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Nutrition Support in Critical Illness

Part 1: Requirements, timing and patient selection

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Nutrition support is widely accepted as beneficial in critical illness. However, optimal requirements, timing and patient selection is disputed.

Resting energy expenditure (REE) constitutes 90 to 95 per cent of total energy expenditure (TEE) in most ICU patients. Daily REE prediction from the PSU(m) equation is as accurate as a single indirect calorimetry measurement. Conversely, non-physiological equations, such as BMR_stress factor or Kcal/kg equations, produce gross under- and overestimates.

Delivering energy equivalent to energy expenditure and >0.19gN/kg/d within 48 hours of admission appears to improve outcome. This applies to high risk patients; low risk patients may require initially lower input, particularly if substrate intolerant. Enteral nutrition (EN) should be started within 24 hours of ICU admission; when contraindicated, start parenteral nutrition (PN). Some studies fail to improve outcome by under- or over-feeding because of inaccurate prediction of EE, inadequate nitrogen input and failure of feeding protocols to maximise nutrition delivery.

We are closer to knowing what nutritional target will improve outcome and to being able to accurately predict that target. Greater definition of patient-specific requirements and timing of intervention is required.

Note: Within this paper energy refers to total energy whether derived from protein or non-protein sources and nitrogen (N) is used as generic term for enteral or parenteral protein equivalents.

Energy and nitrogen requirements

Definition of requirements

This paper discusses adult nutrient requirements in relation to clinical outcome. To improve outcome therefore requires accurate prediction of the optimal nutrient 'dose'. Conversely basing input on inaccurately predicted requirements can be clinically dangerous and waste resources. Because critical illness represents a syndrome, decisions should be based more on physiological measurements and trends than an isolated disease state.

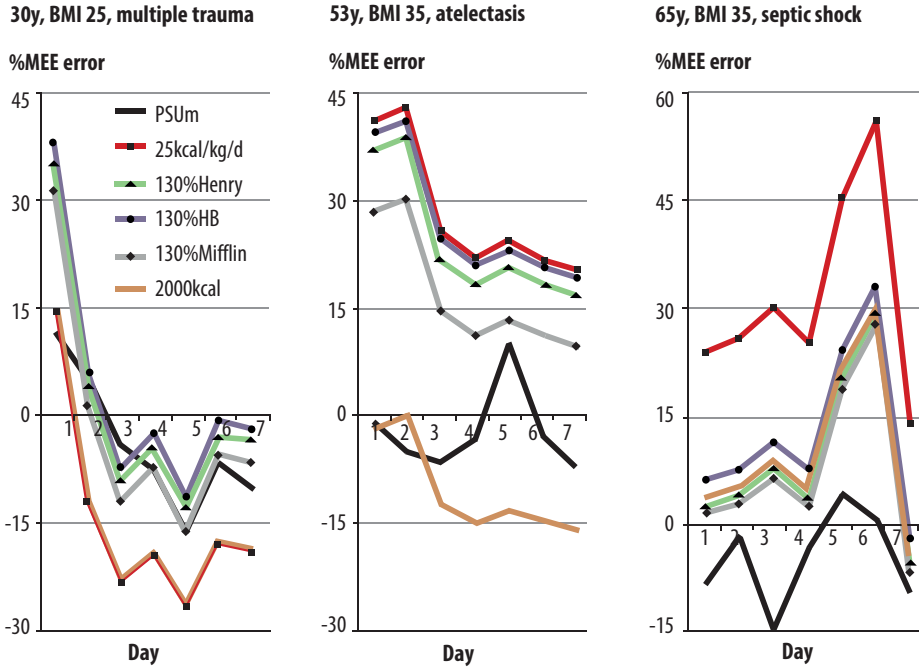
Predicting resting energy expenditure (REE)

Which equation

Dietary-induced thermogenesis plus activity are equivalent to ~5-10 per cent of BMR in most paralysed or sedated ICU patients, respectively,[1,2] the remainder being REE. Indirect calorimetry is more accurate than prediction equations for determining REE[3] but is only practical in 65 per cent of adult intensive care unit (ICU) patients[4] and very few units have the equipment. However, most equations are inaccurate because they fail to track REE.

In mechanically ventilated patients, multi-parameter equations, including physiological variables such as body temperature and minute ventilation, track the inter- and intra-individual variation in EE common to ICU patients. In a series of validation studies, the PSU(m) equation accurately predicted EE (~70% within 10%; only 12-19% >15%) in a mixed ICU population.[5,6] In contrast, BMR equations ± adjustment for obesity ± a 25 per cent stress factor or 25kcal/kg/d predicted within 10 per cent of EE in only 18-53 per cent and are little better than prescribing 2000kcal/d to all patients (see **Figure 1**). Furthermore, the PSU(m) was as accurate over seven days (error: -3.7±5.1%) as a single measurement of EE on day one (error: -4.1±11.1%).[7] If confirmed in larger studies, it means PSU(m) equations can predict REE in most ICU patients where one-off measurement would be clinically impractical and no more accurate. This is important because optimal outcome appears to require tight matching of energy input to expenditure.

Figure 1: Error in Predicted Energy Expenditure as a Percentage of MEE [8,*]



* Patients from [7]. The closer the trend to '0' the more accurate.

Applying the PSU(m) equation

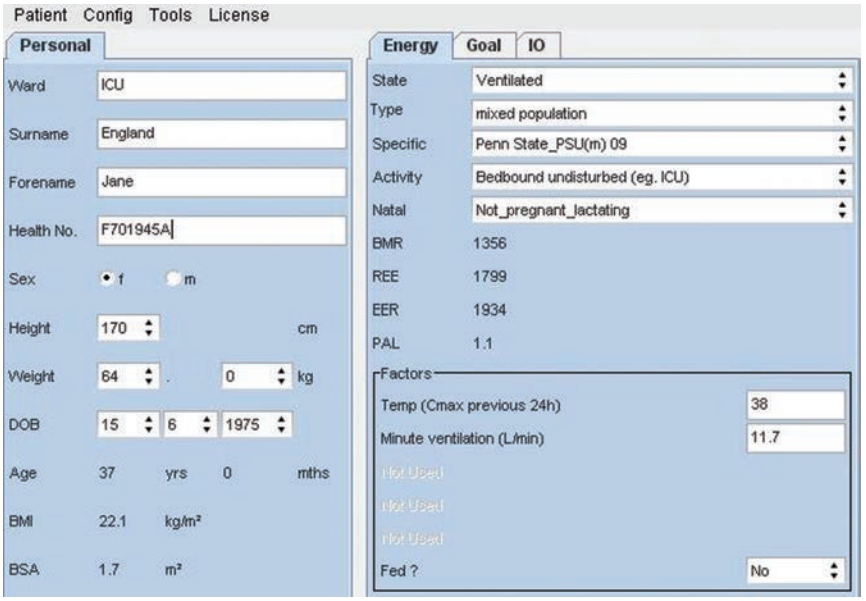
Compared to indirect calorimetry, REE prediction is quick and cheap. Obtain 'dry' weight from records or relatives, and height from measured length. Read maximum temperature (Tmax, ºC) in the last 24 hours and minute ventilation (L/minute) from the ICU record and ventilator, respectively.

Use the PSU(m) equations to predict REE during mechanical ventilation:[5-6, 9]

- **>60y+ BMI >30:**
  Mifflin*0.71+Tmax*85+Vm*64-3085
- **Other patients:**
  Mifflin*0.96+Tmax*167+Vm*31-6212
- **Mifflin:**[10]
  – Men: 10*Kg+6.25*cm-5*Age+5
  – Women: 10*Kg+6.25*cm-5*Age-161

However, the complex equation may discourage daily use. Overcome this by using the alogorithm within a spreadsheet or calculate and store the data within software (see **Figure 2**).

Figure 2: Patient Data Record and PSU(m) Prediction within FeedCalc*



* http://www.nutritionsupport.info/

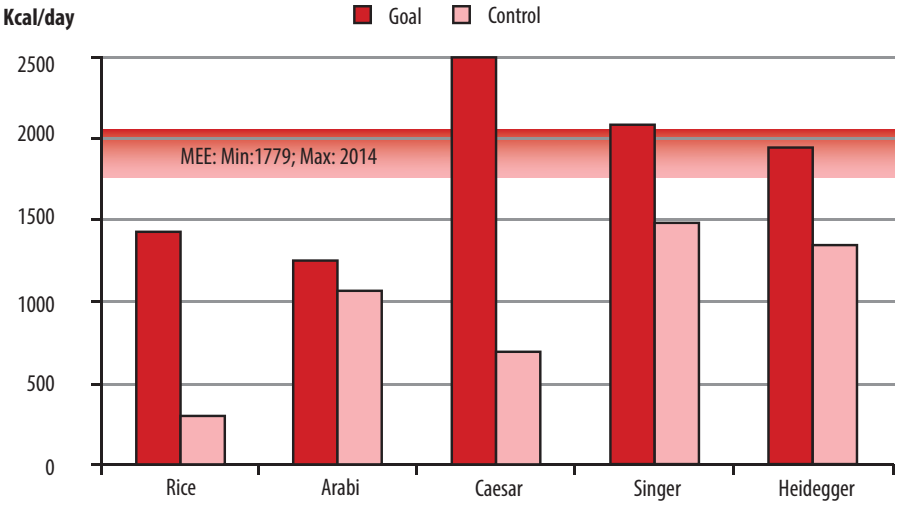
Optimal dose

Dose-dependency of outcome

Definitive RCT evidence is lacking but practice guidelines recommend 'enhanced EN'.[11] This includes starting EN at 80-100 per cent estimated energy requirement (EER) and using a higher threshold of gastric residual volume, prokinetics and nasointestinal feeding to achieve the feeding target. Enhanced EN is associated with reduced nutritional deficit, infection,[12] hospital stay and mortality (trend)[13] (see **Table One**). Similarly, matching EN ± supplemental PN to measured EE reduced mortality (trend),[14] infection and ICU stay.[15] In addition, large cohort studies demonstrate dose-dependent outcomes: Each increment of 1000kcal/d produced a 24 per cent reduction in 60-day mortality and 3.5 days of ventilator-dependence,[16] or a 67 per cent reduction in hospital mortality in females, achieving >90 per cent of measured REE + 10 per cent with 0.19-24gN/kd/d.[17] Trends were stronger **after** 96 hours, when nutrition may have more impact.[18]

In contrast, some medical ICU studies suggest that minimal feeding, <9 or 5 vs 25kcal/kg/d, reduces mortality, pneumonia and C. diff infection,[21, 22] but may be biased. Failure to account for length of stay will show fewer complications on low input,[21] and neglible input in both groups (2 vs 7Kcal/kg/d) was unlikely to affect outcome and bolus feeding and lack of disclosure of pre-ICU pneumonia and stay may all affect infection rates.[22] Conversely, medical patients receiving more energy (%REE: <16%, <32%, <47% or >47% [~14Kcal/kg/d]) had lower mortality (100%, 82%, 79% and 17%, respectively)[23] and reduced S. aureus, ventilator-acquired pneumonia.[24] Importantly, these last two studies used a goal derived from a validated equation,[25, 26] therefore, energy input related to energy requirements rather than an inaccurately predicted goal.

Figure 3: Energy Input vs Measured Energy Expenditure (MEE)



Optimal dose

In five RCTs comparing 'goal' vs underfeeding, intervention only improves outcome when energy input is within the minimum to maximum range of MEE [n=544: [5, 6, 9, 25, 26]] (see **Figure 3**[27]). This is only achieved in the two studies that accurately predicted and delivered energy requirements: a) 106% MEE vs 81% produced a trend to reduced mortality, despite increased infection, ventilation and ICU stay[14] and, b) feeding at 100 per cent MEE vs 73 per cent reduces the risk of developing new infection, antibiotic days, hours of mechanical ventilation and length of stay.[15] Both studies used supplemental PN when EN did not reach 100 per cent MEE. Conversely, intervention patients fed more than controls but still significantly underfed had similar outcomes to controls[28] or increased mortality,[29] and when overfed early PN had increased infection, organ support and cost.[30]

Improved outcome appears to require adequate protein (>0.19gN/kg/d) as well as energy input equivalent to TEE.[20] Importantly, protein input (g/d) of RCT interventions vs controls was only 43 vs 45, 55 vs 6.8, 60 vs 15, 75 vs 60 and 90 vs 60g/d[14, 15, 28-30] when 100g/d would be considered adequate.[27] Total body nitrogen is maintained on 0.27gN/kg/d in mild catabolism (upper GI cancer surgery)[31] and in moderate catabolism (trauma), when substrate intolerance necessitates reduction of energy input from 100 per cent TEE to 75 per cent TEE, 0.27gN/kg/d maintains a similar nitrogen balance.[32, 33] However, in very severe catabolism, such as sepsis requiring continuous renal replacement therapy, nitrogen balance and survival only improved on 0.4gN/kg/d.[34]

Because few EN feeds or PN standard bags have non-protein energy (NPE): gN ratios <100:1 it can be impossible to provide adequate nitrogen,

without overfeeding energy. Substrate intolerance or significant energy input from IV glucose, dialysis solutions, or Propofol, exacerbate the problem by requiring reduction in EN or PN energy while maintaining nitrogen input. In practice, we require an energy dense formulation with an NPE:gN ratio of <80:1. To achieve this requires new formulations, preferably supplemented to the higher end of 0.2-0.5g glutamine/kg/d.[35] In addition, obligatory N loss is partly necessitated by the acute phase protein response requiring higher levels of certain amino acids (e.g. phenylalanine, tryptophan, tyrosine, cysteine) resulting in oxidation of other, 'excess', amino acids.[36, 37] If new feeds complement these needs, improved outcome and nitrogen retention may be achieved[38-40] at a lower nitrogen input and reduced excretory burden.

Table One: Effect of Enhanced EN on Outcome[19]

N	Study Type	Nutritional Variable	Outcome	Risk reduction	95%CI	Reference
2772	Observational, multinational cohort	Every increment: 1000kcal/d	60d mortality Ventilator-free days	24% 3.5d*	5-39% 1.2-5.9d	16 *Only in BMI <25 and >35
275	RCT	EN±supplemental PN to a an energy target determined by indirect calorimetry vs 25-30Kcal/kg/d	 • New infection • Antibiotic free days • Mechanical ventilation (h) • ICU stay	Coefficient: -0.27 3.48 -87.4 -2.7	 -0.5,-0.04 0.94,6.0 -131,-44 -4.7,-0.69	15
462	Cluster randomized controlled trial	Early institution of nutritional support, preferably EN	Hospital stay Mortality (trend, p=0.058)	10d 10%	25 vs 35 27% vs 37%	13
112	RCT, pilot study	EN±supplemental PN energy goal determined by repeated indirect calorimetry measurements vs 25 kcal/kg/day	Mortality (hospital, trend)	15.4%	-	14
423	Observational	Goal: >90% of measured REE + 10%, 0.19-0.24g N/kg/d vs < goal	Mortality in females: • ICU • 28d • Hospital	 90% 92% 67%	 13-95% 53-99% 5-89%	17
886	Prospective observational cohort, mixed medical-surgical	Goal: MEE + >0.192gN/kg/d vs < goal	Hazard ratio of 28d mortality	53%	69-27%	20

Table Two: Systematic Review and Meta-analysis of the Effect of Early EN on Clinical Outcome[19]

Disease state	N	Early EN Delay (h)	Relative Risk (RR), 95%CI Mortality	Infection	Hospital stay (d)	Reference
Acute illness	753	<24^	ns	0.45, 0.3-0.66*	2.2d, 0.81-3.63*	54
Burns	90	4-24	ns	ns	ns	55
ICU, mixed population	440	<24-48	0.24, 0.02-0.41	0.32 (ns)	ns	11
ICU, trauma	126	<24	0.22, 0.044-0.92	-	-	56
GI surgery: Elective, intestinal	494	6-24	0.41, 0.18-0.93	Trends	0.6d, 0.54-0.66	57
Pancreatitis, acute + postoperative	71	<48^^ vs PN	0.26, ns	0.33, ns	-	58

*Heterogeneity. ^32 patients <36h; ^^53 patients <96h.

Timing

Systematic review and meta-analysis indicates that EN within 24 hours of admission or injury improves outcome in acute illness, ICU, GI surgery and possibly pancreatitis requiring surgery; evidence for burns is insufficient (see **Table Two**). Specifically, early EN may reduce infection and mortality by maintaining the gut barrier and gut-associated lymphoid tissue, secretion of IgA and intestinal alkaline phosphatase which detoxifies lipopolysaccharide[41-43] thus reducing risk of multiple organ dysfunction syndrome.[44] However, this protection may require EN delivery within 24 hours because intestinal alkaline phosphatase activity is lost with short-term fasting,[43] conversely mortality risk is reduced when early EN is restricted to within 24 hours[45] rather than up to 72 hours.[46]

There are concerns in giving EN when there is haemodynamic instability[47] or potential for refeeding syndrome. EN increases gut oxygen consumption, potentially promoting gut ischaemia[48] and bowel necrosis,[49] but by less than the increase in oxygen delivery[50] because of increased splanchnic blood flow.[51] In retrospective analysis of critically ill, inotrope-dependent patients, early (<48h vs >48h) EN reduced mortality (ICU: 23% vs 28%; Hospital: 34% vs 44%) especially in those on multiple vasopressors (OR: 0.36: 0.15, 0.85) and requiring >2d support (OR: 0.59: 0.39, 0.90).[52] RCT evidence is needed. In addition, early feeding studies did not identify refeeding risk to preclude early feeding; close surveillance and rapid electrolyte correction is protective. Overall, meta-analysis (B+ evidence with no heterogeneity) found that EN within 24 hours reduced infection compared to PN, but compared to delaying EN >24 hours, early PN reduced mortality.[53]

Supplementary PN, where EN is failing to deliver goal nutrition, and when to start it is the one area lacking consensus between clinical practice guidelines. ASPEN concluded that PN increased complications, unless malnourished, and should be avoided for seven days.[47] Canadian guidelines found no benefit but increased cost, therefore PN should not be started until all methods of maximising EN have been attempted.[11] Conversely, ESPEN recommend PN if EN fails to meet the goal after two days based on reducing the risk of cumulative energy deficit and improving plasma proteins.[14] Casaer, *et al*[30] compared supplemental PN at day two ('ESPEN') with day seven ('ASPEN') but, as discussed above, was a flawed study because most patients did not need PN, IV glucose was given to the early intervention group day 0-2 and patients were overfed. All the above studies used an energy goal that was neither measured or accurately predicted and, therefore, under- and overfeeding in both control and intervention groups would have affected outcomes. In contrast, the two studies supplementing EN with PN from

day two based on the need to meet a measured energy goal, showed a trend to reduced mortality[14] and fewer complications.[15]

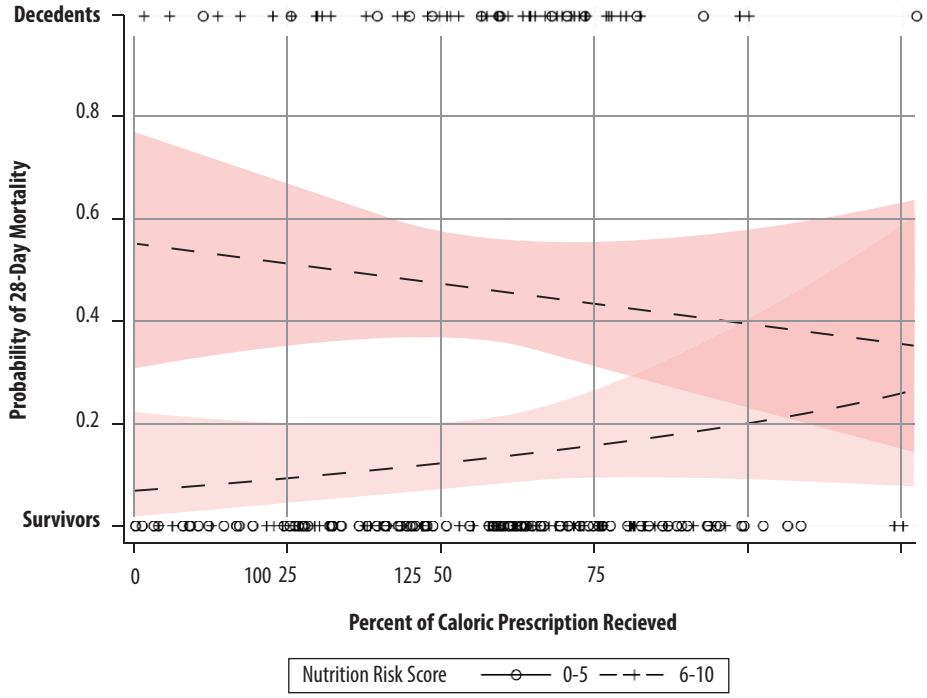
Patient selection

There is a risk:benefit ratio to invasive nutrition support. Delivering a higher percentage of nutrition prescription reduces 28-day mortality in patients with a NUTrition Risk in the Critically ill (NUTRIC) score of 6-10, but may increase risk in those with a score of 1-5 (see **Figure 4**).[59] The NUTRIC score may better guide nutrition support when re-developed using only studies accurately predicting TEE.

Conclusions and recommendations

Starting EN within 24 hours of ICU admission and increasing EN ± supplementary PN to TEE and >0.19gN/kg/d within 48-96 hours appears to improve outcome in high risk patients (NUTRIC score >6); temporary underfeeding energy in low risk patients suffering substrate intolerance may be necessary. The efficacy of nutrition support will only be found if RCTs ensure 'Enhanced EN' ± PN is matched to true requirements and use protocols to ensure those requirements are met.

Figure 4: Effect of Energy Received on 28-day Mortality



Predicted probability (line) and 95%CI (shading) of 28-day mortality versus percent of caloric prescription received. NUTRIC score: Low ('o': 1-5) and high ('+': 6-10).

Look out for Part 2: Nutrition support in critical illness: Routes and achieving goals in the November issue of CN.

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References: **1.** Frankenfield D, et al (1994). Relationships between resting and total EE in injured and septic patients. Critical Care Medicine.; 22: 1796-804. Comment: Crit Care Med.1995; 23:1783-4. **2.** Weissman C, et al (1986). The energy expenditure of the mechanically ventilated critically ill Patient. An Analysis. Chest; 89: 254-9. **3.** Cooney RN, Frankenfield DC (2012). Determining energy needs in critically ill patients: equations or indirect calorimeters. Current Opinion in Critical Care; 18: 174-7. **4.** Berger M (2012). Personal communication regarding reference 15. **5.** Frankenfield DC, Coleman A, Alam S (2009). Analysis of estimation methods for resting metabolic rate in critically ill adults. Journal of Parenteral and Enteral Nutrition; 33: 27-36. **6.** Frankenfield D (2011). Validation of an equation for resting metabolic rate in older obese, critically ill patients. Journal of Parenteral and Enteral Nutrition; 35: 264-269. **7.** Frankenfield D, et al (2012). Longitudinal prediction of metabolic rate in critically ill patients. Journal of Parenteral and Enteral Nutrition; Epub ahead of print. **8.** Taylor SJ. 3.2.2.2 Multi-parameter equations. In: Energy and nitrogen requirements in disease states. 2nd edition. 2012. http://www.nutritionsupport.info/. **9.** Frankenfield D, Smith J, Cooney R (2004). Validation of 2 approaches to predicting resting metabolic rate in critically ill patients. Journal of Parenteral and Enteral Nutrition; 28: 259-64. **10.** Mifflin M, et al (1990). A new predictive equation for resting energy expenditure in healthy individuals. The American Journal of Clinical Nutrition; 51: 241-7. **11.** Heyland D, et al (2009). Canadian Clinical Practice Guidelines for Nutrition Support in Mechanically Ventilated, Critically Ill Adult Patients. Updated recommendations. http://www.criticalcarenutrition.com/index.php?option=com_content&view=article&id=18&Itemid=10. **12.** Taylor SJ, et al (1999). Prospective randomised controlled trial to determine the effect of early enhanced enteral nutrition on clinical outcome in mechanically ventilated patients suffering head injury. Critical Care Medicine; 27: 2525-31. **13.** Martin CM, et al (2004). Multicentre, cluster-randomized clinical trial of algorithms for critical-care enteral and parenteral therapy (ACCEPT). Canadian Medical Association Journal;170:197-204. **14.** Singer P, et al (2011). The tight calorie control study (TICACOS): a prospective, randomized, controlled pilot study of nutritional support in critically ill patients. Intensive Care Medicine; 37:601-609. **15.** Heidegger CP, et al (2011). Supplemental parenteral nutrition (SPN) in intensive care unit (ICU) patients for optimal energy coverage: improved clinical outcome. Clinical Nutrition Supplements; 1: 2-3. **16.** Alberda C, et al (2009). The relationship between nutritional intake and clinical outcomes in critically ill paients: results of an international multicenter observational study. Intensive Care Medicine; 35: 1728-37. **17.** Strack van Schijndel RJM, et al (2009). Optimal nutrition during the period of mechanical ventilation decreases mortality in critically ill, long-term acute female patients: a prospective observational cohort study. Critical Care;13:1-13. **18.** Heyland DK, et al (2011). The success of enteral nutrition and ICU-acquired infections: A multicenter observational study. Clinical Nutrition;30:148-155. **19.** Taylor SJ. 4.3.2 Severe inflammatory states. In: Energy and nitrogen requirements in disease states. 2nd edition. 2012.http://www.nutritionsupport.info/. **20.** Weijs PJM, et al (2012). Optimal protein and energy nutrition decreases mortality in mechanically ventilated, critically ill patients: A prospective observational cohort study. Journal of Parenteral and Enteral Nutrition; 36: 60-68. **21.** Krishnan J, et al (2003). Caloric intake in medical ICU patients: Consistency of care with guidelines and relationship to clinical outcomes. Chest; 124: 297-305. **22.** Ibrahim EH, et al (2002). Early versus late enteral feeding of mechanically ventilated patients: results of a clinical trial. Journal of Parenteral and Enteral Nutrition; 26: 174-81. Comment in: Journal of Parenteral and Enteral Nutrition; 26: 182-3. **23.** Faisy C, et al (2008). Impact of energy deficit calculated by a predictive method on outcome in medical patients requiring prolonged acute mechanical ventilation. British Journal of Nutrition; 101: 1079-87. **24.** Faisy C, et al (2011). Early ICU Energy deficit Is a risk factor for Staphylococcus aureus ventilator-associated pneumonia. Chest; 140:1254-60. **25.** Faisy C, (2003). Assessment of resting energy expenditure in mechanically ventilated patients. The American Journal of Clinical Nutrition; 78: 241-9. **26.** Savard J, (2008). Validation of a predictive method for an accurate assessment of resting energy expenditure in medical mechanically ventilated patients. Critical Care Medicine;36:1175-83. **27.** Singer P, Cohen J (2012). The Unresolved Questions of Nutritional Support in the ICU: Now or Later, More or Less, Enteral or Parenteral? Aktuel Ernahrungsmed; 37: 1-2. **28.** Rice TW, et al (2011). Randomized trial of initial trophic versus full-energy enteral nutrition in mechanically ventilated patients with acute respiratory failure. Critical Care Medicine; 39: 967-73. **29.** Arabi YM, et al (2011). Permissive underfeeding and intensive insulin therapy in critically ill patients: a randomized controlled trial. American Journal of Clinical Nutrition; 93: 569-77. **30.** Casaer MP, (2011). Early versus late parenteral nutrition in critically ill adults. New England Journal of Medicine. Jun 29. [Epub ahead of print] http://www.nejm.org/doi/full/10.1056/NEJMoa1102662. **31.** Sevette A, (2005). Does growth hormone allow more efficient nitrogen sparing in postoperative patients requiring parenteral nutrition? A double-blind, placebo-controlled randomised trial. Clinical Nutrition; 24; 943-955. **32.** Battistella F, (1997). A prospective, randomized trial of intravenous fat emulsion administration in trauma victims requiring total parenteral nutrition. The Journal of trauma; 43: 52-8; discussion 58-60. **33.** Frankenfield DC, Smith JS, Cooney RN (1997). Accelerated nitrogen loss after traumatic injury is not attenuated by achievement of energy balance. Journal of Parenteral and Enteral Nutrition; 21: 324-9. **34.** Scheinkestel C, (2003). Prospective randomised controlled trial to access caloric and protein needs of critically ill, anuric ventilated patients requiring continuous renal replacement therapy. Nutrition; 19: 909-16. **35.** Oliveira GP, et al (2010). Understanding the mechanisms of glutamine action in critically ill patients. Annals of the Brazilian Academy of Sciences; 82: 417-30. **36.** Reeds P, Fjeld C, Jahoor F (1994). Do the differences between the amino acid compositions of acute-phase and muscle protein have a bearing on nitrogen loss in traumatic states? Journal of Nutrition; 124: 906-10. **37.** Scheinkestel C, (2003). Impact of varying parenteral protein loads on amino-acid balance in critically-ill anuric patients on CAVHDF. Nutrition; 19: 813-5. **38.** Berard M, (2002). Qualitative manipulation of amino acid supply during total parenteral nutrition in surgical patients. Journal of Parenteral and Enteral Nutrition; 26: 136-43. **39.** Obled C, Papet I, Breuille D. Sulfur-containing amino acids and glutathione in diseases. In: Cynober LA (editor). Metabolic and therapeutic aspects of amino acids in clinical nutrition, pp667-87. 2003. 2nd edition. CRC Press. Florida. **40.** Reid M, et al (2004). Supplementation with aromatic amino acids improves leucine kinetics but not aromatic amino acid kinetics in Infants with Infection, severe malnutrition and edema. Journal of Nutrition; 134: 3004–10. **41.** Magnotti LJ, Deitch E (2005). Burns, bacterial translocation, gut barrier function, and failure. Burn Care Rehabiitation; 26: 383-391. **42.** Tuin A, et al (2009). Role of alkaline phosphatase in colitis in man and rats. Gut; 58: 379-387. **43.** Goldberg RF, (2008). Intestinal alkaline phosphatase is a gut mucosal defense factor maintained by enteral nutrition. Proceedings of the National Academy of Science;105:3551-6. Se/bp58. **44.** Clark JA, Coopersmith CM (2007). Intestinal crosstalk: a new paradigm for understanding the gut as the "motor" of critical illness. Shock; 28: 384-393. **45.** Doig GS, et al (2009). Early enteral nutrition, provided within 24 h of injury or intensive care unit admission, significantly reduces mortality in critically ill patients: a meta-analysis of randomised controlled trials. Intensive Care Medicine; 35: 2018-27. **46.** Heyland D, (2003). Canadian Critical Care Clinical Practice Guidelines Committee. Journal of Parenteral and Enteral Nutrition; 27: 355-73. **47.** McClave S, et al (2009) . 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.). Journal of Parenteral Enteral Nutrition; 33; 277-317. **48.** Kles KA, Wallig MA,Tappenden KA (2001). Luminal nutrients exacerbate intestinal hypoxia in the hypoperfused jejunum. Journal of Parenteral and Enteral Nutrition;25:246-53. **49.** Melis M, et al (2006). Bowel necrosis associated with early jejunal tube feeding: a complication of postoperative enteral nutrition. Archivs of Surgery; 141: 701-704. **50.** Purcell PN, et al (1993). Continuous duodenal feeding restores gut blood flow and increased gut oxygen utilization during PEEP ventilation for lung injury. Americal Journal of Surgery; 165: 188-193. **51.** Revelly JP, et al (2001). Early metabolic and splanchnic responses to enteral nutrition in postoperative cardiac surgery patients with circulatory compromise. Intensive Care Medicine; 27: 540-547. **52.** Khalid I, Doshi P, DiGiovine B (2010). Early enteral nutrition and outcomes of critically ill patients treated with vassopressors and mechanical ventilation. American Journal of Critical Care; 19: 261-268. **53.** Simpson F, Doig GS (2005). Parenteral versus enteral nutrition in the critically ill patient: a meta-analysis of trials using the intention to treat principle. Intensive Care Medicine; 31:12–23. **54.** Marik P, Zaloga G (2001). Early enteral nutrition in acutely ill patients: A systematic review. Critical Care Medicine; 29: 2264-70. **55.** Wasiak J, Cleland H, Jeffery R (2007). Early versus late enteral nutritional support in adults with burn injury: a systematic review. Journal of Human Nutrition and Dietetics, 20:75–83. **56.** Doig GS, et al (2011). Early enteral nutrition reduces mortality in trauma patients requiring intensive care: A meta-analysis of randomised controlled trials. Injury; 42: 50-56. **57.** Lewis SJ, Andersen HK, Thomas S (2009). Early Enteral Nutrition Within 24 h of Intestinal Surgery Versus Later Commencement of Feeding: A Systematic review and Meta-analysis. Journal of Gastrointestinal Surgery;13:569–575. **58.** McClave S, et al (2006). Nutrition Support in Acute Pancreatitis: A Systematic Review of the Literature. Journal of Parenteral and Enteral Nutrition; 30: 143-156. **59.** Heyland DK, et al (2011). Identifying critically ill patients who benefit the most from nutrition therapy: the development and initial validation of a novel risk assessment tool. Critical Care; 15: R268.

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