What’s New in Parenteral Nutrition?

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7 กรกฎาคม พ.ศ. 2559
Parenteral Nutrition (PN) Used in Critically ill Adults

- Early or Late ??
- Safety ??
- Intravenous lipid emulsions (IVFE) ??
• Overview of Nutrition Support

• Nutritional Support in ICU

• Role of PN in ICU

• Conclusions
OUTLINE

• Overview of Nutrition Support

Nutritional Support in ICU

• Role of PN in ICU

• Conclusions
Definition: Nutrition Support

- **“Nutrition Support”**¹
  : Orally modified formulas or intravenous nutrition necessitated by inability to consume a general diet; administered to malnourished individuals who cannot consume food in its original form.

- **“Nutrition Therapy”**²
  : A component of medical treatment that includes oral, enteral, and parenteral nutrition.

- **“Nutrition Support Therapy”**²
  : Parenteral and/or enteral nutrition.

Algorithm for Delivery of Nutrition Support

Nutrition Screen

Risk or Presence of Malnutrition??

Not-at-Risk

At-Risk or Malnourished

Rescreen at:
- Regularly specified intervals or
- When nutritional/clinical status changes

Nutrition Assessment

At-Risk or Malnourished

Develop Nutrition Care Plan

Reassessment

PN

Nutrition Monitoring

Nutritional Assessment: Goals

1. Assessment of nutritional status
2. Medical problem(s)/disease(s)
3. Energy, macro/micronutrient and fluid requirements
4. Route of administration
5. Follow up
Nutritional Assessment: Goals

1. Assessment of nutritional status
2. Medical problem(s)/disease(s)
3. Energy, macro/micronutrient and fluid requirements
4. Route of administration
5. Follow up
Major goals for Nutrition Prescription

- Energy
- Protein
- Fluids
## Daily Requirements

<table>
<thead>
<tr>
<th>Daily Goals</th>
<th>Stable</th>
<th>Critical Care</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Energy</strong> (Kcal/kg)</td>
<td>30-35</td>
<td>(20-25) 25-30*</td>
</tr>
</tbody>
</table>

- **Refeeding**
  - 10(5) - 20 Kcal/kg/day
  - 80% BEE

- **Obesity**
  - BMI 30 - 40 (adjusted BW): ≥ 2 (IBW)
  - BMI > 40: ≥ 2.5 (IBW)

- **Fluids** (mL/kg)
  - 30 - 35 mL (depending on comorbidities)

References:
- *J Parenter Enteral Nutr. 2016;40(2):159-211*
Pathogenesis of Refeeding Syndrome

Starvation / Malnutrition

Glycogenolysis, gluconeogenesis and protein catabolism

Hypokalaemia
Hypomagnesaemia
Hypophosphataemia
Thiamine deficiency
Salt and water retention - oedema

↑ Glucose uptake
↑ Utilization of thiamine
↑ Uptake of $K^+$, $Mg^{2+}$ & $PO_4^{2-}$

↑ Protein and glycogen synthesis

Fluid, salt, nutrients (CHO major energy source)

Refeeding (switch to anabolism)

Insulin secretion

Protein, fat, mineral, electrolyte and vitamin depletion – salt and water intolerance
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Adjusted BW in “Obese Patients” (BMI ≥ 30 kg/m²)

IDEA = Actual weight

DEA = Ideal weight (IBW)

ACTUA = Adjusted weight

= IBW + \{ 50\% \times (\text{Actual weight} - \text{Ideal weight})\}

= \frac{\text{Actual weight} + \text{IBW}}{2}
Adjusted body weight

\[ = \text{IBW} + [0.5 \times (\text{Actual BW} - \text{IBW})] \]

Where \text{IBW} is calculated as:

- \( \text{♂} = \text{Ht (in cm.)} - 100 \) kg.
- \( \text{♀} = \text{Ht (in cm.)} - 105 \) kg.

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<td>• Obesity</td>
<td>15-20 (adjusted BW)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• 11-14 (actual BW)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• 22-25 (IBW)</td>
</tr>
<tr>
<td><strong>Protein</strong></td>
<td>1.2-1.5(2)</td>
<td>BMI 30-50*</td>
</tr>
<tr>
<td>• Obesity</td>
<td></td>
<td>• 11-14 (actual BW)</td>
</tr>
<tr>
<td></td>
<td>BMI &gt; 50*</td>
<td>• 22-25 (IBW)</td>
</tr>
<tr>
<td><strong>Fluids</strong></td>
<td>30-35 mL</td>
<td>BMI 30-40: ≥ 2 (IBW)</td>
</tr>
<tr>
<td></td>
<td>(depending on comorbidities)</td>
<td>BMI &gt;40: ≥ 2.5 (IBW)</td>
</tr>
</tbody>
</table>

References:
1. Assessment of nutritional status

2. Medical problem(s)/disease(s)

3. Energy, macro/micronutrient and fluid requirements

4. Route of administration

5. Follow up
The Basic Principle

“IF THE GUT WORKS,
...USE IT ”
Route:

Oral diet

Oral supplements

Enteral nutrition (EN)

Parenteral nutrition (PN)

SPN = EN + PN

SPN = Supplemental parenteral nutrition
is the only absolute contraindication to enteral feeding
Feeding Approaches

- Enteral
- Oral
- Tube
- Peripheral vein
- Central vein

"If the gut works, use it"
Plan for Nutritional Support

• Nutritional Prescription
  : How much?

• Route of Administration
Route: Oral diet

Oral supplements

Enteral nutrition (EN)

Parenteral nutrition (PN)

Critically ill patients

$\text{SPN} = \text{EN} + \text{PN}$
IV Lipid Emulsions

- Lipid
- Glucose
- Amino acid
Intravenous Lipid Emulsions (IVLEs)

- An essential component of parenteral nutrition (PN)
- Help to prevent essential fatty acid deficiency (EFAD)
- To decrease the carbohydrate calorie load
- Suitable for patients who need fluid restriction

Evolution of Lipid Emulsions

1961- Soybean oil
(พ.ศ. 2504)

ω-6 fatty acids
Relative pro-inflammatory Eicosanoids from metabolites of ω-6 Fatty Acids

**Omega-6 Fatty Acids**

- **Arachidonic Acid (AA)**
  - 20:4 n6

**Cyclooxygenase (COX)**

- **Prostanoids**
  - Prostaglandin E2 (PGE2)
  - Prostaglandin I2 (PGI2)
  - Thromboxane A2 (TXA2)

**Lipoxygenase**

- **Leukotrienes**
  - Leukotriene B4 (LTB4)
  - Leukotriene C4 (LTC4)
  - Leukotriene E4 (LTE4)

**More Pro-Inflammatory**

(Soybean oil, LCT)
Evolution of Lipid Emulsions

1996 - Olive oil + Soybean oil

1984 - MCT - LCT (coconut + soybean oil) (W.P. 2527)

1961 - Soybean oil (W.P. 2504)

Still continues to be safe & reliable (50 years)

Most recent: S + M + O + F - fish oil

Alternative IVLs

Reproduction from a slide courtesy from Fresenius Kabi.
Potential Benefits of Alternative IVLEs

- Less pro-inflammatory effects
- Less immune suppression
- Improved antioxidant defenses

“No studies showed worse outcomes for alternative IVLEs compared with soybean oil-based IVLEs”

Eicosanoids from metabolites of ω-6 and ω-3 Fatty Acids

**ω-6 Fatty Acids**

- **Arachidonic Acid (AA)**
  - 20:4 n6
- **Cyclooxygenase (COX)**
- **Prostanoids**
  - Prostaglandin E2 (PGE2)
  - Prostaglandin I2 (PGI2)
  - Thromboxane A2 (TXA2)
- **Lipoxygenase**
- **Leukotrienes**
  - Leukotriene B4 (LTB4)
  - Leukotriene C4 (LTC4)
  - Leukotriene E4 (LTE4)

**ω-3 Fatty Acids**

- **Eicosapentaenoic Acid (EPA)**
  - 20:5 n3
- **Cyclooxygenase (COX)**
- **Prostanoids**
  - Prostaglandin E3 (PGE3)
  - Prostaglandin I3 (PGI3)
  - Thromboxane A3 (TXA3)
- **Lipoxygenase**
- **Leukotrienes**
  - Leukotriene B5 (LTB5)
  - Leukotriene C5 (LTC5)
  - Leukotriene E5 (LTE5)

**Pro-inflammatory**

**Anti-inflammatory**
Conclusions:

• Alternative IVLEs are safe and effective.
• They should be made available in the United States of America.

A.S.P.E.N. = The American Society for Parenteral and Enteral Nutrition

When Indicated, Maximize Efficacy of PN

- In the **first week of** hospitalization in the **ICU**, when PN is required and EN is not feasible, patients should be given a parenteral formulation **without soy-based lipids** (Grade D).
H. When Indicated, Maximize Efficacy of PN

H3a. We suggest withholding or limiting SO-based IVFE during the first week following initiation of PN in the critically ill patient to a maximum of 100 g/week (often divided into 2 doses/week) if there is concern for essential fatty acid deficiency.
H. When Indicated, Maximize Efficacy of PN

H3b. Alternative IVFEs may provide outcome benefit over soy-based IVFEs; however, we cannot make a recommendation at this time due to lack of availability of these products in the United States. When these alternative IVFEs (SMOF [soybean oil, MCT, olive oil, and fish oil emulsion], MCT, OO, and FO) become available in the United States, based on expert opinion, we suggest that their use be considered in the critically ill patient who is an appropriate candidate for PN.
- When PN with IV lipids is indicated, IV lipids that reduce the load of omega-6 fatty acids soybean oil emulsion should be considered.
- However, there are insufficient data to make a recommendation on the type of IV lipids to be used in critically ill patients.
The optimal parenteral nutrition regimen for critically ill surgical patients should probably include supplemental n-3 fatty acids. [grade C]
Intravenous Lipids in Intensive Care

ESPEN Guidelines on Parenteral Nutrition: Intensive care

Pierre Singer, Mette M. Berger, Greet Van den Berghe, Gianni Biolo, PhD, Alastair Forbes, Richard Griffiths, Georg Kreyman, Xavier Leverve, Claudia

• Addition of EPA and DHA to lipid emulsions has demonstrable effects on cell membranes and inflammatory processes.

• Fish oil-enriched lipid emulsions probably decrease length of stay in critically ill patients. (Grade B)

ESPEN = The European Society for Clinical Nutrition and Metabolism

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What is the Smartest Way of Nutritional Support in ICU?

“Early Enteral Nutrition”

How Early?

“Within 24-48 hours”

Problems with EN in ICU Practice

- **Fears** about precipitating bowel ischemia the patients with shock
- **EN intolerance**: high GRVs, aspiration, ileus, diarrhea, opiates, pain medications, vasopressors
- Inappropriate cessation of enteral feedings
- Poor adherence to feeding protocols

Inadequate Calorie and Protein Provision

GRV = gastric residual volume
Problems with EN in ICU Practice

- EN is the preferred route of nutritional support in, but it is frequently associated with **underfeeding**, especially in critically ill patients.


- The **average energy** from EN provided to critically ill patients is between **50 - 95%** of requirements.


- The **average protein** intake with enteral feeding ranges from **38 - 82%** of requirements.

Problems with EN in ICU Practice

- **EN**: Physicians prescribed a daily mean volume that was **65.6% of the requirements**, but only **78.1% of the volume prescribed was infused** in critically ill patients in a medical ICU and coronary care unit (CCU)\(^1\)

- The **adequacy of enteral nutritional** intake is associated with nutritional support practice provided by **health care providers** rather than with patients' characteristics \(^2,3\)

\(^2\)Chest. 2003;124:297-305.  
Route: Oral diet

Oral supplements

Enteral nutrition (EN)

Parenteral nutrition (PN)

SPN = EN + PN

Critically ill patients

SPN = Supplemental parenteral nutrition
## When to Start PN/SPN ??

<table>
<thead>
<tr>
<th>Guidelines</th>
<th>Recommendations</th>
</tr>
</thead>
</table>
| **ASPEN 2009** | When **EN is not feasible or available**:  
- **Without** previous *malnutrition*: PN should be reserved and initiated only **after the first 7 days** of hospitalization when EN is not available. *(Grade: E)*  
- **With** *malnutrition* on admission: initiate PN as **soon as possible** following adequate resuscitation. *(Grade: C)* |
| **ESPEN 2009** | All patients receiving **EN less than their target** ed enteral feeding **after 2 days** should be considered for supplementary PN. *(Grade: C)* |

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**ASPEN** = The American Society for Parenteral and Enteral Nutrition  
**ESPEN** = The European Society for Clinical Nutrition and Metabolism

### When SPN ????

<table>
<thead>
<tr>
<th>I. Timing</th>
<th>II. Calories from EN</th>
</tr>
</thead>
<tbody>
<tr>
<td>• May depend on nutritional status of the patients</td>
<td>• &lt; 50-60* % of target energy and protein requirement</td>
</tr>
</tbody>
</table>

*Indirect calorimetry  
*Predictive equations

---

SPN = Supplemental parenteral nutrition

*J Parenter Enteral Nutr. 2016;40(2):159-211
Guidelines for the Provision and Assessment of Nutrition Support Therapy in the Adult Critically Ill Patient: Society of Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.)

Stephen A. McClave, MD1*; Beth E. Taylor, RD, DCN2*; Robert G. Martindale, MD, PhD3; Malissa M. Warren, RD4; Debbie R. Johnson, RN, MS5; Carol Braunschweig, RD, PhD6; Mary S. McCarthy, RN, PhD7; Evangelia Davanos, PharmD8; Todd W. Rice, MD, MSc9; Gail A. Cresci, RD, PhD10; Jane M. Gervasio, PharmD11; Gordon S. Sacks, PharmD12; Pamela R. Roberts, MD13; Charlene Compher, RD, PhD14; and the Society of Critical Care Medicine† and the American Society for Parenteral and Enteral Nutrition†

J Parenter Enteral Nutr. 2016;40(2):159-211
Prospective observational study

Surgical ICU; N = 48 (mean LOS = 15 days)

Energy balance at weeks 1, 2, 3, and 4
Negative impact of hypocaloric feeding and energy balance on clinical outcome in ICU patients

Results:

1. Time to feeding

<table>
<thead>
<tr>
<th>Patients</th>
<th>N</th>
<th>Days</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>48</td>
<td>3.1 ± 2.2 (3)</td>
</tr>
<tr>
<td>Trauma</td>
<td>10</td>
<td>3.8 ± 0.7 (3.5)</td>
</tr>
<tr>
<td>Cardiac surgery</td>
<td>13</td>
<td>3.4 ± 0.6 (3)</td>
</tr>
<tr>
<td>Respiratory failure</td>
<td>7</td>
<td>2.7 ± 0.9 (2.5)</td>
</tr>
<tr>
<td>Gastro-intestinal</td>
<td>3</td>
<td>1.7 ± 1.3 (2)</td>
</tr>
<tr>
<td>Sepsis</td>
<td>3</td>
<td>2.5 ± 1.6 (2.5)</td>
</tr>
<tr>
<td>Transplantation</td>
<td>4</td>
<td>3.0 ± 1.2 (3)</td>
</tr>
<tr>
<td>Other</td>
<td>8</td>
<td>2.9 ± 0.8 (1)</td>
</tr>
</tbody>
</table>

2. Energy delivery

<table>
<thead>
<tr>
<th>Routes</th>
<th>Days</th>
<th>Energy delivery</th>
</tr>
</thead>
<tbody>
<tr>
<td>No feeding*</td>
<td>101 (4/3/1.75)</td>
<td>345 ± 410 (225)</td>
</tr>
<tr>
<td>Oral Feeding</td>
<td>433 (1320)</td>
<td>805 ± 490 (880)</td>
</tr>
<tr>
<td>Enteral†</td>
<td>81 (2175)</td>
<td>1365 ± 770 (1320)</td>
</tr>
<tr>
<td>Combined§</td>
<td>36 (1710)</td>
<td>2160 ± 650 (2175)</td>
</tr>
<tr>
<td>Parenteral</td>
<td>36 (1710)</td>
<td>1915 ± 625 (1710)</td>
</tr>
</tbody>
</table>

Results as mean ± SD (median).
*As defined: days without oral or artificial feeding.
†Enteral feeding includes 416 with pure enteral and 17 days with transition to oral feeding.
‡P < 0.0001 between enteral and either parenteral or combined nutrition.
§Combined = combination of EN and PN.
Progression of energy delivery compared to energy target over 4 weeks: the figure shows that energy delivery increases with time, reducing daily deficit.
Relationship between complications and cumulated energy deficit

<table>
<thead>
<tr>
<th>Variables</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Length of stay</td>
<td>0.0001</td>
</tr>
<tr>
<td>Complications</td>
<td>0.0003</td>
</tr>
<tr>
<td>Infections</td>
<td>0.0042</td>
</tr>
<tr>
<td>Days on antibiotics</td>
<td>0.0003</td>
</tr>
<tr>
<td>Start of nutrition</td>
<td>0.0002</td>
</tr>
<tr>
<td>Days of mechanical ventilation</td>
<td>0.0002</td>
</tr>
</tbody>
</table>

At 1 week: Cumulated energy balance was between $-12,600 \pm 10,520$ kcal.
• **Objective**: To examine the relationship between the amount of energy and protein administered and clinical outcomes, and the extent to which pre-morbid nutritional status (BMI) influenced this relationship

• **167 ICUs** across **21 countries/ N = 2,772**

• **Mechanically ventilated** patients
The relationship between increasing calories/day and 60-day mortality by BMI
Critical pathways in nutrition support:

Route:

1. Oral diet
2. Oral supplements
3. Enteral nutrition (EN)
4. Parenteral nutrition (PN)

SPN = Supplemental parenteral nutrition

- Calories
- Protein

Critically ill patients

SPN = EN + PN
OUTLINE

• Overview of Nutrition Support
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Supplemental Parenteral Nutrition (SPN)

- = EN + PN
- EN $\rightarrow$ $\rightarrow$ + PN

**when EN is insufficient to cover caloric needs**
Propective, randomized, single-center, pilot clinical trial

**Adult general ICU**: N 112 with mechanical ventilator (56/56)

**PURPOSE**: To determine whether nutritional support guided by repeated measurements of resting energy requirements using indirect calorimetry (STUDY GROUP) improves the hospital mortality of critically ill patients, compared to a weight-based formula using 25 Kcal/kg/day (CONTROL GROUP)

**STUDY GROUP**: Dietitian / + SPN to reach target within 24 hrs

**CONTROL GROUP**: Ward staff
STUDY group: IC / dietitians/ + early SPN

IC = Indirect calorimetry
CONTROL group: 25 Kcal/kg/day + ward staff
### Table 1: Nutritional Outcomes

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Study group (n = 56)</th>
<th>Control group (n = 56)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean REE (kcal/day)</td>
<td>1,976 ± 468</td>
<td>1,838 ± 468</td>
<td>0.6</td>
</tr>
<tr>
<td>Mean energy delivered/day (kcal/day)</td>
<td>2,086 ± 460</td>
<td>&gt; 1,480 ± 356</td>
<td>0.01</td>
</tr>
<tr>
<td>Mean enterally delivered energy/day (kcal/day)</td>
<td>1,515 ± 756</td>
<td>&gt; 1,316 ± 456</td>
<td>0.09</td>
</tr>
<tr>
<td>Mean parenterally delivered energy/day (kcal/day)</td>
<td>571 ± 754</td>
<td>&gt; 164 ± 294</td>
<td>0.001</td>
</tr>
<tr>
<td>Route of administration (n)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Enteral</td>
<td>34</td>
<td>48</td>
<td></td>
</tr>
<tr>
<td>Parenteral</td>
<td>3</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Enteral and parenteral</td>
<td>19</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>Mean protein delivered/day (g/day)</td>
<td>76 ± 16</td>
<td>&gt; 53 ± 16</td>
<td>0.001</td>
</tr>
<tr>
<td>Mean daily energy balance (kcal)</td>
<td>186 ± 206</td>
<td>&gt; −312 ± 481</td>
<td>0.001</td>
</tr>
<tr>
<td>Cumulative energy balance (kcal)</td>
<td>2,008 ± 2,177</td>
<td>&gt; −3,550 ± 4,591</td>
<td>0.01</td>
</tr>
<tr>
<td>Maximum negative energy balance (kcal)</td>
<td>15.7 ± 883</td>
<td>&lt; −3.895 ± 4,144</td>
<td>0.01</td>
</tr>
<tr>
<td>Daily mean blood glucose (mg/dL)</td>
<td>119.6 ± 21.8</td>
<td>127.3 ± 33.7</td>
<td>0.82</td>
</tr>
</tbody>
</table>

REE resting energy expenditure, kcal kilocalories; SPN, Supplemental parenteral nutrition
STUDY: + Early SPN

CONTROL

Cum Survival

Days

Conclusions: Actively supervised nutritional intervention and providing near target energy requirements based on repeated IC was achievable in a general ICU and may be associated with lower hospital mortality.
Comparison the inflammatory effects of early supplemental parenteral nutrition plus enteral nutrition versus enteral nutrition alone in critically ill patients

1Abrishami R., 2Ahmadi A., 1Abdollahi M., 1Moosivand A., 1Khalili H., 2Najafi A., 1Gholami K., 1,3Hamishehkar H., 4Peivandi Yazdi A., 51Mojtahedzadeh M.

• Single center (teaching hospital) RCT; Iran
• N = 20 mixed ICU pts with SIRS and APACHE score > 10
• Day 0, 3, and 7:
  • Inflammatory indices: IL-6
  • Pre-albumin
• Objectives: To compare inflammatory parameters of EN and EN+PN regimens during the first week of nutritional support in the ICU
Comparison the inflammatory effects of early supplemental parenteral nutrition plus enteral nutrition versus enteral nutrition alone in critically ill patients

• Supplemental PN

  = 50% dextrose 500 mL

  + 10% amino acid solution 500 mL

\[ \therefore \text{PN calories} = 1,050 \text{ Kcal w/ volume } 1,000 \text{ mL} \]
Comparison the inflammatory effects of early supplemental parenteral nutrition plus enteral nutrition versus enteral nutrition alone in critically ill patients

Results: Differences in mean IL-6 levels between groups were not significant

p > 0.05
Results: Differences in mean serum pre-albumin between groups were not significant.

\[ p > 0.05 \]
Comparison the inflammatory effects of early supplemental parenteral nutrition plus enteral nutrition versus enteral nutrition alone in critically ill patients

- Mean length of hospitalization were not different
- **OMEGA score**: Higher score in EN+PN group
  → higher nursing workload (30 mins more)

**CONCLUSION**
No difference was found between EN and EN+PN regimens in regard to effects on inflammatory responses. Severity of illness may not change with these regimens. Nursing workload increases with implementation of supplemental PN. Until sufficient data from large randomized clinical trials is available using EN with parenteral supplementation is not recommended.
• **Objective:** Individually optimized energy provision by **SPN for 5 days after day 3 of ICU admission** *(early PN)* could improve clinical outcome for whom EN alone is insufficient.

• **Primary outcome:** **Nosocomial infection** at D8 and D28

• **Population:** Severely ill patients on **day 3 of ICU admission + received EN < 60% of energy target** *(N = 305)*
Optimisation of energy provision with supplemental parenteral nutrition in critically ill patients: a randomised controlled clinical trial

• **Energy targets**: at Day 3
  • Indirect calorimetry (IC)
  • If not possible, set targets as:
    — ♀: 25 kcal/kg IBW/day
    — ♂: 30 kcal/kg IBW/day

• **Intervention**: Day 4-7 (4 days)
  
  EN (n = 152) vs. SPN (n = 153)

Only 65% done
Findings

<table>
<thead>
<tr>
<th></th>
<th>EN</th>
<th>SPN (EN+PN)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean <strong>energy</strong> delivery between D 4-8</td>
<td>20 kcal/kg per day (77% of target)</td>
<td>&lt; 28 kcal/kg per day (103% of target)</td>
</tr>
<tr>
<td>Mean <strong>protein</strong> delivery between D 4-8</td>
<td>0.8 g/kg/day</td>
<td>&lt; 1.2 g/kg/day</td>
</tr>
<tr>
<td><strong>Nosocomial infection</strong> between D 9 - 28</td>
<td>58/152 (38%)</td>
<td>&gt; 41/153 (27%)</td>
</tr>
<tr>
<td></td>
<td>Hazard ratio 0.65, 95% CI 0.43–0.97; p=0.0338</td>
<td></td>
</tr>
</tbody>
</table>

**SPN group** had a **lower** mean number of **nosocomial infections** per patient (−0.42 [−0.79 to −0.05]; p=0.0248).

**Early PN ดีกว่า **
• **Interpretation:** Individually optimized energy supplementation with SPN starting 4 days after ICU admission could reduce nosocomial infections and should be considered as a strategy to improve clinical outcome in patients in the ICU for whom EN is insufficient.
Trial of the Route of Early Nutritional Support in Critically Ill Adults


- N = 2,400
- Early nutritional support: EN vs. PN

CONCLUSIONS

We found no significant difference in 30-day mortality associated with the route of delivery of early nutritional support in critically ill adults.

Evolution of PN Concept

**Past**
- PN was associated with ↑infectious complications and mortality in ICU patients
- 1980s: Hyperalimentation
  - Impaired immunity
  - ↑CO2 production
  - Organ dysfunction

**Present**
- Not that Bad !!!!!!!
- Goal-directed nutrition strategies
  - Safe
  - Improved quality of IVFE
  - Better IC, line care and glucose control

- PN should be considered in critically ill patients who cannot meet calorie and protein targets with EN alone

IVEF = intravenous lipid emulsion; IC = infectious control
### Early versus Late Parenteral Nutrition in Critically Ill Adults

- **Prospective, randomized, controlled, parallel-group multicenter (7) trial**
- **Critically ill adults** in the ICU who were nutritionally at risk but who were not chronically malnourished
- **Early EN**

<table>
<thead>
<tr>
<th>+ Early PN</th>
<th>V S.</th>
<th>+ Late PN</th>
</tr>
</thead>
<tbody>
<tr>
<td>- European guideline</td>
<td></td>
<td>- American and Canadian guidelines</td>
</tr>
<tr>
<td>- Start PN on D3</td>
<td></td>
<td>- Start PN on D8</td>
</tr>
<tr>
<td>- n = 2,312</td>
<td></td>
<td>- n = 2,328</td>
</tr>
</tbody>
</table>

**Early versus Late Parenteral Nutrition in Critically Ill Adults**

### Early EN +

<table>
<thead>
<tr>
<th>Early PN</th>
<th>Late PN</th>
</tr>
</thead>
<tbody>
<tr>
<td>• n = 2,312</td>
<td>• n = 2,328</td>
</tr>
<tr>
<td>• D1: 20% glucose solution (TC = 400 Kcal)</td>
<td>• 5% glucose solution</td>
</tr>
<tr>
<td>• D2: 20% glucose solution (TC = 800 Kcal)</td>
<td>• ** Withhold PN for 1 week</td>
</tr>
<tr>
<td>• ** D3: + 3-in-1 PN at 100% of caloric goal</td>
<td></td>
</tr>
</tbody>
</table>

*EPaNIC*
# Results: Safety and Primary Outcome

<table>
<thead>
<tr>
<th>Variable</th>
<th>Late-Initiation Group (N=2328)</th>
<th>Early-Initiation Group (N=2312)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Safety outcome</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vital status — no. (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Discharged live from ICU within 8 days</td>
<td>1750 (75.2)</td>
<td>&gt; 1658 (71.7)</td>
<td>0.007</td>
</tr>
<tr>
<td>Death</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>In ICU</td>
<td>141 (6.1)</td>
<td>146 (6.3)</td>
<td>0.76</td>
</tr>
<tr>
<td>In hospital</td>
<td>242 (10.4)</td>
<td>251 (10.9)</td>
<td>0.63</td>
</tr>
<tr>
<td>Within 90 days after enrollment†</td>
<td>257 (11.2)</td>
<td>255 (11.2)</td>
<td>1.00</td>
</tr>
<tr>
<td>Nutrition-related complication — no. (%)</td>
<td>423 (18.2)</td>
<td>434 (18.8)</td>
<td>0.62</td>
</tr>
<tr>
<td>Hypoglycemia during intervention — no. (%)‡</td>
<td>81 (3.5)</td>
<td>&gt; 45 (1.9)</td>
<td>0.001</td>
</tr>
<tr>
<td><strong>Primary outcome</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duration of stay in ICU§</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median (interquartile range) — days</td>
<td>3 (2–7)</td>
<td>4 (2–9)</td>
<td>0.02</td>
</tr>
<tr>
<td>Duration &gt;3 days — no. (%)</td>
<td>1117 (48.0)</td>
<td>&lt; 1185 (51.3)</td>
<td>0.02</td>
</tr>
<tr>
<td>Hazard ratio (95% CI) for time to discharge alive from ICU</td>
<td>1.06 (1.00–1.13)</td>
<td>0.04</td>
<td></td>
</tr>
</tbody>
</table>
### Results: Secondary Outcomes

<table>
<thead>
<tr>
<th>Variable</th>
<th>Late-Initiation Group (N=2328)</th>
<th>Early-Initiation Group (N=2312)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Secondary outcome</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>New infection — no. (%)</td>
<td>531 (22.8)</td>
<td>605 (26.2)</td>
<td>0.008</td>
</tr>
<tr>
<td>Any</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Airway or lung</td>
<td>381 (16.4)</td>
<td>447 (19.3)</td>
<td>0.009</td>
</tr>
<tr>
<td>Bloodstream</td>
<td>142 (6.1)</td>
<td>174 (7.5)</td>
<td>0.05</td>
</tr>
<tr>
<td>Wound</td>
<td>64 (2.7)</td>
<td>98 (4.2)</td>
<td>0.006</td>
</tr>
<tr>
<td>Urinary tract</td>
<td>60 (2.6)</td>
<td>72 (3.1)</td>
<td>0.28</td>
</tr>
<tr>
<td><strong>Inflammation</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median peak C-reactive protein level during ICU stay (interquartile range) — mg/liter</td>
<td>190.6 (100.8–263.2)</td>
<td>159.7 (84.3–243.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Mechanical ventilation</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median duration (interquartile range) — days</td>
<td>2 (1–5)</td>
<td>2 (1–5)</td>
<td>0.02</td>
</tr>
<tr>
<td>Duration &gt;2 days — no. (%)</td>
<td>846 (36.3)</td>
<td>930 (40.2)</td>
<td>0.006</td>
</tr>
<tr>
<td>Hazard ratio (95% CI) for time to definitive weaning from ventilation</td>
<td>1.06 (0.99–1.12)</td>
<td>1.62 (7.0)</td>
<td>0.07</td>
</tr>
<tr>
<td>Tracheostomy — no. (%)</td>
<td>134 (5.8)</td>
<td></td>
<td></td>
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<table>
<thead>
<tr>
<th>Parameters</th>
<th>Early EN +</th>
<th>Early PN</th>
<th>Late PN</th>
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<tr>
<td>Mortality</td>
<td>No significant difference</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fewer ICU infection</td>
<td>☣️</td>
<td>☣️</td>
<td>☬️ * but higher degree of acute inflammation*</td>
</tr>
<tr>
<td>Shorter duration of MV</td>
<td>☣️</td>
<td>☣️</td>
<td>☬️</td>
</tr>
<tr>
<td>Shorter duration of RRT</td>
<td>☣️</td>
<td>☣️</td>
<td>☬️</td>
</tr>
<tr>
<td>Shorter ICU stay</td>
<td>☣️</td>
<td>☣️</td>
<td>☬️ * but slightly increase in hypoglycemic episode *</td>
</tr>
<tr>
<td>Shorter hospital stay</td>
<td>☣️</td>
<td>☣️</td>
<td>☬️</td>
</tr>
<tr>
<td>Reduced health care cost</td>
<td>☣️</td>
<td>☣️</td>
<td>☬️</td>
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In conclusion, the early initiation of parenteral nutrition to supplement insufficient enteral nutrition during the first week after ICU admission in severely ill patients at risk for malnutrition appears to be inferior to the strategy of withholding parenteral nutrition until day 8 while providing vitamins, trace elements, and minerals. Late parenteral nutrition was associated with fewer infections, enhanced recovery, and lower health care costs.

Considerations of EPaNIC Trial

(** Late PN ดีกว่า **) 

- 61% elective heart surgery
- Need nutrition support ??
- 50% stayed in ICU < 3 days

Early versus Late Parenteral Nutrition in Critically Ill Adults

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<td></td>
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Considerations of EPaNIC Trial

- 61% elective heart surgery
  ?? Need nutrition support ??

- 50% stayed in ICU < 3 days

- Early PN group:
  Early hypertonic glucose load → hyperglycemia → poorer outcome??

(* * Late PN ดีกว่า **)
Conclusions: The increased costs by early PN were mainly pharmacy-related and explained by higher expenditures for PN and anti-infective agents. The use of Early-PN in critically ill patients can thus not be recommended for both clinical (no benefit) and cost-related reasons.
Trial of the Route of Early Nutritional Support in Critically Ill Adults


• N = 2,400
• Early nutritional support: EN vs. PN

CONCLUSIONS

We found no significant difference in 30-day mortality associated with the route of delivery of early nutritional support in critically ill adults.

Different recommendations on PN initiation in ICU

: 24 hrs $\rightarrow$ 7 days


Review

Nutrition therapy in critically ill patients- a review of current evidence for clinicians

Emma Ridley a,b,*, Dashiell Gantner a,c,d, Vincent Pellegrino c

Parenteral Nutrition (PN):
When to Start PN

Although the conflicting recommendations, it appears sensible to consider PN when EN cannot be delivered at all in patients who:

1. Malnourished (regardless of duration). PN should be commenced as early as possible if EN is contraindicated.

2. In surgical patients who have impaired GI function (pre- or postop) which would prevent oral or EN being commenced within 5-7 days.

3. In critically ill patients whom EN or oral nutrition is contraindicated or not expected to commence within 3 days.

Supplemental PN (SPN):

- Relatively new concept
- SPN should be considered in ICU when EN is insufficient for more than 2 days to prevent energy and protein deficiency: as recommended by ESPEN 2009

Guidelines for the Provision and Assessment of Nutrition Support Therapy in the Adult Critically Ill Patient: Society of Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.)

Stephen A. McClave, MD¹; Beth E. Taylor, RD, DCN²; Robert G. Martindale, MD, PhD³; Malissa M. Warren, RD⁴; Debbie R. Johnson, RN, MS⁵; Carol Braunschweig, RD, PhD⁶; Mary S. McCarthy, RN, PhD⁷; Evangelia Davanos, PharmD⁸; Todd W. Rice, MD, MSc⁹; Gail A. Cresci, RD, PhD¹⁰; Jane M. Gervasio, PharmD¹¹; Gordon S. Sacks, PharmD¹²; Pamela R. Roberts, MD¹³; Charlene Compher, RD, PhD¹⁴; and the Society of Critical Care Medicine† and the American Society for Parenteral and Enteral Nutrition‡

J Parenter Enteral Nutr. 2016;40(2):159-211
G. When to Use PN

G3. We recommend that, in patients at either low or high nutrition risk, use of supplemental PN be considered after 7–10 days if unable to meet > 60% of energy and protein requirements by the enteral route alone.

  Initiating supplemental PN prior to this 7- to 10-day period in critically ill patients on some EN does not improve outcomes and may be detrimental to the patient.
H. When Indicated, Maximize Efficacy of PN

H1. Based on expert consensus, we suggest the use of protocols and nutrition support teams to help incorporate strategies to maximize efficacy and reduce associated risk of PN.
• Overview of Nutrition Support
• Nutritional Support in ICU
• Role of PN in ICU

• Conclusions
Conclusions: Benefit of PN

: To easily meet calories and protein target
  ** regardless of GI function**

How to maximize efficacy and minimize complications of PN:

1) **Always + EN when possible** (SPN is better than PN alone)
2) As GI tolerance improves: ↑ EN and ↓ PN
3) Use PN for the **shortest possible duration**
4) Mode: complete **all-in-one bag** is preferred

(ESPEN 2009: Grade B)
Conclusions

• **EN** support is *always the preferred route* as compared to **PN**

• The *optimum timing of PN initiation in critically ill adults* in whom caloric targets cannot be met by **EN** alone is still *controversial but tend to be beneficial*

• **Combination of PN with EN** constitutes a strategy to *prevent nutritional deficit, but can easily cause overfeeding*
Conclusions

• Understanding the **barriers for enteral nutrition is essential** for health care providers to optimize nutritional support

• **SPN** could be the optimal modality to provide the calculated **energy targets** if this **cannot be reached by EN alone**

• Appropriate use of **PN** can minimize risk of **its complications** to the patients.
Conclusions

• In severely ill patients, route of energy delivery may not affect patient outcome, and delivering enough energy and substrate to hypercatabolic critically ill patients may be more important. Higher demands of these patients must be matched with an appropriate supply.
Parenteral Nutrition (PN) Used in Critically ill Adults

- Early or Late ??
- Safety ?? Yes
- Intravenous lipid emulsions (IVFE) ??

Alternative IVFE
QUESTIONS
???