

# Enteral nutrition in medical ICU patients : review of advances in last five years

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Our food should be our medicine and our medicine  
should be our food.

—Hippocrates

# Introduction

- Nutritional support in the ICU is a highly controversial subject
- Emphasis has shifted from nutritional *support* to nutritional *therapy*
- Variety of guidelines and extensive data is available

# What is enteral nutrition?

- Nutrition provided through the gastrointestinal tract via a tube, catheter, or stoma that delivers nutrients distal to the oral cavity
  - A.S.P.E.N. Enteral Nutrition Practice Recommendations: JPEN 2009
- All forms of nutritional support that imply the use of “dietary foods for special medical purposes” independent of the route of application. It includes oral nutritional supplements (ONS) as well as tube feeding via nasogastric, nasoenteral or percutaneous tubes
  - ESPEN GUIDELINES ON ENTERAL NUTRITION: Clinical Nutrition 2006

# Enteral vs parenteral

- Ongoing debate
- Though the balance is in favour of EN there is no hard evidence to support it
- Earlier trials showing increased mortality from PN have been criticized for not considering the effect of hyperglycemia on the rate of infections

- Rationale of EN
  - lower cost
  - fewer and less severe complications
  - lower rates of infection
  - better rates of wound healing
  - association with lower gut mucosal permeability

Deitch EA, Winterton J, Li M, et al. The gut as a portal of entry for bacteremia: role of protein malnutrition. *Ann Surg* 1987;205:681–692

- However, achieving targeted nutritional goals with exclusive enteral nutrition is difficult
- Inability to deliver adequate energy results in energy deficits that cannot be compensated later on during the ICU stay and that have been associated with increased morbidity and mortality in ICU patients
  - Villet S, Chiolero RL, Bollmann MD, et al. Negative impact of hypocaloric feeding and energy balance on clinical outcome in ICU patients. *Clin Nutr* 2005; 24:502–509
  - Dvir D, Cohen J, Singer P. Computerized energy balance and complications in critically ill patients: an observational study. *Clin Nutr* 2006; 25:37–44

- ***Total parenteral nutrition or ‘Total poisonous nutrition’***

- Marik PE, Pinsky M. Death by parenteral nutrition. *Intensive Care Med* 2003;29:867–869

- **Problems**

- gut mucosal atrophy related to bowel starvation
- metabolic complications such as hyperglycemia and hypertriglyceridemia
- endocrine abnormalities,
- immunological dysfunction
- infections



**Table 1 Relevant meta-analyses comparing enteral with parenteral nutrition in the critically ill patient showing no worsened clinical outcome**

References	Group comparison	Studies		Clinical outcome	
		Number included	Year of publication	Mortality	Infection
Braunschweig <i>et al.</i> [36]	EN vs. TPN	20	1986–1992	NS	Decreased
Heyland <i>et al.</i> [40]	EN vs. TPN	12	1986–2001	NS	Decreased
Dhaliwal <i>et al.</i> [39]	EN + TPN vs. EN	5	1987–2000	NS	NS
Gramlich <i>et al.</i> [37]	EN vs. TPN	13	1983–2001	NS	Decreased
Peter <i>et al.</i> [38]	EN vs. TPN	24	1980–2002	NS	Decreased
Simpson and Doig [35]	EN vs. TPN	11	1983–2002	Decreased	Decreased

EN, enteral nutrition; TPN, total parenteral nutrition.

significant mortality benefit in favor of PN [OR 0.51, 95% CI 0.27–0.97]

confined to trials comparing it with late enteral nutrition

Simpson F, Doig GS. Parenteral vs. enteral nutrition in the critically ill patient: a meta-analysis of trials using the intention to treat principle. *Intensive Care Med* 2005; 31:12–23.

- **Current practice in nutritional support and its association with mortality in septic patients—Results from a national, prospective, multicenter study**
  - Elke *et al.* Crit Care Med 2008 Vol. 36, No. 6
- Studied 415 patients with severe sepsis or septic shock in Germany
  - 20.1% EN
  - 35.1% PN
  - 34.6% mixed nutrition
- Mortality was significantly higher in patients receiving exclusively parenteral (62.3%) or mixed nutrition (57.1%) than in patients with exclusively enteral nutrition (38.9%) (*p* 0.005)

- Jury still out on parenteral nutrition
- Most guidelines recommend enteral nutrition upfront, in the absence of specific contraindications
- Parenteral nutrition indicated only if enteral nutrition is insufficient or contraindicated
- Concept of '***supplemental parenteral nutrition***' to optimize enteral nutrition, when the latter is unable to cover energy needs
  - Enteral vs. parenteral nutrition for the critically ill patient: a combined support should be preferred. Heidegger CP, Darmon P and Pichard C. Current Opinion in Critical Care 2008, 14:408–414

# Early vs late

- Early nutrition support is defined as starting within the first 24–48 h following admission to an ICU in all critically ill patients
  - Dhaliwal R, Heyland D. Nutrition and Infection in the intensive care unit: what does the evidence show? *Curr Op Crit Care* 2005; 11:461–467
- Well designed interventional trials demonstrating the specific role for routine early nutrition support are lacking

- Early enteral nutrition can improve clinical outcome by
  - attenuating the hypercatabolic response after trauma
  - improving wound healing and the immune response
  - preserving gastrointestinal structure and function
  - favorably modulates the inflammatory cascade and subsequent hypermetabolic/hypercatabolic response
    - Oltermann M. Nutrition support in the acutely ventilated patient. *Respir Care Clin* 2006; 12:533–545
- Delayed nutrition support is associated with a prolonged acute phase response and poor outcome in brain-injured patients
  - Debaveye Y, Van den Berghe G. Risk and benefit of nutritional support during critical illness. *Annu Rev Nutr* 2006; 26:513–538

- **Vasken A, Hicham K, Bruno D. Effects of early enteral feeding on the outcome of critically ill mechanically ventilated patients. Chest 2006; 129:960–967**
- Early enteral nutrition reduced ICU and hospital mortality despite being associated with increased ventilator associated pneumonia (VAP) rates; however, this did not statistically change the mortality
- The overall ICU and hospital mortality were lower in the early feeding group (18.1% vs 21.4%,  $p = 0.01$ ; and 28.7% vs 33.5%,  $p = 0.001$ , respectively)
- The lower mortality rates in the early feeding group were most evident in the sickest group as defined by quartiles of severity of illness scores

- A prospective study of ICU patients found that an *energy debt* begins in the first several days of critical illness and that debt cannot be recompensed despite aggressive nutritional support
  - Villet S, Chiolerio R, Berger M. Negative impact of hypocaloric feeding and energy balance on clinical outcome in ICU patients. Clin Nutr 2005; 24:502–509

# Route

## **Long-term nutrition:**

- Gastrostomy
- Jejunostomy

## **Short-term nutrition:**

- Nasogastric feeding
- Nasoduodenal  
feeding
- Nasojejunal feeding



- Problems of NG tubes
  - Inadequate calories delivered
  - Risk of aspiration and VAP
- Supposedly, post-pyloric feeding could resolve these issues
- No difference in incidence of pneumonia or in length of ICU stay in patients receiving gastric vs post-pyloric feedings
  - Ho KM, Dobb GJ, Webb SAR. A comparison of early gastric and post-pyloric feeding in critically ill patients: a meta-analysis. *Intens Care Med.* 2006;32:639-649

- Patients who received ND feedings achieved nutritional goals earlier than those who received NG feeding. ND feeding group also has a lower rate of vomiting and VAP in the medical ICU setting
  - Duodenal versus gastric feeding in medical intensive care unit patients: A prospective, randomized, clinical study. Hsu et al .Crit Care Med 2009; 37:1866 –1872
- Intestinal tube placement
  - Is technically more demanding
  - Delivers 200 – 300 kcal/d extra
  - Unlikely to significantly affect nutritional status over the course of an average ICU stay (8 – 10 d)

# General recommendations

1. EN should be initiated in the critically ill patient who is unable to maintain volitional intake
2. EN is the preferred route of feeding over PN
3. Feeding should be started early within the first 24–48 hours following admission
4. Feedings should be advanced toward goal over the next 48–72 hours

5. In the setting of hemodynamic compromise (patients requiring significant hemodynamic support, including high-dose catecholamine agents, alone or in combination with large volume fluid or blood product resuscitation to maintain cellular perfusion), EN should be withheld until the patient is fully resuscitated and/or stable
  
6. In the ICU patient population, neither the presence nor the absence of bowel sounds and evidence of passage of flatus and stool is required for the initiation of enteral feeding

7. Either gastric or small bowel feeding is acceptable in the ICU setting. Critically ill patients should be fed via an enteral access tube placed in the small bowel if at high risk for aspiration or after showing intolerance to gastric feeding

- A.S.P.E.N. Enteral Nutrition Practice Recommendations JPEN 2009

# Dosing

1. Target goal of EN (defined by energy requirements) should be determined and clearly identified at the time of initiation of nutrition support therapy
  - Energy requirements can be calculated by predictive equations or measured by indirect calorimetry
2. >50% - 65% of goal calories should be achieved over the first week of hospitalization

3. If unable to meet energy requirements(100% of target goal calories) after 7–10 days by the enteral route alone, consider initiating supplemental PN
4. Initiating supplemental PN before this 7–10-day period in the patient already on EN may be detrimental
5. During the acute and initial phase of critical illness: in excess of 20–25 kcal/kg/day may be associated with a less favourable outcome
6. During the anabolic recovery phase, the aim should be to provide 25–30 kcal/kg/day

# Monitoring

1. Patients should be monitored for tolerance of EN
  - complaints of pain and/or distention
  - physical examination
  - passage of flatus and stool
  - abdominal radiographs
2. Inappropriate cessation of EN should be avoided
3. Holding EN for gastric residual volumes  $<500$  ml\* in the absence of other signs of intolerance should be avoided
4. Making the patient NPO *surrounding the time of diagnostic* tests or procedures should be minimized to prevent inadequate delivery of nutrients and prolonged periods of ileus. Ileus may be propagated by NPO *status*



5. Use of enteral feeding protocols increases the overall percentage of goal calories provided
  
6. Patients placed on EN should be assessed for risk of aspiration & steps taken to reduce it
  - head of the bed should be elevated 30°– 45°
  - for high-risk patients or those shown to be intolerant to gastric feeding, EN should be given by continuous infusion
  - agents to promote motility, such as prokinetic drugs (metoclopramide and erythromycin) or narcotic antagonists (naloxone and alvimopan), should be used when needed
  - postpyloric tube placement should be considered
  - use of chlorhexidine mouthwash twice a day should be considered to reduce risk of VAP

# Specific disease state recommendations

## ***Respiratory failure***

1. Specialty high-lipid low-carbohydrate formulations designed to manipulate the respiratory quotient and reduce CO<sub>2</sub> production are not recommended for routine use in ICU patients with acute respiratory failure
2. Should be placed on an enteral formulation characterized by an antiinflammatory lipid profile (i.e., omega 3 fish oils, borage oil) and antioxidants
3. Fluid-restricted calorically dense formulations should be considered
4. Serum phosphate levels should be monitored closely, and replaced appropriately when needed

## ***Acute renal failure***

1. Patients should receive standard enteral formulations, and standard ICU recommendations for protein and calorie provision should be followed
2. If significant electrolyte abnormalities develop, a specialty formulation designed for renal failure (with appropriate electrolyte profile) may be considered
3. Patients receiving hemodialysis or continuous renal replacement therapy should receive increased protein, up to a maximum of 2.5 g/kg/day
4. Protein should not be restricted as a means to avoid or delay initiation of dialysis therapy

## ***Hepatic failure***

1. EN is the preferred route of nutrition therapy in ICU patients with acute and/or chronic liver disease
2. Avoid protein restriction in patients with liver failure
3. Standard enteral formulations should be used
4. Branched chain amino acid formulations should be reserved for encephalopathic patients who are refractory to standard therapy with luminal-acting antibiotics and lactulose

## ***Acute pancreatitis***

1. At admission, patients should be evaluated for disease severity
2. Patients with ***severe acute pancreatitis*** should have a nasoenteric tube placed and EN initiated as soon as fluid volume resuscitation is complete
3. Patients with ***mild to moderate acute pancreatitis*** do not require nutrition support therapy (unless an unexpected complication develops or there is failure to advance to oral diet within 7 days)

4. Patients may be fed enterally by the gastric or jejunal route
  
5. Tolerance to EN in patients with severe acute pancreatitis may be enhanced by the following measures:
  - a) Minimizing the period of ileus after admission by early initiation of EN
  - b) Displacing the level of infusion of EN more distally
  - c) Switching from bolus to continuous infusion

- d) Changing the content of the EN delivered from intact protein to small peptides, and long-chain fatty acids to medium-chain triglycerides or a nearly fat-free elemental formulation
- 7. For the patient with severe acute pancreatitis when EN is not feasible, use of PN should be considered
- 8. PN should not be initiated until after the first 5 days of hospitalization

## ***Nutrition Therapy End-of-Life Situations***

- Specialized nutrition therapy is not obligatory in cases of futile care or end-of-life situations. The decision to provide nutrition therapy should be based on effective patient/family communication, realistic goals, and respect for patient autonomy



# Adjunctive therapy

- Administration of probiotic agents has been shown to improve outcome (most consistently by decreasing infection) in specific critically ill patient populations involving transplantation, major abdominal surgery, and severe trauma
- No recommendation can currently be made for use of probiotics in the general ICU population because of a lack of consistent outcome effect

- A combination of antioxidant vitamins and trace minerals (specifically including selenium) should be provided to all critically ill patients receiving specialized nutrition therapy
- The addition of enteral glutamine to an EN regimen (not already containing supplemental glutamine) should be considered in burn, trauma, and mixed ICU patients
- Soluble fiber may be beneficial for the fully resuscitated, hemodynamically stable critically ill patient receiving EN who develops diarrhea. Insoluble fiber should be avoided in all critically ill patients. Both soluble and insoluble fiber should be avoided in patients at high risk for bowel ischemia or severe dysmotility

# Hyperglycemia

# Immunonutrition

- Some nutrients, when given in therapeutic doses, appear to serve as pharmacologic agents and they can positively or negatively effect clinical outcome just as any other pharmacologic agent would
- May be required to replace acute deficiencies brought on by specific injury or disease states
- Glutamine, arginine, and omega-3 fatty acids are three of the well studied pharmaconutrients

- **Glutamine**

- Induces heat shock proteins, which are essential to the cell's ability to survive injury and to attenuate the SIRS response during critical illness

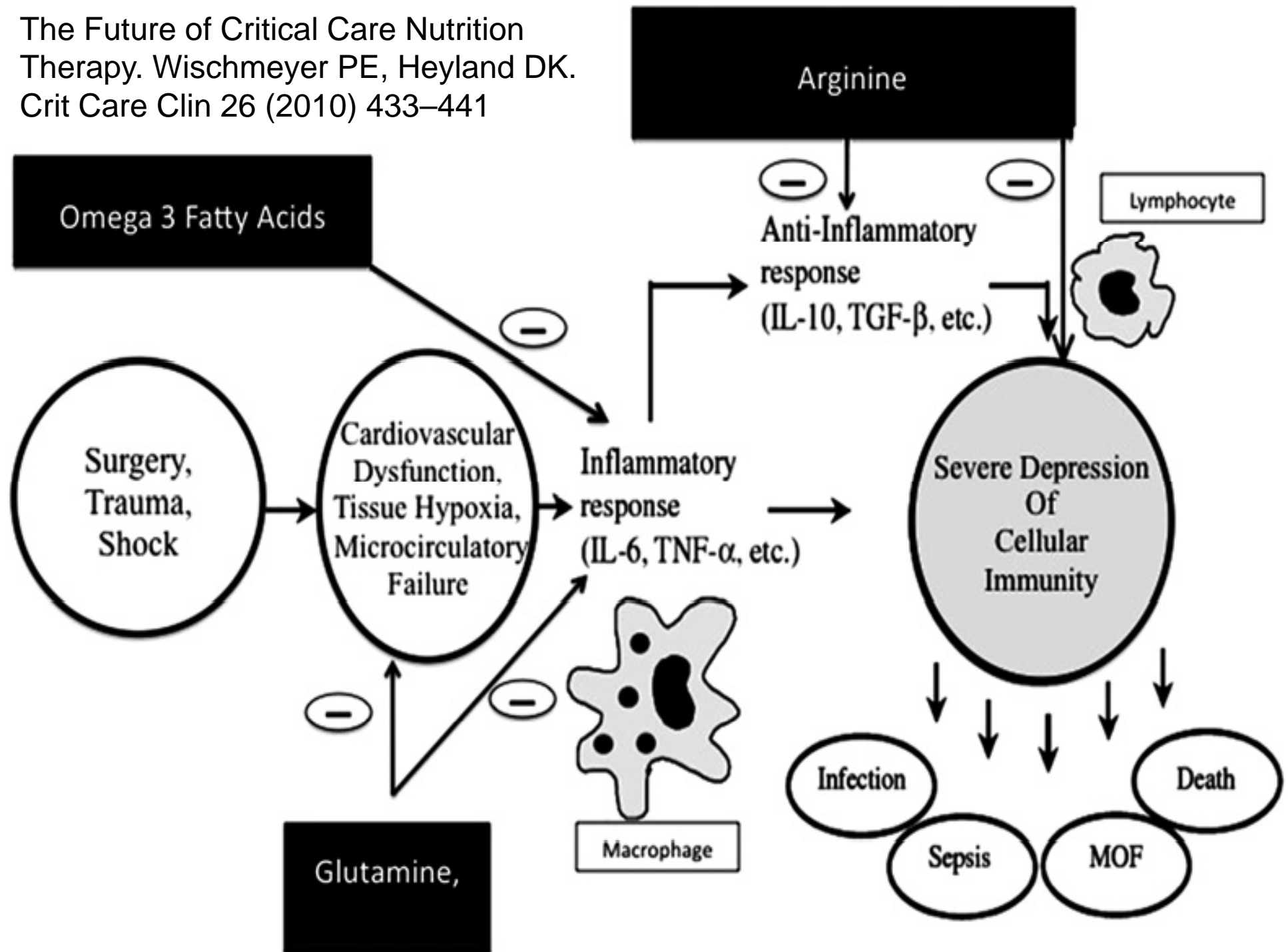
- **Arginine**

- Prevents T-lymphocyte dysfunction following physical injury

- **Omega-3 fatty acids** (specifically eicosapentaenoic acid and docosahexaenoic acid)

- Serve as precursors for resolvins and protectins, which assist in resolution of inflammation and decrease tissue injury.

The Future of Critical Care Nutrition Therapy. Wischmeyer PE, Heyland DK. Crit Care Clin 26 (2010) 433–441



- Specific nutrients appear to have specific roles following particular injury and illness states
- ***Arginine deficiency*** occurs rapidly after physical injury (trauma and surgical injury) but not after sepsis
- Clinical outcome data in more than 30 trials and 3000 patients studied support a significant treatment effect of arginine supplementation to reduce rate of infection (RR, 0.58 [95% CI, 0.48, 0.69,  $P < .00001$ ]) and overall LOS (weighted mean difference, 2.09 [95% CI, 3.20, 0.97,  $P < .0002$ ]) after major surgery versus standard enteral nutrition
  - Weitzel L, Dhaliwal R, Drover J, et al. Should perioperative immune-modulating nutrition therapy be the standard of care? A systematic review. Crit Care Med 2009;13:132

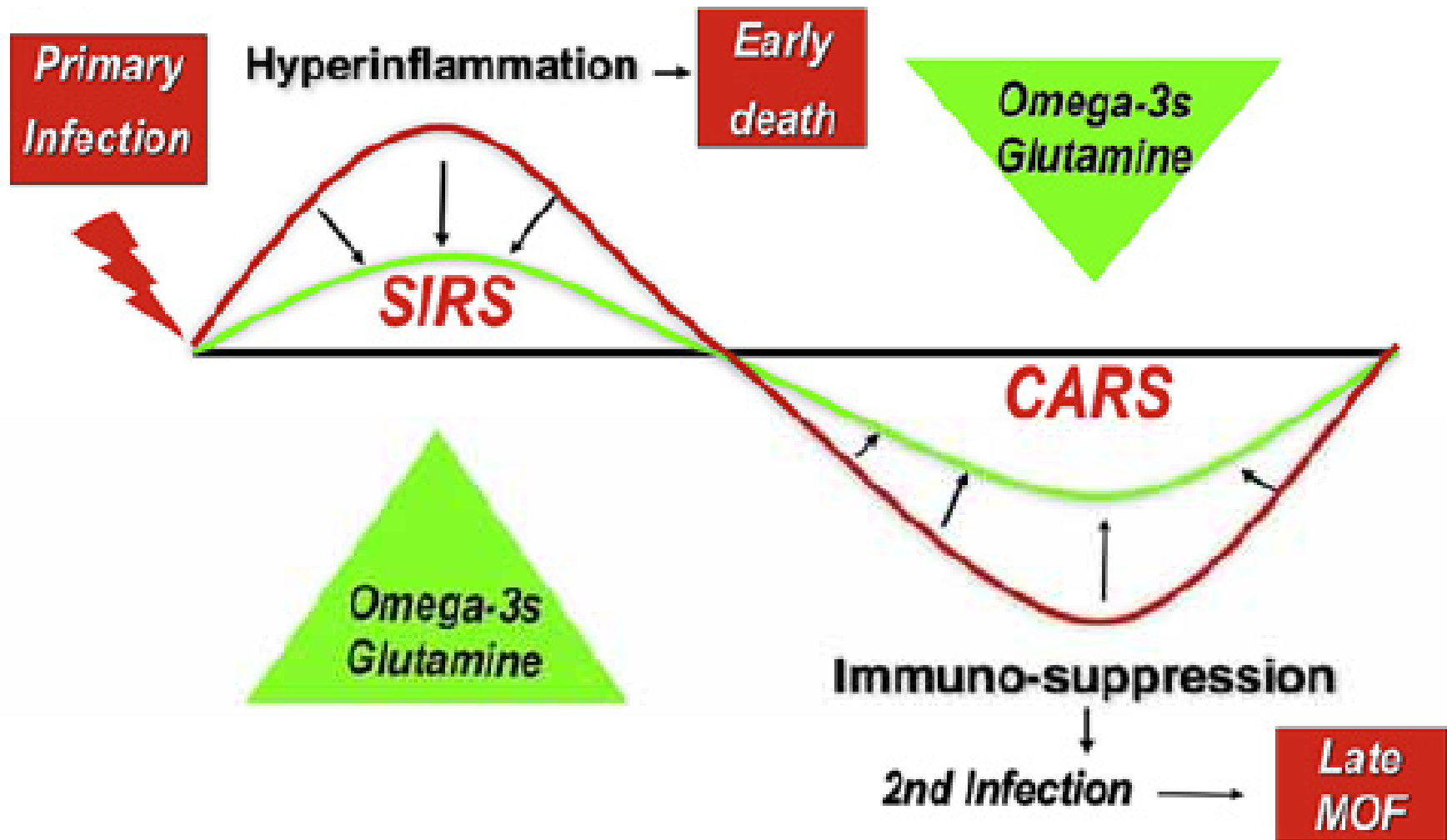
- However, very little benefit, and perhaps harm, is observed in septic patients
- **Glutamine** is likely of the greatest benefit in acutely ill patients with sepsis and organ failure, who typically have the most severe glutamine deficiency
- This has been correlated with increased mortality at ICU admission
  - Oudemans-van Straaten HM, Bosman RJ, Treskes M, et al. Plasma glutamine depletion and patient outcome in acute ICU admissions. *Intensive Care Med* 2001;27(1):84–90



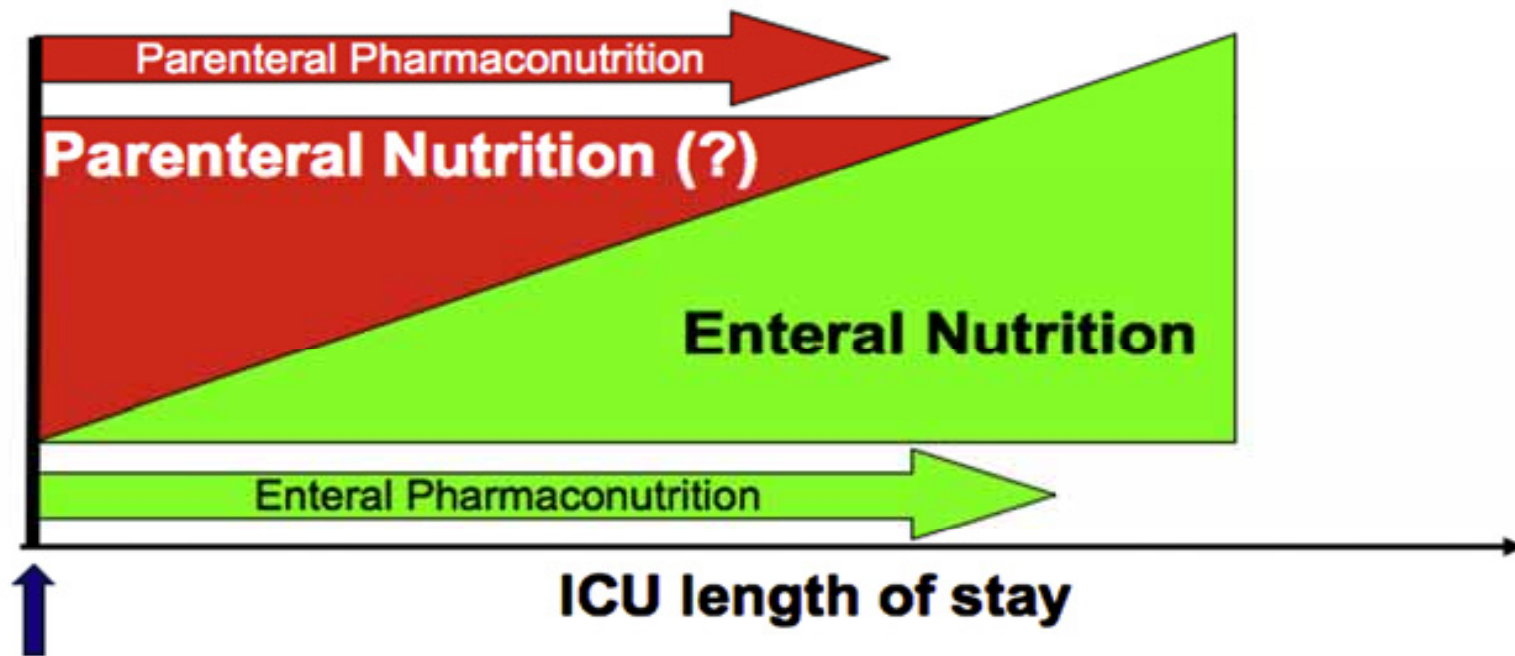
## Clinical effects of immunomodulating nutrients in specific states of critical illness and injury<sup>a</sup>

Nutrient	Infections	LOS	Mortality
Glutamine <sup>22</sup>	↓ Critical illness ↓ Surgery	↓ Critical illness ↓ Surgery	↓ Critical illness
Arginine <sup>18,19</sup> (all studies used arginine as part of "cocktail" formula)	↓ Surgery ↓ Trauma	↓ Surgery ↓ Trauma	↑ (?) Sepsis following infection
Omega-3 Fatty Acids <sup>15</sup>		↓ ARDS	↓ ARDS (?)

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- Assessment of nutritional risk
- Measurement of biomarker(s) to determine which pharmaconutrient/aggressiveness of caloric intake
- Set of tools/biomarkers to monitor response to nutrition/nutrient therapy
- Evaluate gut function in the sick patient, with biomarkers to assess if the gut is able to function to absorb nutrients

-The Future of Critical Care Nutrition Therapy.

Wischmeyer PE, Heyland DK. Crit Care Clin 26 (2010) 433–441