What’s New In Nutrition Research?

Dr Lee-anne Chapple
Who am I?
Not Carol Hodgson
Who am I?
Who am I?

Critical Care Dietitian, RAH
Post-Doctoral Research Fellow, ICU Research
Click to add title

- Click to add text
THE GREATEST PRESENTATION IN THE WORLD...
TRIBUTE
What do we want to achieve for our patients?
Acute Skeletal Muscle Wasting in Critical Illness

Days 1, 3, 7 & 10

17.7% decrease in CSA-RF at day 10
(p<0.001)
22 pts
Thickness: VI, VL, RF; CSA: RF
Days 3, 5, 7 & 10, awakening, & ICU D/C
30% ↓ in RF & VI thickness & RF CSA
14% ↓ in VL thickness
2 weeks into adm
2.58 cm

6 weeks into adm
1.28 cm

Chapple et al, 2017, CCR
Day 21 measure
3.66 cm

3 month follow-up
2.74 cm

Chapple et al, 2017, CCR
March 2003

One-Year Outcomes in Survivors of the Acute Respiratory Distress Syndrome

Margaret S. Herridge, M.D., M.P.H., Angela M. Cheung, M.D., Ph.D., Catherine M. Tansey, M.Sc., Andrea Matte-Martyn, B.Sc., Natalia Diaz-Granados, B.Sc., Fatima Al-Saidi, M.D., Andrew B. Cooper, M.D., Cameron B. Guest, M.D., C. David Mazer, M.D., Sangeeta Mehta, M.D., Thomas E. Stewart, M.D., Ailala Bar; Ph.D., Deborah Cook, M.D., and Arthur S. Slutsky, M.D., for the Canadian Critical Care Trials Group

April 7, 2011

Functional Disability 5 Years after Acute Respiratory Distress Syndrome

Margaret S. Herridge, M.D., M.P.H., Catherine M. Tansey, M.Sc., Andrea Matté, B.Sc., George Tomlinson, Ph.D., Natalia Diaz-Granados, M.Sc., Andrew Cooper, M.D., Cameron B. Guest, M.D., C. David Mazer, M.D., Sangeeta Mehta, M.D., Thomas E. Stewart, M.D., Paul Kodlow, B.Sc., Deborah Cook, M.D., Arthur S. Slutsky, M.D., and Angela M. Cheung, M.D., Ph.D., for the Canadian Critical Care Trials Group
What might ameliorate muscle wasting?
What do we know about protein in critical illness?
Plethora of opinion pieces!
Summary Points and Consensus Recommendations From the International Protein Summit

Ryan T. Hurt, MD, PhD; Stephen A. McClave, MD; Robert G. Martindale, MD, PhD; Juan B. Ochoa Gautier, MD, FACS, FCCM; Jorge A. Coss-Bu, MD; Roland N. Dickerson, PharmD; Daren K. Heyland, MD, MSc; L. John Hoffer, MD, PhD; Frederick A. Moore, MD; Claudia R. Morris, MD; Douglas Paddon-Jones, PhD; Jayshil J. Patel, MD; Stuart M. Phillips, PhD; Saul J. Rugeles, MD; Menaka Sarav, MD; Peter J. M. Wejs, PhD; Jan Wernerman, MD, PhD; Jill Hamilton-Reeves, PhD, RD, CSO; Craig J. McClain, MD; and Beth Taylor, DCN, RD-AP
What do the guidelines say?
**American ICU Guidelines:**

**Question:** Does the amount of protein provided make a difference in clinical outcomes of adult critically ill patients?

**C4.** We suggest that sufficient (high-dose) protein should be provided. Protein requirements are expected to be in the range of 1.2–2.0 g/kg actual body weight per day and may likely be even higher in burn or multitrauma patients (see sections M and P).

[Quality of Evidence: Very Low]
Level of evidence

- Expert consensus: 53
- Very low: 16
- Low to very low: 3
- Low: 11
- Moderate to low: 1
- Moderate: 6
- Moderate to high: 3
- High: 1
European ICU Guidelines:

1.3 g/kg/day delivered progressively
‘There are insufficient data to make a recommendation regarding the use of high protein diets for head injured patients and other critically ill patients’
But what’s the evidence?
Provision of protein and energy in relation to measured requirements in intensive care patients

Matilde Jo Allingstrup 1,2, Negar Esmailzadeh 3, Anne Wilkens Knudsen 2, Kurt Espersen 2, Tom Hartvig Jensen 4, Jørgen Wiis 4, Anders Perner 4, Jens Kondrup 5

1 Department of Intensive Care 4121, Copenhagen University Hospital, Rigshospitalet, Blegdamsvej 9, 2100 Copenhagen, Denmark
2 Department of Human Nutrition, Faculty of Life Sciences, University of Copenhagen, 3030 Copenhagen, Denmark
Lowest mortality was in those patients that met protein targets.
119 patients

0.8 vs 1.2 g/kg amino acids

Higher protein:
- Greater amelioration of ultrasound-derived muscle loss
- Trend towards improved hand-grip strength
RCT level evidence for augmented protein?

Figure 2. Effect of protein delivery on mortality*

<table>
<thead>
<tr>
<th>Author (year)</th>
<th>OR (95% CI)</th>
<th>% Weight</th>
</tr>
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<tbody>
<tr>
<td>Keams (2000)</td>
<td>1.13 (0.29–4.44)</td>
<td>3.10</td>
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<tr>
<td>Goeters (2002)</td>
<td>1.70 (0.57–5.10)</td>
<td>4.38</td>
</tr>
<tr>
<td>Ibrahim (2002)</td>
<td>1.45 (0.68–3.12)</td>
<td>7.14</td>
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<tr>
<td>Ozgultekin (2008)</td>
<td>1.11 (0.37–3.31)</td>
<td>4.41</td>
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<tr>
<td>Hsu (2009)</td>
<td>0.80 (0.39–1.65)</td>
<td>7.58</td>
</tr>
<tr>
<td>Rice (2011)</td>
<td>1.19 (0.60–2.35)</td>
<td>8.11</td>
</tr>
<tr>
<td>Singer (2011)</td>
<td>2.33 (1.07–5.09)</td>
<td>6.94</td>
</tr>
<tr>
<td>Huang (2012)</td>
<td>0.77 (0.34–1.75)</td>
<td>6.50</td>
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<tr>
<td>Heyland (2013)</td>
<td>0.78 (0.61–1.00)</td>
<td>15.09</td>
</tr>
<tr>
<td>Braunschweig (2014)</td>
<td>0.28 (0.10–0.83)</td>
<td>4.51</td>
</tr>
<tr>
<td>Ferrie (2015)</td>
<td>0.69 (0.27–1.79)</td>
<td>5.39</td>
</tr>
<tr>
<td>Doig (IV AA) (2015)</td>
<td>1.22 (0.76–1.98)</td>
<td>11.04</td>
</tr>
<tr>
<td>Doig (refeeding) (2015)</td>
<td>0.37 (0.19–0.70)</td>
<td>8.52</td>
</tr>
<tr>
<td>Qiu (2015)</td>
<td>1.20 (0.57–2.54)</td>
<td>7.29</td>
</tr>
<tr>
<td>Overall (I² = 48.2%, P = 0.023)</td>
<td>0.93 (0.72–1.22)</td>
<td>100.00</td>
</tr>
</tbody>
</table>

Davies, et al. Critical Care & Resus. 2017
The number of powered, blinded RCTs conducted to evaluate EN protein dose?
The number of powered, blinded RCTs conducted to evaluate EN protein dose? 

ZERO
And in fact....

In a review of RCTs of nutrition interventions in critically ill adults over a 10 year period only ONE included a functional outcome measure

Chapple et al, *manuscript in preparation*
So....
What evidence do we need to generate in order to change practice?
Does increased protein delivery to critically ill patients improve ICU survival and recovery in survivors?
How is additional protein handled in the stomach?
Is additional protein absorbed and taken up into muscle?

How is additional protein handled in the stomach?
Can we feasibly deliver additional protein? How is additional protein handled in the stomach? Is additional protein absorbed and taken up into muscle?
How is additional protein handled in the stomach?
Gastric emptying

% retention at 240 mins

ICU patients

Healthy subjects

P<0.001

Chapman et al, Gut 2011
Does protein dose of an enteral nutrition formula affect rate of gastric emptying?
Cross-over RCT

40 ICU patients:
20 feed intolerant
20 feed tolerant

12 healthy subjects
Receive bolus of high vs low protein EN formula

Measure gastric emptying over 4 hours
4 hour fast

Test Meal

-5 0 240

Time (min)

Blood samples for the measurement of BGL, 3-OMG and gut hormones

Scintigraphy
What do we want to measure?

1. Rate of gastric emptying
2. Gut hormone levels
3. Glucose absorption
Is additional protein absorbed and taken up into muscle?
Glucose absorption and gastric emptying in critical illness

Marianne J Chapman1,2, Robert JL Fraser2,5, Geoffrey Matthews4, Antonietta Russo2, Max Bellon5, Laura K Besanko3, Karen L Jones2, Ross Butler4, Barry Chatterton5 and Michael Horowitz2

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This is an open access article distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/2.0), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.
Effect of Critical Illness on Triglyceride Absorption

Yasmine Al Abdelhamid, MBBS; Caroline E. Cousins, BSc (Hons); Jennifer A. Sim, B Med Sci (Hons); Max S. Bello, Dip Med Tech, A Dip Nut Med; Nan Q. Nguyen, MBBS, PhD, FRACP; Michael Horowitz, MBBS, PhD, FRACP; Marianne J. Chapman, BMBS, PhD, FANZCA, FCICM; and Adam M. Deane, MBBS, PhD, FRACP, FCICM.
But what about protein?
We try to increase protein delivery in practice

Not known if additional protein will be:
- absorbed adequately for an effect
- incorporated into muscle
Protein Absorption in Critical Illness
PACE study
Are:

- protein digestion
- exogenous amino acid absorption
- basal muscle protein fractional synthesis
- post-prandial muscle protein fractional synthesis

impaired in critical illness compared to health?
Protein Kinetics

Stable isotope-labelled amino acids

Delivered intravenously

Enteral protein dilutes amino acid pool
Intrinsically Labeled Milk

\[
\text{●} = \text{L-[1-^{13}\text{C}]-phenylalanine}
\]
Single study day
~10-12 hours

20 ICU patients
10 healthy controls
L-[ring-$^2$H$_5$]-phenylalanine
L-[3,5-$^2$H$_2$]-tyrosine
L-[1-$^{13}$C]-leucine
Milk protein infusion:
240 ml, 20g protein

L-[1-^{13}C]-phenylalanine
L-[1-^{13}C]-leucine
Muscle biopsy
Tracer enrichment

Measured by mass spectroscopy in blood and muscle tissue
Understanding of basic metabolism

?  ?  ?

Improved patient-centred outcomes
Can we feasibly deliver additional protein?
Who is familiar with TARGET?
The Augmented versus Routine approach to Giving Energy Trial (TARGET)
4000 patients

≥ 18 years age

MV, expected to stay ventilated >48hrs

Received <12hrs EN or planned to commence EN
4000 patients

1 kcal/ml
EN formula

or

1.5 kcal/ml
EN formula
Does augmentation of calorie delivery using an energy-dense enteral nutrition formulation in mechanically ventilated patients increase 90-day survival compared with routine care?
31st Annual Congress
Paris
TARGET – PROTEIN

Rinaldo Bellomo, Marianne Chapman, Lee-anne Chapple, Andrew Davies, Adam Deane, Suzie Ferrie, Mark Finnis, Stephanie O’Connor, Sandra Peake, Emma Ridley, Matthew Summers, Trish Williams and Paul Young.
Are we able to conduct a randomised double-blinded study in which administration of formula X (high protein) when compared to formula Y (standard care) will result in the delivery of more protein to enterally-fed critically ill patients?

+ Formula X will delivery protein dose within international guidelines
What is standard care?

INS data of 2776 patients from ANZ

Prescription: 1.12 (0.25) g/kg/d

Delivery: 0.6 g/kg/d

Data are mean (SD) from International Nutrition Survey
Ridley, et al. 2018, JPEN
High protein: aim between 1.2-2 g/kg/d
120 patients, 8 ANZ sites

Inclusion

• ≥ 18 years
• (Invasive) Mechanical Ventilation
• EN < 12 hours
• Anticipate EN in ICU until at least the day after tomorrow

Exclusion

• Anticipate any oral nutritional intake before the day after tomorrow
• PN > 12 hours this ICU
• Any other trial of nutritional therapy
• Treating clinician considers goal rate or protein dose to be C/I
• Requirement for specific nutritional therapy
1° Separation of protein dose between groups

2° Feasibility outcomes:
   - Blinding, tolerance of intervention, recruitment rate, biochemical outcomes, protein dose for intervention within international guidelines

3° Clinical outcomes:
   - Mortality, LOS, ventilatory requirements, need for RRT, functional recovery
RAH, Alfred, QEH, Austin, Frankston, RPAH, RMH, and Wellington

Project Managers: Lee-anne Chapple & Matthew Summers

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Industry supported

PI: Adam Deane
2020 Funding
Phase 3 trial from ~2021
Where will this all lead?
Thank you

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Thank you