order to assist clinicians in coping with PN shortages for their patients.
Self-Assessment Questions

1. It is recommended to limit sodium and fluid during the early phases of refeeding syndrome due to the risk of:
   a. Wernickes encephalopathy
   b. pulmonary edema
   c. muscle paralysis
   d. seizures

2. What is the recommended protein intake for obese patients with BMI 30-39.9 kg/m²?
   a. 1.2 g protein/kg IBW per day
   b. 1.5 g protein/kg IBW per day
   c. 2 g protein/kg IBW per day
   d. ≥ 2.5 g protein/kg IBW per day
Self-Assessment Questions

3. An ICU patient with severe hypophosphatemia is MOST LIKELY to exhibit:
   a. acute kidney injury
   b. respiratory muscle weakness
   c. cholestasis
   d. decreased gastric motility

4. Deficiency of the following micronutrient has been associated with the development of Wernicke’s encephalopathy:
   a. niacin
   b. magnesium
   c. thiamine
   d. folic acid
Self-Assessment Answers

1. b – pulmonary edema
2. c – 2 g protein/kg IBW per day
3. b – respiratory muscle weakness
4. c - thiamine