Protein Supplementation in the Pediatric Intensive Care Unit

Jan Hau Lee, MBBS, MRCPCH, MCI
Children’s Intensive Care Unit
28th July 2017
Objectives

• Basis for protein supplementation
• Challenges in monitoring protein balance
• Current evidence for and against protein supplementation
• Future directions
Protein Homeostasis During Critical Illness

Protein Synthesis

Protein Catabolism

- PICU support
- Drugs
- Inflammation
- Underlying disease

Protein provision

Coss-Bu et al. *Nutr Clin Pract* 2017
Challenges to Assessment of Protein Homeostasis in the PICU

- Traditional markers are not robust
  - BMI, skin-fold thickness

- Body composition measurements
  - Dual-energy x-ray absorptiometry, CT, MRI

- Serum biomarkers
  - Albumin, pre-albumin, plasma amino acid

- Nitrogen balance

Ong C et al. *Clin Nutr* 2014
Coss-Bu et al. *Nutr Clin Pract* 2017
A Deeper Look Into Serum Biomarkers

Review

Nutrition biomarkers and clinical outcomes in critically ill children: A critical appraisal of the literature

Chengsi Ong a,*, Wee Meng Han a, Judith Ju-Ming Wong b, Jan Hau Lee c, d

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b Department of Pediatric Medicine, KK Women’s and Children’s Hospital, Singapore
c Children’s Intensive Care Unit, Department of Pediatric Subspecialties, KK Women’s and Children’s Hospital, Singapore
d Office of Clinical Sciences, Duke-NUS Graduate School of Medicine, Singapore

- Adults: Prealbumin and retinol binding protein
- Children: Albumin
- Mindful of limitations of albumin

Ong C et al. Clin Nutr 2014
Objectives

• Basis for protein supplementation

• Challenges in monitoring protein balance

• Current evidence for and against protein supplementation

• Future directions
Clinical Impact of Protein Inadequacy

Adequate enteral protein intake is inversely associated with 60-d mortality in critically ill children: a multicenter, prospective, cohort study

Nilesh M Mehta,2–5* Lori J Bechard,4,5 David Zurakowski,3,5,6 Christopher P Duggan,4,5 and Daren K Heyland6

2Critical Care Medicine, Department of Anesthesiology, Perioperative and Pain Medicine, 3Department of Anesthesiology, Perioperative and Pain Medicine, and 6Center for Nutrition, Division of Gastroenterology, Hepatology and Nutrition, Boston Children’s Hospital, Boston, MA; 4Harvard Medical School, Boston, MA; and 6Kingston General Hospital, Kingston, Canada

Nutrition Delivery Affects Outcomes in Pediatric Acute Respiratory Distress Syndrome

Judith Ju-Ming Wong, MBCh BAO, MRCPCH¹; Wee Meng Han, PhD²; Rehena Sultana, MSc³; Tsee Foong Loh, MBBS, MRCPCH⁴; and Jan Hau Lee, MBBS, MRCPCH, MCT⁴.⁵

- 109 children with ARDS
- Nutritional data over the first 7 days of ARDS
- Adequate calories: ≥ 80% of resting energy expenditure by day 3 of ARDS
- Adequate protein: ≥ 1.5 g/kg/day of protein by day 3 of ARDS
- Primary clinical outcomes: PICU mortality
- Secondary outcomes: Ventilator-free days and PICU-free days, multi-organ dysfunction and need for ECMO
Wong et al. *JPN* 2016
After adjusting for severity illness scores, oxygenation index, presence of comorbidities, inadequate protein intake was associated with mortality.

Wong et al. *JPEN* 2016
The New Power Couple

**Protein + Energy**

A minimum intake of **57 kcal/kg/day** and **1.5 g protein/kg/day** associated with positive protein balance

Bechard et al. *J Peds* 2012
How much protein and energy are needed to equilibrate nitrogen and energy balances in ventilated critically ill children?

Corinne Jotterand Chaparro a, 1, Jocelyne Laure Depeyre a, 1, David Longchamp b, Marie-Hélène Perez b, Patrick Taffé c, Jacques Cotting b, *

a Department of Nutrition and Dietetics, School of Health Professions, University of Applied Sciences Western Switzerland (HES-SO), Rue des Caroubiers 25, 1227 Carouge, Geneva, Switzerland
b Paediatric Intensive Care Unit, Medico-Surgical Department of Paediatrics, Lausanne University Hospital (CHUV), Rue du Bugnon 46, 1011 Lausanne, Switzerland
c Institute for Social and Preventive Medicine (IUMSP), Biopôle 2, Route de la Corniche 10, 1010 Lausanne, Switzerland

- 74 children [median: 21 (4-35) months]
  - 54 patients had surgical diagnoses
- 402 measurements of total urinary nitrogen and resting energy expenditure
Nitrogen balance was achieved with $1.5$ (95% CI: $1.4 - 1.6$) g/kg/day

Energy balance was achieved with $58$ (95% CI: $53 - 63$) kcal/kg/day

Early versus Late Parenteral Nutrition in Critically Ill Children

Tom Fivez, M.D., Dorian Kerklaan, M.D., Dieter Mesotten, M.D., Ph.D., Sascha Verbruggen, M.D., Ph.D., Pieter J. Wouters, M.Sc., Ilse Vanhorebeek, Ph.D., Yves Debaveye, M.D., Ph.D., Dirk Vlasselaers, M.D., Ph.D., Lars Desmet, M.D., Michael P. Casaer, M.D., Ph.D., Gonzalo Garcia Guerra, M.D., Jan Hanot, M.D., Ari Joffe, M.D., Dick Tibboel, M.D., Ph.D., Koen Joosten, M.D., Ph.D., and Greet Van den Berghe, M.D., Ph.D.

- RCT across 3 sites involving 1440 critically ill children
- Early PN (within 24 hours of PICU admission) vs. Late PN (8th day of PICU stay)
- No difference in mortality between the groups
- Late PN group
  - Reduced risk of nosocomial infection
  - Shorter duration of mechanical ventilation
  - Higher chance to discharge from PICU earlier

Fivez et al. NEJM 2016
Effect of early supplemental parenteral nutrition in the paediatric ICU: a preplanned observational study of post-randomisation treatments in the PEPaNIC trial

Ilse Vanhorebeek, Sascha Verbruggen, Michaël P Casaer, Jan Gunst, Pieter J Wouters, Jan Hanot, Gonzalo Garcia Guerra, Dirk Vlasselaers, Koen Joosten, Greet Van den Berghe

- Examined the doses of glucose, lipids and amino acids
- Analysis focused on first 7 days of PICU admission
- Adjusted for appropriate covariates
  - Diagnostic groups
  - Age
  - Severity of illness scores
  - Risk of malnutrition
  - Site

Infection freedom from mechanical ventilation

Day of PICU Stay

<table>
<thead>
<tr>
<th></th>
<th>Glucose</th>
<th>Aminoacids</th>
<th>Lipids</th>
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<tbody>
<tr>
<td></td>
<td>Early PN</td>
<td>Late PN</td>
<td>Early PN</td>
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<tr>
<td>Total dose†</td>
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<tr>
<td>Day 1</td>
<td>1440</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>58.2% (33.8–81.1)</td>
<td>16.8% (11.4–24.6)</td>
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<tr>
<td>Day 2</td>
<td>1188</td>
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<td></td>
<td>68.4% (44.2–86.4)</td>
<td>19.2% (14.3–31.6)</td>
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<td>Day 3</td>
<td>924</td>
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<td></td>
<td>60.9% (41.7–77.6)</td>
<td>19.8% (14.6–31.0)</td>
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<tr>
<td>Day 4</td>
<td>747</td>
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<tr>
<td></td>
<td>58.7% (40.1–72.9)</td>
<td>20.9% (14.7–31.5)</td>
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<tr>
<td>Day 5</td>
<td>611</td>
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<tr>
<td></td>
<td>56.6% (39.5–71.0)</td>
<td>21.8% (14.9–32.6)</td>
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<tr>
<td>Day 6</td>
<td>517</td>
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<tr>
<td></td>
<td>55.2% (39.3–71.6)</td>
<td>24.4% (16.1–35.2)</td>
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<tr>
<td>Day 7</td>
<td>443</td>
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<tr>
<td></td>
<td>54.2% (39.0–70.3)</td>
<td>25.8% (16.3–35.5)</td>
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<tr>
<td>Enteral dose</td>
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<tr>
<td>Day 1</td>
<td>1440</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>0% (0–0)</td>
<td>0% (0–0)</td>
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<tr>
<td>Day 2</td>
<td>1188</td>
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<tr>
<td></td>
<td>0% (0–3.5)</td>
<td>1.2% (0–8.8)</td>
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<tr>
<td>Day 3</td>
<td>924</td>
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<tr>
<td></td>
<td>0% (0–8.8)</td>
<td>1.2% (0–9.4)</td>
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<td>Day 4</td>
<td>747</td>
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<td></td>
<td>1.8% (0–14.1)</td>
<td>2.6% (0–16.4)</td>
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<td>Day 5</td>
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<td></td>
<td>3.3% (0–18.4)</td>
<td>4.4% (0–18.8)</td>
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<td>Day 6</td>
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<td></td>
<td>4.2% (0–19.3)</td>
<td>7.0% (0–22.7)</td>
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<td>Day 7</td>
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<td></td>
<td>4.8% (0–21.1)</td>
<td>9.2% (0–24.2)</td>
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<td>Parenteral dose</td>
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<tr>
<td>Day 1</td>
<td>1440</td>
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<tr>
<td></td>
<td>56.6% (32.0–79.7)</td>
<td>16.3% (10.7–23.6)</td>
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<td>Day 2</td>
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<td></td>
<td>63.9% (34.5–81.3)</td>
<td>16.9% (12.5–23.4)</td>
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<td>47.8% (25.5–68.7)</td>
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<td>Day 5</td>
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<td>42.6% (22.5–66.8)</td>
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<td>Day 7</td>
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<tr>
<td></td>
<td>38.2% (19.3–66.1)</td>
<td>11.8% (7.7–16.2)</td>
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</table>

Take Home Messages from PEPaNIC trial

• Limitations of the study
  – > 55% of the patients in early PN group were discharged by day 4
  – > 77% of patients in the late PN group were discharged by day 8 without having received any PN

• The pre-planned analysis did not take into account which group the patient came from

• Delaying PN with early initiation and stepwise advancement of EN seems sensible in most patient

• Nutrition prescription needs to be individualized

Metha. NEJM 2016
Ong and Lee. Lancet Resp Med 2017
Objectives

• Basis for protein supplementation
• Challenges in monitoring protein balance
• Current evidence for and against protein supplementation
• Future directions
Muscle Ultrasound: Novel Biomarker

Ong et al. J Parenter Enteral Nutrition 2017
1. A minimum protein intake of 1.5 g/kg/day

2. Optimal protein dose associated with improved clinical outcomes is not known

3. Provide protein early in the course of critical illness

Q34: What is the minimum protein intake that is adequate for critically ill children?
R34: On the basis of evidence from RCTs and as supported by observational cohort studies, we recommend a minimum protein intake of 1.5 g/kg/d. Protein intake higher than this threshold has been shown to improve outcomes in critically ill children. In critically ill children, the optimal protein intake required to attain a positive protein balance may be much higher than this minimum threshold. Negative protein balance may result in loss of lean muscle mass, which has been associated with poor outcomes in critically ill patients. Based on large observational studies, higher protein intake may be associated with lower 90-day mortality in mechanically ventilated children.

Q3-B: What is the optimal protein delivery strategy in the PICU?
R3-B: On the basis of evidence, we recommend provision of protein early in the course of critical illness to attain protein delivery goals and promote positive nitrogen balance. Delivery of a higher proportion of the protein goal has been associated with positive clinical outcomes in observational studies.

Q3-C: How should protein delivery goals be determined in critically ill children?
R3-C: The optimal protein dose associated with improved clinical outcomes is not known. We do not recommend the use of RDA values to guide protein prescription in critically ill children. These values were developed for healthy children and often underestimate the protein needs during critical illness.
Conclusion

• We need to be mindful of caloric and protein provision in critically ill children

• Too much and too little can be bad

• Future studies will need to focus on novel biomarkers for protein balance and address the issue of the clinical impact of protein supplementation
Thank you

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