Objectives

- Review the metabolic response of critical illness and their associated clinical outcomes
- Discuss assessment of nutritional status in the critically ill patient
- Describe the advantages and disadvantages of enteral and parenteral nutrition
- Evaluate the latest guideline recommendations for nutrition support in the critically ill

Historical Perspective

- 1870: First described enteral feeding
- 1960s: More refined mixtures of enteral feedings
- 1972: Development of 2-3 compartment TPN bags
- 1937: First successful intragastric feeding
- 1980s: PN in its complete form developed
- 1980s: Hyperalimentation with large glucose loads
Recent Guidelines

Effects of Critical Illness
- Muscle mass loss
- Impaired healing
- Immobility
- Susceptibility to infections
- Cognitive impairment

Metabolic Response to Stress

- Stressor (trauma, surgery, infection)
- Neuroendocrine
- Inflammatory/immune
- Adipokines
- GI tract hormones
- Uncontrolled catabolism
- Resistance to anabolic signals
Clinical Consequences

- Metabolic Stress
  - Hyperglycemia
  - Muscle Wasting/Changes in Body Composition
  - Changes in metabolic rate

Consequences of Malnutrition

- Malnutrition
  - Morbidity ↑
    - Wound healing ↓
    - Infections ↑
    - Complications ↑
    - Convalescence ↑
  - Mortality ↑
  - Treatment ↑
  - Hospital LOS ↑

 Need for Nutrition

- Widespread underfeeding in ICU patients
- Underfed, critically ill patients have worse outcomes
  - Mortality, longer duration of mechanical ventilation (MV)

<table>
<thead>
<tr>
<th>Citation</th>
<th>Methods/ Patients</th>
<th>Intervention</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heyland et al. 2015</td>
<td>Prospective, multi-institutional study 201 ICUs in 20 countries (n=13190 MV patients)</td>
<td>Determine prevalence of iatrogenic underfeeding (&lt;80% of prescribed energy needs) in nutritionally at-risk patients (&gt;96h MV)</td>
<td>8% received &lt;1.2% of prescribed calories (57.6% protein) and 7.7% pts failed to meet 80% of energy targets. ICUs in US had the worst outcomes (13% of prescribed requirements)</td>
</tr>
</tbody>
</table>
Nutritional Risk

- Risk of acquiring complications and other forms of adverse outcomes that might have been prevented by timely and adequate nutrition support
  - Traditional serum protein markers (albumin, prealbumin) are acute phase reactants
  - Davis et al. 2012
    - Changes in prealbumin (PAB) correlated only with changes in CRP ($P<0.001$)
    - PAB may not be a sensitive marker for adequacy of nutrition support in the critically ill

Surrogate Nutrition Markers

<table>
<thead>
<tr>
<th>Serum Protein</th>
<th>Half-life</th>
<th>Factors Resulting in Increased Values</th>
<th>Factors Resulting in Decreased Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Albumin</td>
<td>14-20 days</td>
<td>Dehydration</td>
<td>Liver disease, infection, nephrotic syndrome, post-op edema, overhydration, malabsorption</td>
</tr>
<tr>
<td>Prealbumin</td>
<td>2-3 days</td>
<td>Chronic renal failure</td>
<td>Acute catabolic states, post surgery, altered energy and nitrogen balance, liver disease, infection, dialysis</td>
</tr>
<tr>
<td>Transferrin</td>
<td>8-10 days</td>
<td>Pregnancy, hepatitis, iron deficiency, dehydration, chronic blood loss</td>
<td>Chronic infection, acute catabolic states, nephrotic syndrome, increased iron stores, liver damage, overhydration, malnutrition</td>
</tr>
</tbody>
</table>
Nutrition Risk Scores

- Screening tools available:
  - Mini Nutritional Assessment
  - Malnutrition Universal Screening Tool
  - Short Nutritional Assessment Questionnaire
  - Malnutrition Screening Tool
  - Subjective Global Assessment
  - Nutritional Risk Screening (NRS) 2002
  - Canadian NUTRition Risk in the Critically Ill (NUTRIC) score

### NRS 2002

<table>
<thead>
<tr>
<th>Impaired Nutritional Status</th>
<th>Severity of Disease</th>
<th>Normal nutritional requirements</th>
<th>Normal nutritional requirements</th>
</tr>
</thead>
<tbody>
<tr>
<td>Absent</td>
<td>Absent</td>
<td>Score 0</td>
<td>Score 0</td>
</tr>
<tr>
<td>Score 1</td>
<td>Weight loss &gt;5% in 3 months or fluid intake below 50% of normal requirements preceding event</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Score 2</td>
<td>Weight loss &gt;5% in 2 months or BMI &gt; 18.5 - 20.5 + impaired general condition or food intake 25 - 60% of normal requirement in preceding week</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Score 3</td>
<td>Weight loss &gt;5% in 1 month (&gt;15% in 3 months) or BMI &lt;18.5 + impaired general condition or food intake 0 - 25% of normal requirement in preceding week</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Score: \( \chi \) (impaired nutritional status) + \( \chi \) (severity of disease) = Total Score

Age if ≥70 years: add 1 point to total score above

Total Score ≥3: the patient is nutritionally at risk and a nutritional care plan is initiated

Score <3: weekly rescreening of patient; if patient is scheduled for a major operation, a preventative care plan is considered

**NUTRIC Score**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Range</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>≥70</td>
<td>+1</td>
</tr>
<tr>
<td>60 - &lt;75</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;60</td>
<td></td>
<td></td>
</tr>
<tr>
<td>APACHE II</td>
<td>≥15</td>
<td>+1</td>
</tr>
<tr>
<td>11 - &lt;15</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;11</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SOFA</td>
<td>≥2</td>
<td>+1</td>
</tr>
<tr>
<td>1 - &lt;2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of Co-morbidities</td>
<td>≥2</td>
<td>+1</td>
</tr>
<tr>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Days from hospital to ICU admission</td>
<td>≥15</td>
<td>+1</td>
</tr>
<tr>
<td>11 - &lt;15</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;11</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IL-6</td>
<td>≥496</td>
<td>+1</td>
</tr>
<tr>
<td>448 - &lt;496</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;448</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

NUTRIC Score

NUTRIC Score scoring system: if IL-6 available

<table>
<thead>
<tr>
<th>Sum of Points</th>
<th>Category</th>
<th>Explanation</th>
</tr>
</thead>
<tbody>
<tr>
<td>6-10</td>
<td>High</td>
<td>Associated with worse clinical outcomes (mortality, ventilation). These patients are the most likely to benefit from aggressive nutrition therapy.</td>
</tr>
<tr>
<td>0-5</td>
<td>Low</td>
<td>These patients have low malnutrition risk</td>
</tr>
</tbody>
</table>

NUTRIC Score scoring system: if no IL-6 available*

<table>
<thead>
<tr>
<th>Sum of Points</th>
<th>Category</th>
<th>Explanation</th>
</tr>
</thead>
<tbody>
<tr>
<td>5-9</td>
<td>High</td>
<td>Associated with worse clinical outcomes (mortality, ventilation). These patients are the most likely to benefit from aggressive nutrition therapy.</td>
</tr>
<tr>
<td>0-4</td>
<td>Low</td>
<td>These patients have low malnutrition risk</td>
</tr>
</tbody>
</table>

*It is acceptable to not include IL-6 data points if IL-6 is not consistently available. A score of 0 or 1 can be attributed to missing data as it has minimal prediction of the NUTRIC score.

Assessment of Nutritional Status

ASPEN/SCCM Recommendations

- Suggest not using traditional nutrition surrogate markers, as they are not validated in critical care (expert consensus)
- Suggest a determination of nutrition risk 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 enteral therapy (expert consensus)
- IC be used to determine energy requirements when available in absence of variables that affect the accuracy (very low)
- In the absence of IC, suggest a published predictive equation or a simplistic weight-based equation be used to determine energy requirements (expert consensus)

Calculating Energy Needs

1. **Indirect calorimetry (IC)**
   - Gold standard
   - Measures O₂ consumption and CO₂ production → energy expenditure (EE) of whole body
   - Limited in some institutions
   - Factors affecting IC
     - Ventilator settings, continuous renal replacement therapy, excessive movement/physical therapy

### Calculating Energy Needs

2. **Published predictive equations**
   - Less accurate in obese and underweight patients
   - Ex: Ireton-Jones, Harris-Benedict

3. **Weight-based equations**
   - Advantage: simplistic; generally 25-30 kcal/kg/day
   - Obesity?

### Controversies of Nutrition Support

- Type
- Timing
- Quantity

### Type of Nutrition: Enteral (EN) vs Parenteral (PN)
Benefits of Enteral Nutrition

- Reduce gut/lung inflammation
- Attenuate oxidative stress
- Muscle function, mobility, return to baseline function
- Maintain gut integrity
- Absorb capacity, absorptive capacity
- Promote insulin sensitivity
- Provide micro & macronutrients, antioxidants
- Maintain lean body mass
- Absorption capacity
- Dominance of anti-inflammatory T2 over pro-inflammatory T1 responses
- Increased absorptive capacity
- Modality, contractility
- Virulence of pathogenic organisms
- Increase absorptive capacity
- Th2 over Th1 responses
- Reduce gut/lung inflammation
- Muscle function, mobility, return to baseline function
- Maintain gut integrity
- Absorb capacity, absorptive capacity
- Promote insulin sensitivity
- Provide micro & macronutrients, antioxidants
- Maintain lean body mass
- Absorption capacity
- Dominance of anti-inflammatory T2 over pro-inflammatory T1 responses
- Increased absorptive capacity
- Modality, contractility
- Virulence of pathogenic organisms
- Increase absorptive capacity
- Th2 over Th1 responses

Location of EN Delivery

- **Gastric feeding**
  - Stomach
    - Nasogastric (NG) or orogastric tube (OG)
    - Percutaneous endoscopic gastrostomy (PEG) tube or surgical gastrostomy tube (G-tube)
  - **Postpyloric feeding**
    - Duodenum
    - Jejunum

Issues With EN Delivery

- Reducing aspiration risk
  - Postpyloric feeding
  - Deliver greater number of goal calories
  - Administration of prokinetic agents
  - Erythromycin, metoclopramide
  - Elevation of head of bed 30°-45°
Location of EN Delivery

- Davies et al.
  - Largest prospective, RCT to compare small bowel feeding (nasojejunal) vs gastric (naso gastric) to increase energy delivery
  - 17 med/surg ICUs; n=181 on MV with elevated GRV
  - No difference energy delivery (P=0.66), mortality, LOS, or incidence of pneumonia

APEN/SCCM Recommendations

- In most critically ill patients, it is acceptable to initiate EN in the stomach (expert consensus)
- Recommend the level of infusion be diverted to lower in the GI tract in those critically ill patients at high risk for aspiration (moderate to high)

What is TPN?

- Parenteral nutrition (PN) or total parenteral nutrition (TPN)
  - Macronutrients (protein, carbs, fats)
  - Micronutrients
  - Vitamins/minerals
  - Water
  - Administered through central venous catheter
    - Infection risk
    - Peripheral parenteral nutrition (PPN) → limitations

Indications for PN

- Gastrointestinal (GI) ileus
- Severe GI motility disorder
- Bowel obstruction
- Multiple fistulas
- Severe pancreatitis (w/o jejunostomy access)
- Short bowel syndrome (<150cm small bowel)
- Excessive energy needs
- Prolonged severe hyperemesis gravidarum
### Enteral vs Parenteral Nutrition

<table>
<thead>
<tr>
<th>Type of Nutrition</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enteral (EN)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Simplest, less monitoring</td>
<td>Dependent on GI function</td>
</tr>
<tr>
<td></td>
<td>Physiologically</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Decrease in GI mucosal atrophy</td>
<td>Increased gastric residual volume</td>
</tr>
<tr>
<td></td>
<td>Reduced incidence of hyperglycemia vs PN</td>
<td>Frequent interruptions</td>
</tr>
<tr>
<td></td>
<td>Cost-effective</td>
<td></td>
</tr>
<tr>
<td>Parenteral (PN)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Independent of GI function</td>
<td>Requires venous access</td>
</tr>
<tr>
<td></td>
<td>Able to reach nutritional goals quicker</td>
<td>Nonphysiologic</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Increased rate of infectious complications</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Expensive</td>
</tr>
</tbody>
</table>

### EN vs PN in Critically Ill

<table>
<thead>
<tr>
<th>Design</th>
<th>Systematic literature review and meta-analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methods</td>
<td>Critically ill adults (&gt;18y.o.) admitted to ICU</td>
</tr>
<tr>
<td></td>
<td>18 RCTs with 3347 patients (1681 EN vs 1666 PN)</td>
</tr>
<tr>
<td>Intervention</td>
<td>EN vs PN; subgroup: differences in caloric intake</td>
</tr>
<tr>
<td>Outcomes</td>
<td>1°: overall mortality</td>
</tr>
<tr>
<td></td>
<td>2°: infections, ICU and hospital LOS, duration of mechanical ventilation (MV)</td>
</tr>
<tr>
<td>Results</td>
<td>1°: no difference (RR 1.04, 95% CI 0.82, 1.33, P=0.75)</td>
</tr>
<tr>
<td></td>
<td>2°: ↓ incidence of infections (RR 0.64, 95% CI 0.48, 0.87, P=0.004)</td>
</tr>
<tr>
<td></td>
<td>↓ subgroup: ↓ incidence of infections (RR 0.55, 95% CI 0.37, 0.82, P=0.039)</td>
</tr>
<tr>
<td></td>
<td>↓ ICU LOS: ↓ LOS (WMD -0.80, 95% CI -1.23, -0.37, P=0.0003)</td>
</tr>
<tr>
<td></td>
<td>↓ Hospital LOS and duration of MV: no overall difference</td>
</tr>
<tr>
<td>Conclusion</td>
<td>EN vs PN had no effect on overall mortality but decreased infectious complications and ICU LOS</td>
</tr>
</tbody>
</table>

### Type of Nutrition

**ASCPEN/SCCM Recommendations**
- Suggest the use of EN over PN in critically ill patients who require nutrition support therapy (low to very low)

- Biggest benefit of EN vs PN
  - Reduction in infectious complications
    - Pneumonia, central line infections
  - Reduction in ICU length of stay (LOS)
**CALORIES trial**

<table>
<thead>
<tr>
<th>Hypothesis</th>
<th>Parenteral route is superior to enteral route</th>
</tr>
</thead>
<tbody>
<tr>
<td>Design</td>
<td>Pragmatic, open, multicenter, parallel-group, RCT</td>
</tr>
<tr>
<td>Methods</td>
<td>33 adult ICUs in England Parenteral vs enteral nutrition within 36hr of ICU admission continued up to 5 days (PN n=1191, EN n=1197)</td>
</tr>
<tr>
<td>Outcomes</td>
<td>1°: 30 day all-cause mortality 2°: duration of organ support, infectious complications, ICU and hospital LOS, mortality at ICU and hospital discharge</td>
</tr>
<tr>
<td>Results</td>
<td>1°: PN (33.1%) vs EN (34.2%), RR in PN 0.97, 95% CI, 0.86-1.08, P=0.57 2°: PN vs EN significantly less hypoglycemia (P=0.006) and vomiting (P&lt;0.001); no other differences in secondary outcomes</td>
</tr>
<tr>
<td>Conclusion</td>
<td>No significant difference in 30-day mortality associated with the route of early nutritional support in critically ill adults</td>
</tr>
</tbody>
</table>

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**When to Use PN**

**ASPER/SCCM Recommendations**

- Patients at low nutrition risk, exclusive PN should be withheld over first 7 days of ICU admission if patient cannot maintain volitional intake and if early EN is not possible
- Patients at high nutrition risk or severely malnourished, when EN is not feasible, should be initiated on exclusive PN as soon as possible following ICU admission
- Supplemental PN can be considered after 7-10 days if unable to meet >60% of energy and protein requirements by EN route alone
Early vs Delayed EN

ET has many nutritional and nonnutritional benefits

- Early: 24-48 hr of initiating mechanical ventilation

<table>
<thead>
<tr>
<th>Citation</th>
<th>Methods/Patients</th>
<th>Intervention</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Doig et al. 2009</td>
<td>Meta-analysis: 6 RCTs (214 medical/surgical ICU MV patients) Outcomes: 1*: mortality (2*: N/V, pneumonia, sepsis, MODS, bacteremia)</td>
<td>Standard EN formula within 24hr within initial injury or ICU admission vs delayed</td>
<td>Reduction in mortality (OR=0.34, 95% CI 0.14-0.85) and pneumonia (OR=0.31, 95% CI 0.12-0.78). Trend toward fewer failed organ systems in early EN (2.5 ± 0.7 vs 3.1 ± 0.8, P=0.057).</td>
</tr>
</tbody>
</table>

When to Initiate PN?

<table>
<thead>
<tr>
<th>Patient Type</th>
<th>When to Start PN</th>
</tr>
</thead>
<tbody>
<tr>
<td>EN not feasible and patient previously well nourished</td>
<td>Only after first 7 days of hospitalization</td>
</tr>
<tr>
<td>Low nutrition risk (NRS 2002 ≤3 or NUTRIC score ≤5)</td>
<td>Quality of evidence: very low</td>
</tr>
<tr>
<td>EN not feasible and patient showing signs of malnutrition</td>
<td>During first week of hospitalization</td>
</tr>
<tr>
<td>High nutrition risk (NRS 2002 ≥3 or NUTRIC score ≥5)</td>
<td></td>
</tr>
<tr>
<td>Severely malnourished (BMI &lt;18.5, actual weight &lt;90% of IBW, or 10-15% weight loss over previous 6 months)</td>
<td>Quality of evidence: expert consensus</td>
</tr>
</tbody>
</table>
**When to Initiate PN?**

- Supplemental PN: PN given in addition to EN to help achieve caloric goals

<table>
<thead>
<tr>
<th>Citation</th>
<th>Methods/Patients</th>
<th>Intervention</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Casaer et al 2013 EPaNIC trial</td>
<td>Multicenter RCT (n=4640 med/surg ICU)</td>
<td>Early (within 48hr) vs late (&gt;day 8) PN to supplement insufficient EN</td>
<td>Late PNE: 6.3% likelihood being d/c from hospital &amp; ICU alive (P=0.04), fewer infections (22.8% vs 26.2%, P=0.006), ↓ ICU LOS (P=0.02), reduction in healthcare costs (P=0.04) Rates of survival similar</td>
</tr>
</tbody>
</table>

**ASPEN/SCCM Recommendation**

- Recommend patients at low or high risk, supplemental PN be considered after 7-10d if unable to meet >60% energy and protein requirements by enteral route alone (quality of evidence: moderate)

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**Quantity of Nutrition: What is the optimal dose?**

**Rationale:**

- Optimal EN attenuates malnutrition and protein catabolism
- Permissive underfeeding: restriction of nonprotein calories while supplying full protein requirements
- Trophic (trickle) feeding: administering small volumes of EN (10-20mL/hr), does not provide adequate nutrition support

MORE

- Give extra calories to prevent catabolism

LESS

- Illness-induced anorexia is adaptive

---

**Quantity of Nutrition Support**

MORE

- Give extra calories to prevent catabolism

LESS

- Illness-induced anorexia is adaptive
EDEN trial


Objective
Initial trophic enteral feeding would increase ventilator-free days and decrease GI intolerance compared with initial full enteral feeding.

Design
Randomized, open-label, multicenter (ARDS Net)

Methods
1000 pts within 48hr of acute lung injury (ALI) requiring MV starting EN to receive trophic EN 10-20 mL/hr (n=508) vs full (n=492) EN for up to 6 days.

Outcomes
Calories per day: trophic=400kcal/day (25%) vs full=1300kcal/day (80%)

Results
1*: No difference in VFDs in trophic (14.9d) vs full (15d), P=0.89
2*: No differences in secondary outcomes
   Full EN had more GI intolerance (vomiting, higher residuals); overall prevalence low.

Full or Permissive Underfeeding?

<table>
<thead>
<tr>
<th>Study</th>
<th>Methods / Patients</th>
<th>Intervention</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Casaer et al. 2013</td>
<td>EPANC trial post-hoc Multicenter RCT (n=440 med/surg ICU)</td>
<td>Hypocaloric (15.7 kcal/kg/d) vs full (25-30 kcal/kg/d) feeding</td>
<td>Early PN: longer ICU LOS, longer MV, no difference in mortality</td>
</tr>
<tr>
<td>Braunschweig et al. 2015</td>
<td>INACT trial         Multicenter RCT (n=76 medical ICU)</td>
<td>Intensive nutrition (54.7% goal calories) vs standard therapy (35.5% goal calories) from diagnosis of ALI to hospital discharge</td>
<td>Trial stopped midway. Greater mortality in intensive group (66% vs 16%, P&lt;0.02)</td>
</tr>
<tr>
<td>Charles et al. 2014</td>
<td>Single-center RCT   (n=68 trauma ICU)</td>
<td>Hypocaloric (12.5 kcal/kg/d) vs full (25-30 kcal/kg/d) feeding full protein (1.5 g/kg/d)</td>
<td>No significant difference in mortality, ICU/hospital LOS, or infection</td>
</tr>
<tr>
<td>Arabi et al. 2015</td>
<td>PermiT trial        Multicenter RCT (n=894 med/surg ICU requiring MV)</td>
<td>Permissive (40-60% goal calories) vs standard (70-100%) feeding for up to 14d</td>
<td>Permissive 46% calories vs standard 73% goal calories 60 day mortality similar (P=0.58)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Protein intake similar in groups (1.2-1.5 g/kg/d)</td>
<td>No differences in infections, VFDs, ICU LOS, ICU mortality</td>
</tr>
</tbody>
</table>

Higher Nutrition Risk

- Increased nutritional adequacy associated with increased survival in patients with higher NUTRIC scores (26)
Who Should Get What & When?

- What we know...
  - Start trophic EN (10-20 mL/hr)
    - Low nutrition risk: continue trophic EN for first week of hospitalization
    - High nutrition risk: advance EN to goal as tolerated over 24-48 hr
  - ANY absolute contraindication to EN, start PN as soon as possible following ICU admission

Protein Requirements: More is More?

- Provided as essential and nonessential amino acids
  - Critical illness: rate of protein breakdown > rate of protein synthesis
  - Goal: to administer adequate protein to maintain body protein stores and prevent catabolism of these stores
  - Studies suggest improved survival with higher protein
    - Mostly observational

ASPEN/SCCM Recommendations

- Suggest that sufficient (high-dose) protein should be provided. Protein requirements are expected to be in the range of 1.2-2 gm/kg/day of actual body weight and may likely be even higher in burn or multitrauma patients (quality of evidence: very low)

Protein Requirements in the Critically Ill: A Randomized Controlled Trial Using Parenteral Nutrition


<table>
<thead>
<tr>
<th>Design</th>
<th>Double-blinded, RCT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methods</td>
<td>Compare standard amino acid (AA) 0.8gm/kg/d vs higher 1.2gm/kg/d in critically ill patients on PN 119 general med/surgical ICU patients; standard (n=60) vs high (n=59)</td>
</tr>
<tr>
<td>Outcomes</td>
<td>1°: increased hand-grip strength at ICU discharge 2°: fatigue score, muscle mass, and/or nitrogen balance, mortality, &amp; LOS</td>
</tr>
<tr>
<td>Results</td>
<td>Actual AA delivery 0.8gm/kg/d (standard) and 1.1gm/kg/day (higher) 1°: No difference (P=0.054); improved at day 7 in higher AA group (P&lt;0.025) 2°: Less fatique at day 7 in higher AA group (P=0.045) Greater forearm muscle thickness at day 7 in higher AA group (P=0.0001) No difference in mortality or LOS</td>
</tr>
<tr>
<td>Conclusion</td>
<td>In the higher AA group, there were improvements in a number of different outcomes supporting the use of guideline recommendations for protein delivery in critically ill patients</td>
</tr>
</tbody>
</table>
Greater Protein and Energy Intake May Be Associated with Improved Mortality in Higher Risk Critically Ill Patients

**Compher et al. Crit Care Med 2017;45:156-163.**

| **Design** | Multicenter, multinational, observational study |
| **Methods** | 202 ICUs; 2853 MV patients in ICU ≥4 days (subset 1605 patients in ICU ≥12 days) |
| **Outcomes** | Mortality and time to discharge alive (TDA) in high and low risk patients (NUTRIC score: high risk ≥5 and low risk <5; no interventions) |
| **Results** | Mean NUTRIC 4.8 in both ≥4d and ≥12d groups 75.5% EN, 8.7% PN, 13.8% EN & PN, 2% neither 4d: mortality decreased by 6.6% (P=0.003) in high risk and TDA shorter by 5.1% (P=0.01) in high risk group 12d: significant interaction between NUTRIC score, protein, and mortality (P=0.02) |

**Compher et al.**

**Outcomes**
- TDA
  - Significantly shorter in high risk patients at 4 days and 12 days in ICU for both increased protein and energy intake

**Conclusion**
- Greater protein and energy intake is associated with a decrease in mortality and a faster time to discharge alive in high risk patients who stay in the ICU for at least 12 days
- These outcomes did not differ significantly in the low risk group
## Protein Requirements

<table>
<thead>
<tr>
<th>Condition</th>
<th>Protein (gm/kg/day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild stress</td>
<td>0.8 – 1</td>
</tr>
<tr>
<td>Moderate stress</td>
<td>1 – 1.2</td>
</tr>
<tr>
<td>Severe stress</td>
<td>1.2 – 2</td>
</tr>
<tr>
<td>Trauma/burns</td>
<td>2 – 2.5</td>
</tr>
<tr>
<td>Hemodialysis (traditional)</td>
<td>1.2 – 1.5</td>
</tr>
<tr>
<td>CRRT (CVVHDF mode)</td>
<td>2 – 2.5</td>
</tr>
<tr>
<td>Renal insufficiency</td>
<td>0.5 – 0.6</td>
</tr>
<tr>
<td>CAPD</td>
<td>1.3 – 1.5</td>
</tr>
<tr>
<td>Liver failure</td>
<td>0.6 – 0.8</td>
</tr>
</tbody>
</table>

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**One size does **NOT** fit all!**

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**Select Issues in Nutrition Support**
Promoting EN Delivery

- Many factors prevent EN delivery
  - Patients get ~50% of goal calories/protein required
  - Many interruptions in EN
    - Inappropriate 66% of the time
- Common misconceptions → feeding is inappropriate in...
  - High gastric residual volumes
  - Stable blood pressure while on vasopressors
  - Hypoactive bowel sounds with evidence of ileus

Promoting EN Delivery

Monitoring Tolerance of EN

- Tolerance should be assessed daily
  - Physical exam, passing flatus/stool, radiologic evaluations, absence of patient complaints (ex: abdominal pain)
- GI intolerance
  - Vomiting, abdominal distention, discomfort, high NG output, high gastric residual volumes (GRVs), diarrhea

Underordering + inadequate delivery = Calorie deficit
Gastric Residual Volumes

- Overall, poor correlation of GRVs to gastric emptying
  - Increasing cutoff of GRVs did not increase risk for aspiration
- Downfalls of using GRVs:
  - Increased enteral access device clogging, inappropriate cessation of EN, consumption of nursing time

**ASPEN/SCCM Recommendations**

- Suggest that GRVs not be used as part of routine care to monitor ICU patients receiving EN
- Suggest for ICUs that still utilize GRVs, hold EN for GRVs <500mL in the absence of other signs of intolerance should be avoided

Nutrition Support in Shock

- 2 major concerns with EN in shock:
  - Ischemic bowel
  - Steal phenomenon
  - Potential consequence: nonocclusive bowel necrosis (NOBN)
    - Rare (0.29% - 1.14%); most common in jejunal feeding

**DO NOT** initiate EN in the following:

- Hypotensive or vasopressors being initiated or escalating doses

**ASPEN/SCCM Recommendations**

- Suggest in the setting of hemodynamic compromise or instability, EN should be withheld until the patient is fully resuscitated and/or stable (expert consensus).
GI Contractility & EN Initiation

- Many patients experience GI dysfunction in the ICU
- Bowel sounds only indicative of contractility
  - Do not relate to mucosal integrity, barrier functions, or absorptive capacity
- Data mainly from surgical ICU patients
- Feasibility and safety of EN within 36-48hr of ICU admission

**ASPREN/SCCM Recommendations**

- Suggest in majority of MICU and SICU patients, while GI contractility factors should be evaluated when initiating EN, overt signs of contractility should not be required prior to initiation of EN (expert consensus).

Intravenous Fat Emulsions

- US: Primarily soybean oil (SO) based
- Necessary to prevent essential fatty acid (EFA) deficiency
- Growing interest in medium-chain triglycerides (MCTs), olive oil (OO), and fish oil (FO) based products

![Fat Emulsions Diagram](image)

- **1st Generation:** 100% SO
- **2nd Generation:** 50:50 MCT:SO
- **3rd Generation:** OO containing
- **4th Generation:** FO containing

Intravenous Fat Emulsions

- Limitations with SO IVFEs
  - **Inflammatory effects**
    - Contain omega-6 fatty acids and long-chain triglycerides
    - No eicosapentaenoic (EPA) of docosahexaenoic acid (DHA)
  - **Allergic reactions**
    - Soy allergies
  - **PN-associated liver disease (PNALD)**
    - Steatosis and cholestasis
### IVFE Products in the US

<table>
<thead>
<tr>
<th>Product</th>
<th>Total FA Concentration, %</th>
<th>Composition, %</th>
<th>IVFE Generation</th>
<th>kcal/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intralipid</td>
<td>10</td>
<td>100 SO</td>
<td>First</td>
<td>1100</td>
</tr>
<tr>
<td>Intralipid</td>
<td>20</td>
<td>100 SO</td>
<td>First</td>
<td>2000</td>
</tr>
<tr>
<td>Nutrilipid</td>
<td>20</td>
<td>100 SO</td>
<td>First</td>
<td>2000</td>
</tr>
</tbody>
</table>

### Alternative Lipid Emulsions in the Critically Ill


**Design:** Systematic review and meta-analysis

**Methods:** SO-based vs SO-sparing lipid emulsions (LEs)

12 RCTs (866 patients)

**Outcomes:**

1. ICU & hospital LOS, infections, and duration of mechanical ventilation

**Results:**

1. **Primary:** Reduction in mortality with SO-sparing LEs: significant (RR: 0.83; 95% CI 0.62, 1.11; P=0.2)
2. **Secondary:** Trend toward ↓ ICU LOS with SO-sparing (WMD = -2.31; 95% CI -5.28, 0.66; P=0.13)
3. Overall ↓ duration of MV with SO-sparing: not significant (WMD = -2.57; 95% CI -5.51, 0.37; P=0.09)

**Conclusion:** Alternative LEs may be associated with improved clinical outcomes but lack of statistical precision precludes any clinical recommendations at this time.


**Study:** Systematic review and meta-analysis

8 RCTs (391 patients)

**Outcomes:** Hospital LOS ↓ (WMD=9.49; 95% CI -16.5, 2.5; P=0.008) with FO-based IVFEs vs others

No differences in ICU LOS or infections.

No improvements with omega-3 LEs in mortality, ICU LOS, or infections. Weak evidence did show decrease in hospital LOS.

**Conclusions:** No differences in ICU-acquired infections.
**Lipids in Critically Ill PN Patients**

**ASPEN/SCCM Recommendation**

- Suggest withholding or limiting SO-based IVFE during first week following initiation of PN in the critically ill patient to a max of 100gm/week if there is a concern for essential fatty acid deficiency
- Alternative IVFEs may provide outcome benefit over soy-based IVFEs

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**Feeding the Critically Ill Obese**

- Obesity ≠ additional nutrition reserve
  - Issues with fuel utilization (greater loss of lean body mass), increased risk for insulin resistance
- More complications
  - Greater incidence of infection, prolonged hospital/ICU LOS, ↑ risk of organ failure, longer duration of mechanical ventilation
- Mortality
  - Underweight (BMI <18.5) and obesity class III (BMI ≥ 40) have highest mortality

---

**Feeding the Critically Ill Obese**

- Body Mass Index (BMI) = Wt (kg) / Ht (m)²
  - <18.5 – Underweight
  - 20-25 – Normal
  - 25-30 – Borderline; moderately excessive body fat
  - >30 – Obesity
- Obesity
  - Class I = BMI 30 – 34.9
  - Class II = BMI 35 – 39.9
  - Class III = BMI ≥ 40

---


Feeding the Critically Ill Obese

- ASPEN/SCCM suggest:
  - Lower total calories, lower carbohydrates, high amino acids
  - Protein
    - BMI 30-40: 2 gm/kg/day on ideal body weight (IBW)
    - BMI ≥40: up to 2.5 gm/kg/day on IBW
  - Weight-based equations
    - BMI 30-50: 11-14 kcal/kg/day of actual body weight
    - BMI >50: 22-25 kcal/kg/day of IBW

ASPN/SCCM Nutrition Bundle

- Assess patients on admission to the ICU for nutrition risk, and calculate both energy and protein requirements to determine goals of nutrition therapy
- Initiate EN within 24-48hr following the onset of critical illness and admission to the ICU, and increase to goals over the first week of ICU stay
- Take steps as needed to reduce risk of aspiration or improve tolerance to gastric feeding
- Implement EN protocols with institution-specific strategies to promote delivery of EN
- Do not use gastric residual volumes as part of routine care to monitor ICU patients receiving EN
- Start PN early when EN is not feasible or sufficient in high-risk or poorly nourished patients

Summary

- EN should still be considered first-line over PN in critically ill patients with a functioning GI tract
- Need for protocols to deliver specialized nutrition therapy to critically ill patients
- Need for large, RCTs in order to provide more data to guide nutritional support for critically ill patients
Learning Question 1
• What is the most appropriate indication for parenteral nutrition?
  a) Lack of bowel sounds/flatus
  b) Gastrointestinal ileus
  c) Gastric residual volumes of 250mL
  d) On stable, low-dose vasopressors

Learning Question 2
• HD is a 45 year female admitted to the MICU s/p COPD exacerbation who is currently receiving tube feeds (TF) at 50mL/hr. While reviewing the patient’s chart you notice the RN has documented a GRV of 200mL on the flowsheet. What is your recommendation to the nurse?
  a) Hold TFs due to high GRV and start a prokinetic agent
  b) Hold TFs until GRV is <250mL then restart
  c) Continue TFs and hold for residuals >400mL
  d) Continue TFs and do not check residuals unless signs of GI intolerance develop

Learning Question 3
• JT is a 57 year old male admitted to the SICU s/p bowel resection who is now being started on PN. His measurements are as follows: BMI 35 kg/m², IBW 75kg, actual body weight (act BW) 114kg. What are your recommendations for energy and protein requirements?
  a) 22 kcal/kg IBW and 2.5 gm/kg act BW
  b) 30 kcal/kg IBW and 2.5 gm/kg IBW
  c) 25 kcal/kg act BW and 1.5 gm/kg act BW
  d) 14 kcal/kg act BW and 2 gm/kg IBW
Learning Question 4

- RW is a 65 year old male POD#3 from total gastrectomy and jejunostomy feeding tube placement for gastric cancer. He is currently NPO with no flatus or bowel movements yet. What is your nutrition plan?
  a) Start trophic feeds now
  b) Start parenteral nutrition now
  c) Wait until hospital day 7 then start parenteral nutrition
  d) Continue NPO status until bowel function returns

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Detroit Receiving Hospital
February 3rd, 2017