Immunomodulatory Therapy:

When & How to Use It in the Critically Ill Patient?

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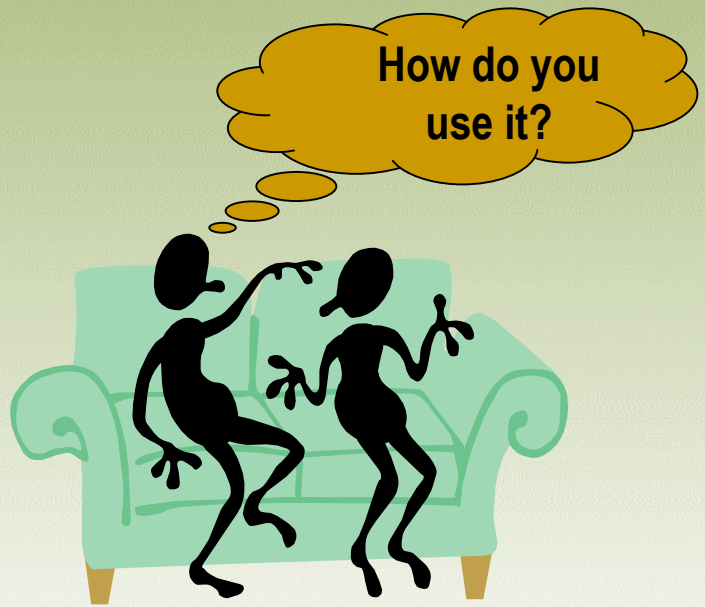
Outline

- Review the current CPGs for Immunonutrition in Critically Ill Patients
- Nutrients:
  - Arginine
  - Glutamine
  - Fish Oils
  - Antioxidants
- Nutrient administration:
  - Route, timing, duration and dosage



Canadian Clinical Practice Guidelines for Nutrition Support in Mechanically Ventilated, Critically Ill Adult Patients*

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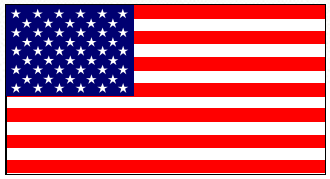
Guidelines for the Provision and Assessment of Nutrition Support Therapy in the Adult Critically Ill Patient:

Society of Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.)

Stephen A. McClave, MD; Robert G. Martindale, MD, PhD;
Vincent W. Vanek, MD; Mary McCarthy, RN, PhD; Pamela Roberts, MD;
Beth Taylor, RD; Juan B. Ochoa, MD; Lena Napolitano, MD; Gail Cresci, RD;
the A.S.P.E.N. Board of Directors; and the American College of Critical Care Medicine

SCCM and ASPEN Guidelines:

Released May 2009



http://intl.elsevierhealth.com/journals/clnu

ESPEN GUIDELINES

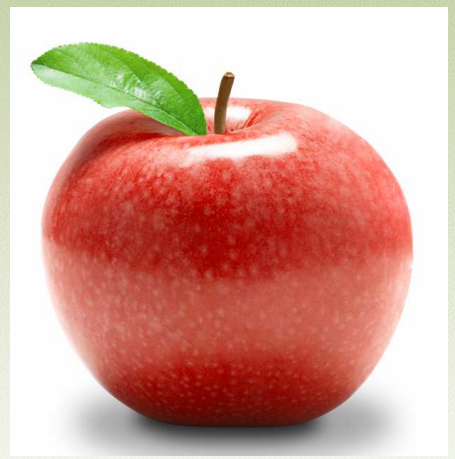
ESPEN Guidelines on Enteral Nutrition: Intensive care ☆

K.G. Kreymann[a,*], M.M. Berger[b], N.E.P. Deutz[c], M. Hiesmayr[d], P. Jolliet[e], G. Kazandjiev[f], G. Nitenberg[g], G. van den Berghe[h], J. Wernerman[i], DGEM: ☆☆ C. Ebner, W. Hartl, C. Heymann, C. Spies

Clinical Nutrition (2006) 25, 210-223

www.espen.org/espenguidelines.html

Are all critically ill patients equal?



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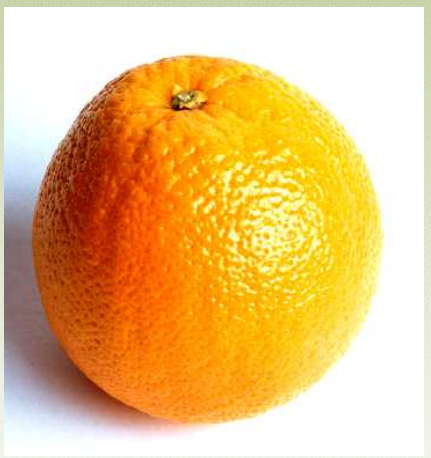
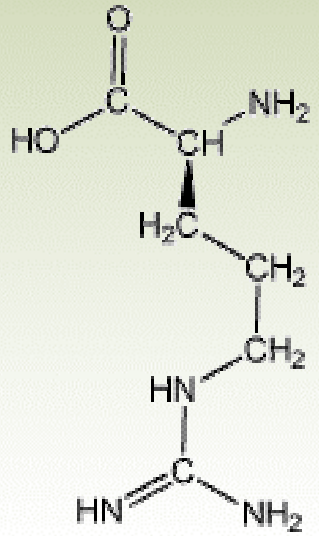



Arginine
Antioxidants
Glutamine
ω-3 Fatty Acids
Selenium

Should we expect the impact of immunomodulating diet therapy to be the same?

Arginine Supplemented Diets?



Arginine Containing Enteral Formulas

Product	Arginine	Manufacturer
Impact	12.5 g/L	Novartis/Nestle
Immun-Aid	14.0 g/L	McGraw Inc.
Perative*	6.8g/L (8.05 g/L)	Abbott Laboratories
Optimental*	5.5 g/L (3.6g/L)	Abbott Laboratories
Stresson	9.0 g/L	Nutricia
Recovan	10.0 g/L	Fresenius-Kabi
Crucial	10.0 g/L	Novartis/Nestle

* Available in Canada

Diets Supplemented with Arginine:

- No effect on mortality.
- No effect on rate of infectious complications.
- May reduce length of ICU stay, hospital stay and mechanical ventilation.

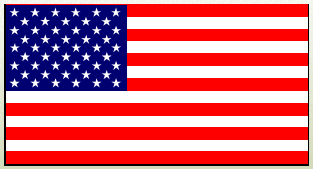
Canadian CPG, January 2009

Recommendation:

- "Based on 4 level 1 studies and 18 level 2 studies, we recommend that diets supplemented with arginine NOT be used for critically ill patients."

Canadian CPG, January 2009

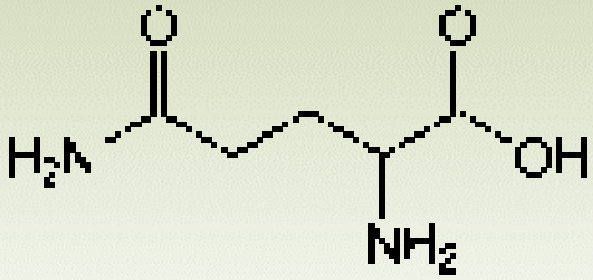
Recommendation:



- "Immune-modulating formulations containing arginine are safe enough to use in mild to moderate sepsis (APACHE II <15), but that caution should be employed if utilized in patients with severe sepsis."

McClave et al., *JPEN (*2009); 33; 277.

Enteral Glutamine Supplementation?



Glutamine Containing Enteral Formulas

Product	Glutamine	Manufacturer
Immun-Aid	9.0 g/L	McGraw Inc.
Recovan	15.0 g/L	Fresenius-Kabi
Stresson	13.0 g/L	Nutricia

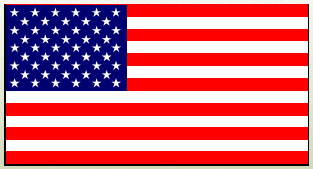
Recommendation: ESPEN

- Enteral glutamine should be considered in burn and trauma patients.
  - reduction in mortality in burn patients
  - reduction in infectious complications in burn and trauma patients
  - reduction in hospital length of stay in burn and trauma patients

- Insufficient data to support the routine use of enteral glutamine in other critically ill patients.

Canadian CPG, January 2009

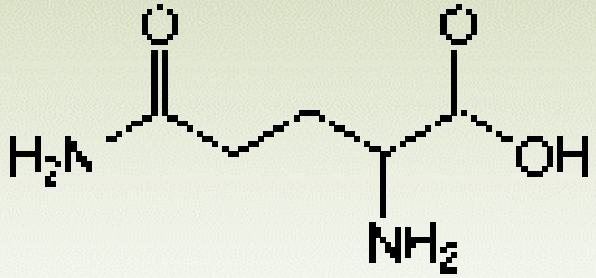
Recommendation:



- The addition of enteral glutamine to an EN regimen (not already containing supplemental glutamine) should be considered in burn, trauma, and mixed ICU patients.
- 0.3-0.5 g/kg/day in 2 or 3 divided doses

McClave et al., *JPEN (*2009); 33; 277.

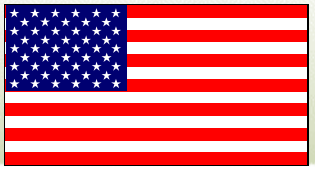
Parenteral Glutamine Supplementation?



Parenteral Glutamine (0.5g/kg/day)

- Associated with a significant ↓ in mortality.
- Associated with a significant ↓ in infectious complications.
- Associated with a significant ↓ in hospital length of stay.

Recommendation:



- Parenteral supplementation with glutamine, where available, is **strongly recommended** for critically ill patients.

McClave et al., *JPEN (*2009);33; 277.

Canadian CPG, January 2009

Parenteral Glutamine Supplementation

- "Supplementation of critically ill patients requiring TPN should be the standard of care unless new trials refute this clear evidence of benefit."

Wischmeyer PE. Curr Opin Gastroenterol (2008): 24: 192

ω-3 Supplemented Diets?

Recommendation:

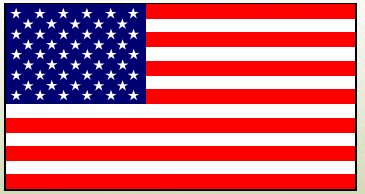


Table 14. Anti-inflammatory Immune-Modulating Enteral Nutrition (Oxepa) vs Standard Enteral Nutrition (Stand EN) in Patients With Acute Respiratory Distress Syndrome (ARDS), Acute Lung Injury (ALI), and Sepsis

Study	Population	Study Groups	Mortality	LOS Days, Mean ± SD	Ventilator Days, Mean ± SD	New Organ Dysfunction
Gadek et al, 1999[207] Level I	ARDS ICU (n = 146)	Oxepa	11/70 (16%) ICU	11.0 ± 0.9 ICU[a]	9.6 ± 0.9[a]	7/70 (10%)[a]
		Stand EN	19/76 (25%) ICU	14.8 ± 1.3 ICU	13.2 ± 1.4	19/76 (25%)
		Oxepa		27.9 ± 2.1 Hosp		
		Stand EN		31.1 ± 2.4 Hosp		
Singer et al, 2006[208] Level I	ARDS and ALI (n = 100)	Oxepa	14/46 (30%) at 28 d[a]	13.5 ± 11.8 ICU	12.1 ± 11.3	NR
		Stand EN	26/49 (53%) at 28 d	15.6 ± 11.8 ICU	14.7 ± 12.0	
Pontes-Arruda et al, 2006[209] Level I	Severe sepsis ICU (n = 165)	Oxepa	26/83 (31%) at 28 d[a]	17.2 ± 4.9 ICU[a]	14.6 ± 4.3[a]	32/83 (39%)[a]
		Stand EN	38/82 (46%) at 28 d	23.4 ± 3.5 ICU	22.2 ± 5.1	66/82 (80%)

SD, standard deviation; NR, not reported; ICU, intensive care unit; LOS, length of stay; d, day(s).
[a] $P \leq .05$.
Oxepa: Abbott Nutrition; Columbus, OH.

McClave et al., *JPEN* (2009);33; 277

Canadian CPG, January 2009

Combined antioxidants and trace elements?

Recommendation:

"Based on 3 level 1 and 13 level 2 studies, the use of supplemental combined vitamins and trace elements should be considered in critically ill patients."

Canadian CPG, January 2009

WHEN?

Nutrient	Candidates
Arginine	NO
Enteral Glutamine	Burn/Trauma
Parenteral Glutamine	✓
Omega – 3 FA	✓ ARDS/ALI
Antioxidants	✓
Parenteral Selenium	NO

WHEN?

- Patients with mild sepsis (APACHE II <15) should receive an immune-modulating formula.
- May be harmful in patients with severe sepsis, therefore is not recommended.

Clin Nutr (2006) 25, 210-223

How Long?

- Minimum duration of 5 days – then switch to standard formula

OR

- While patient is in ICU or until infectious complications are reduced.

- Criteria for discontinuation:
  - ↓ CRP and ↑ Prealbumin

JPEN (2001); 25; S61

Dosage

- Minimum 50% - 60% of goal energy requirements should be delivered.
- If the patient cannot tolerate >700 ml/day then immune-modulating formula is **NOT** recommended.

McClave et al., *JPEN (*2009);33; 277

Clin Nutr (2006) 25, 210-223

Saskatoon Health Region

"The role of immuno-modulating diets in critically ill patients is controversial…"

Marik & Zaloga, Intensive Care Med (2008) 34:1984.

Thank-you!

CANADA
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