Nutritional Support in the Critically Ill

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Little work has been done looking at nutritional status in the critically ill, and as they are a very heterogeneous group this may be a vital determinant of outcome and have a significant bearing on how aggressive we should be in feeding to requirements.
Not all patients are the same

Clapped out and in deficit  Tuned up and fit to go
Main issues

• Why feed?
• How much?
• Protein?
• Which route?
• Supplementary PN?
• Modulation of contents?
Shall we NG Feed Mr Jones?

Let's not complicate things!
The nutrition merry go round
Baseline requirements

- Water
- Electrolytes
- Macronutrients:
  "energy" = CHO / fat and protein
- Micronutrients: vitamins / trace elements
How much?

- Water = 25-30 ml/kg/day (+ losses)
- Energy = 25-30 kcal/kg/day
- CHO and Fat
- Protein = 1g/kg/day \( (1g \text{ N}_2 = 6.25 \text{ g protein}) \)

- Na = 1-2 mmol/kg/day
  K = 0.5-1mmol/kg/day
- Mg / PO$_4$
WHY FEED?

Catabolism with breakdown of muscle protein, fat and other complex molecules occurs faster than anabolism.
Why feed?

• The major goal of nutritional support during this period of acute illness has been to ensure the body has adequate energy and nutrients available to slow down this process of fat and muscle loss.

• PREVENT A CALORIE “DEBT”

• Better management of ventilatory failure, fever, anxiety, and pain, calorie consumption, as measured by calorimetry, has been dramatically reduced
Why feed?

• Loss of lean muscle mass is associated with worse outcomes including prolonged need for ventilatory support and disability

• Nutritional support should preserve protein and energy stores and bolster bodily processes needed to survive critical illness without lasting impairment
Why feed?

• Modify the inflammatory processes?

• Enhance the immune activity / anti-oxidant activity of the body?

• Is the catabolic process not physiological?
Baseline nutritional status

- MUST score
- Height / weight (BMI)
- History of intake / disease process

- Likely nutritional intake
Nutritional risk score 2002

- Nutritional status
  Wt. loss / BMI
  0-3
- Severity of disease
  Hip #
  Major surgery / stroke
  Head injury / ICU patient
  0-3

- Score > 3 “at risk”
- Score >5 “high risk”
NUTRIC score

- Age <50; 50-75; >75 0/1/2
- APACHE II <15; 15-20; 20-28; >28 0/1/2/3
- SOFA <6; 6-10; >10 0/1/2
- Co-morbidities 0-1; >1 0/1
- Days to ITU admission 0-1; >1 0/1
- (IL6 <400; >400 0/1)

- 5-9 High Score Associated with worse clinical outcomes (mortality, ventilation) most likely to benefit from aggressive nutrition therapy.
- 0-4 Low Score these patients have a low malnutrition risk
What should we do?

• *Feed the gut early, if you can*

• *You usually can*

• *If you can’t feed the gut, wait before starting TPN*
Reduce gut/lung axis of inflammation
Maintain MALT tissue
↑ Production of Secretory IgA at epithelial surfaces

↑ Muscle function, mobility, return to baseline function

Provide micro & macronutrients, antioxidants
Maintain lean body mass
↓ Muscle and tissue glycosylation
↑ Mitochondrial function
↑ Protein synthesis to meet metabolic demand

Maintain gut integrity
↓ Gut permeability
Support commensal bacteria
Stimulate oral tolerance
↑ Butyrate production
Promote insulin sensitivity, ↓ hyperglycemia (AGEs)

↑ Absorptive capacity
Influence anti-inflammatory receptors in GI tract
↓ Virulence of pathogenic organisms
↑ Motility, contractility

Attenuate oxidative stress
↓ Systemic Inflammatory Response Syndrome (SIRS)

↑ Dominance of anti-inflammatory Th2 over pro-inflammatory Th1 responses
Modulate adhesion molecules to ↓ transendothelial migration of macrophages and neutrophils
## Benefit of early EN: the evidence

<table>
<thead>
<tr>
<th>Yes: McLave / Heyland</th>
<th>No: Casaer / Van den Bergh</th>
</tr>
</thead>
<tbody>
<tr>
<td>1) Small RCTs and multiple meta-analyses</td>
<td>Meta analysis of 234 patients in 6 studies; poor studies</td>
</tr>
<tr>
<td>2) Meta-analyses of early EN in surgical patients</td>
<td></td>
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<tr>
<td>3) Observational cohort studies showing calorific deficit</td>
<td>No large high quality RCTs</td>
</tr>
<tr>
<td>4) Protocol driven EN delivery</td>
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</table>
How much?

25 – 30 kcals / kg / day

Extremes of BMI may differ
(16-18kcal / kg BMI > 30)

“The development of an accurate, easy-to-use, and affordable calorimeter is eagerly awaited” Heyland
How much should we give?

Much debate
Estimated with “adjustments”

Indirect calorimetry

TICACOS STUDY
Singer et al
Intensive Care Med 2011
37; 601-609
Optimising delivery

“The largest analysis of an international database (n = 7872) with robust statistical adjustment for potential confounders had shown that providing at least 80% of calories target is associated with improved clinical outcomes; the same result was also found for protein”

• Greater protein and calorie intake may be associated with improved mortality in higher risk critically ill patients: a multicentre, multinational observational study. Compher et al Crit Care Med Feb 2017

• What is best achievable practice in implementing the enhanced protein-energy provision via the enteral route feeding protocol in ICUs in the USA? Results of a multicentre quality improvement collaborative. Heyland et al JPEN Oct 2016
PERFECT study

Protein & Energy Requirements Fed for Every Critically ill patient every Time

• Early feeding 24 – 48 hours & quick progression to target rate
• Dietetic prescription or ‘starter’ regime
• GRV accepted and replaced up to 500ml
• Nurse-led strategies to increase feed rate
• End-of-day feed bolus (max 200ml)
• Bed end chart documentation
• Whole protein feeds: 28% more protein than Heyland group
• No prophylactic prokinetics

Sue Brierley-Hobson; Head of Dietetics YGC unpublished
## Energy & Protein

<table>
<thead>
<tr>
<th>Variable</th>
<th>RBF (n=46)</th>
<th>VBF (n=46)</th>
<th>Change</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ENERGY</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Energy (kcal/day):</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>1540.6 (±380.2)</td>
<td>1784.5 (±245.1)</td>
<td>&gt;243.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>% energy (all):</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>87.9 (±13.8)</td>
<td>101.3 (±11.7)</td>
<td>&gt;13.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>&gt;90% delivered</td>
<td>22 (47.8)</td>
<td>39 (84.8)</td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>PROTEIN</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Protein (g/day):</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>78.1 (±19.4)</td>
<td>98.1 (±23.7)</td>
<td>&gt;20</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>% protein (all):</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>89.2 (±19.5)</td>
<td>97.6 (±14.8)</td>
<td>&gt;8.6</td>
<td>0.022</td>
</tr>
<tr>
<td>&gt;90% delivered</td>
<td>26 (56.5)</td>
<td>34 (73.9)</td>
<td></td>
<td>0.134</td>
</tr>
</tbody>
</table>
Why can’t we feed the gut?

No access
Gut “dysfunction”

- High GRV
- Interuptions

*Gastric residual volumes, prokinetics and postpyloric feeding may not matter*
Gastric residual volumes

- Among adults requiring mechanical ventilation and receiving early enteral nutrition, the absence of gastric volume monitoring was not inferior to routine residual gastric volume monitoring in terms of development of VAP.

  Reignier J et al
  JAMA 2013: 309 (3); 249-256
  NUTRIREA 1 trial (449 pts)

- Diet volume: ratio of mechanically ventilated patients treated with enteral nutrition is unaffected by increasing the limit in GRV. A limit of 500 ml is not associated with adverse effects in gastrointestinal complications or in outcome variables. A value of 500 ml can be equally recommended as a normal limit for GRV.

  Montejo JC et al
  Intensive Care Med 2010: 36 (8); 1386 – 1393 REGANE study
Use of metoclopramide

- Neurological and cardiac side effects rarely reported in critically ill patients
- Feeding intolerance is common
- Alternative therapeutic strategies are limited
- The use of metoclopramide in critically ill patients to improve gastric emptying in patients with high gastric residual volumes to enhance enteral feeding

van der Meer YG, Venhuizen WA, Heyland DK, van Zanten ARH. Critical Care 2014, 18:502
Use of prokinetics

- Maximum duration of 7 (5) days is recommended
- Combination therapy with erythromycin if monotherapy is ineffective.
- If treatment failure: a post-pyloric feeding tube should be considered
PERFECT STUDY : Feed Tolerance

• No difference!

• GRV – change of nasogastric tubes…
  • RBF 38ml (±68ml); VBF 154ml (±240ml)

• Replaced 100% GRV (p = 0.521)
  • RBF IQR 20 -100 / VBF IQR 61-100

• Prokinetics: no difference (p = 0.819)
Post pyloric tubes?

- Early use of post-pyloric feeding instead of gastric feeding in critically ill adult patients with no evidence of impaired gastric emptying was not associated with significant clinical benefits.


- No difference between groups in the percentage of intended calories delivered: both received ~70% of their caloric goals.

- No difference in 2ndy outcomes, including VAP (~20%), ICU LOS, duration of mechanical ventilation, in-hospital mortality, GI side effects. Patients in the nasojejunal feeding group had higher rates of minor gastrointestinal bleeding (12% vs. 3%).
• **Clinical Takeaway:** Nasojejunal tube placement for enteral feedings doesn’t provide a detectable benefit in most critically ill patients, even those with clearly impaired gastric motility. Nasogastric tube feedings seem to achieve similar caloric goals, if pro-motility agents like metoclopramide and erythromycin are used. Certain patients (e.g., severe pancreatitis, post-abdominal surgery, gut stenosis), **may still benefit from postpyloric tube feedings.**

PERFECT outcomes

• Mortality
  – No difference
  – ICU: 14 in both groups (30.4%)
  – Hospital: RBF 17 (37%); VBF 18 (39%), p = 0.830
  – Probability (LR): % energy/protein; group; APACHE-II (25%) $p = 0.001$
  – Kaplan-Meier: 60-day hospital survival rate: $p = 0.693$
  – Cox regression: % energy/protein; group; APACHE-II (17%) $p = 0.001$

  – LOICUS (survivors ‘ready for discharge’)
  – No difference
  – Kaplan-Meier: RBF 11.1 days; VBF 8.4 days: $p = 0.367$
  – Cox regression: for protein $p = 0.112$
Ventilation (survivors)

- No group difference

- Cox regression 1:
  - Adj APACHE-II; group; % energy
  - Each 1% protein delivered, ↑ daily probability of extubation 1.022 fold (2.2%), \( p=0.040 \), 95% CI [1.001-1.043].

- Cox regression 2:
  - Adj APACHE-II; resp diagnosis
  - Daily probability extubation tripled if receiving >90% protein compared to receiving <80%, \( p=0.021 \) (HR 3.473, 95% CI [1.205-10.014]).

Key: Horizontal lines: bold dash=75th centile; pale dash=probability remaining ventilated; colour vertical lines: 25% of group extubated by day shown
What about Parenteral Nutrition?

ASPEN GUIDELINES 2016

• UNLESS NUTRITIONALLY COMPROMISED AND UNLIKELY TO RECEIVE EN FOR A NUMBER OF DAYS

• WAIT FOR 7 DAYS

ESPEN GUIDELINES 2009

• ALL PATIENTS WHO ARE NOT EXPECTED TO BE ON NORMAL NUTRITION WITHIN 3 DAYS SHOULD RECEIVE PN WITHIN 24 – 48 HRS IF EN CONTRAINDICATED OR NOT TOLERATED
PERCEIVED RISKS FROM PARENTERAL NUTRITION

• INFECTION
• OVER FEEDING
• HYPERGLYCAEMIA
• ACIDAEMIA
SUPPLEMENTAL PN

Conflicting evidence as to HARM

EPaNIC study: Early versus late PN in critically ill adults

Optimisation of energy provision with supplemental PN in critically ill patients:
Heidegger et al. Lancet 2013; 381: 385-393

Early PN in critically ill patients with short term relative contraindications to early EN. A RCT
Doig et al. JAMA 2013; 309: 2130-2138
CALORIES STUDY 2014

Pragmatic study: ~2400 patients / 33 ICU

1191 in PN group / 1197 in EN group

30 days mortality: 33.1% PN versus 34.2% EN

Significant reduction in rate of hypoglycemia (44 patients [3.7%] vs. 74 patients [6.2%]; P=0.006) and incidence of vomiting (100 patients [8.4%] vs. 194 patients [16.2%]; P<0.001).
No significant differences in the mean number of treated infectious complications (0.22 vs. 0.21; P=0.72) in 90-day mortality (442 of 1184 patients [37.3%] vs. 464 of 1188 patients [39.1%], P=0.40) or in the rates of 14 other secondary outcomes, or in rates of adverse events.

Caloric intake was similar in the two groups, with the target intake not achieved in most patients.
Where does this leave us?

- ASPEN 2016 guidelines
- Optimise PROTEIN intake 1.2 – 1.5 G / kg in high risk patients
- Volume base feeding
ASPEN 2016 summary

- Assess patients on admission to the ICU for nutrition risk, and calculate both energy and protein requirements to determine goals of nutrition therapy.

- Initiate enteral nutrition (EN) within 24–48 hours 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 (use prokinetic agent, continuous infusion, chlorhexidine mouthwash, elevate the head of bed, and divert level of feeding in the gastrointestinal tract).
ASPEN 2016 summary

• Implement enteral feeding 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 on EN.

• Start parenteral nutrition early when EN is not feasible or sufficient in high-risk or poorly nourished patients
Doses of protein in the range of 1.2-2.5 g/kg/d may be required in the setting of the intensive care unit (ICU) to optimize nutrition therapy and reduce mortality. Protein doses in this range may be needed to best stimulate new protein synthesis and preserve muscle mass. Achieving protein goals the first week following admission to the ICU should take precedence over meeting energy goals. High-protein hypocaloric (providing 80%-90% of caloric requirements) feeding may evolve as the best strategy during the initial phase of critical illness to avoid overfeeding, improve insulin sensitivity, and maintain body protein homeostasis, especially in the patient at high nutrition risk.
Role of anti-oxidants?

8 trials published between 2004 and 2013

They should be considered!
No clear recommendation with respect to composition or dose of micronutrients and trace elements

Signal towards reduced mortality

Antioxidant micronutrients in the critically ill: a systematic review and meta-analysis
Manzanares W et al. Crit Care 2012;16(2): R66
Selenium?

7 trials published between 2004 to 2013

Parenteral selenium should be considered
Significant treatment effect with respect to reduced infections

High dose bolus monotherapy?
Systematic review and meta analysis of RCTs
Alhazzanni et al Crit Care Med 2013;41:1555-1564
Glutamine?

• Parenteral supplementation
  Early evidence was of benefit
  SIGNET trial (0.1 – 0.2g / day): no benefit
  REDOX trial (0.6 – 0.8 g / day): harm

  Scandanavian trial 2011 stopped early
www.criticalcarenutrition.com