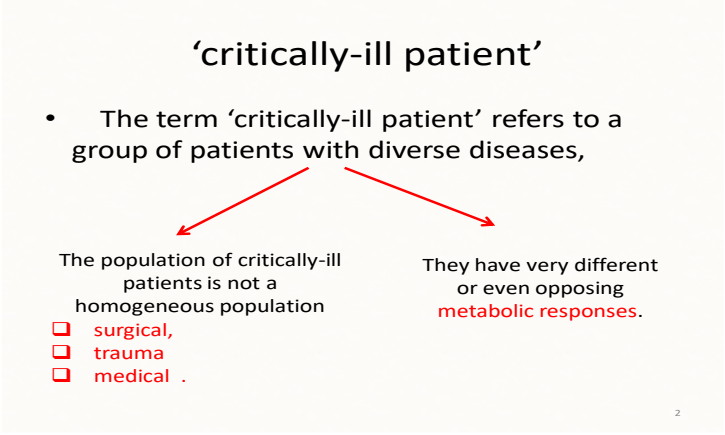
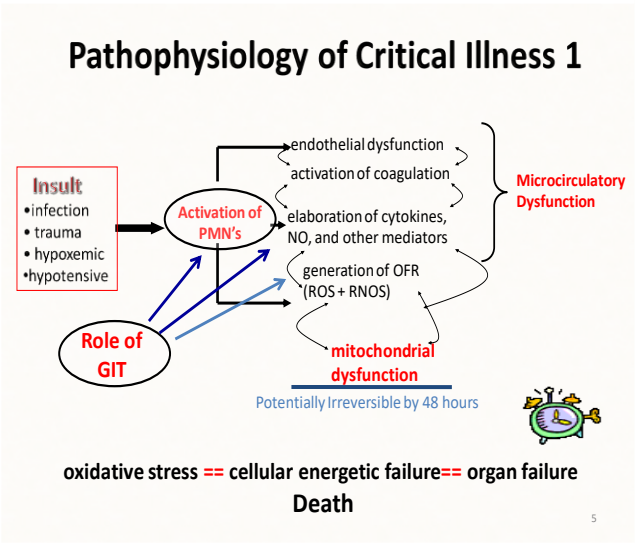
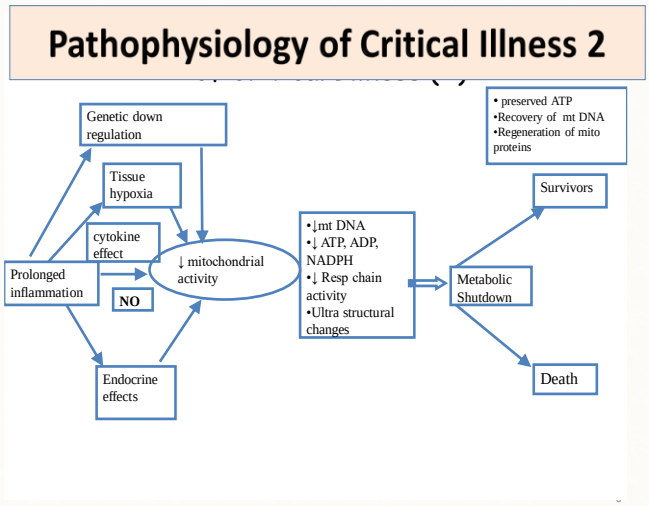
Role of Nutrients in Critically Ill Patients



the population of critically-ill patients is not a homogeneous population, based on their assignment to either the surgical, trauma or medical area, and within these, to their specific disease, whose level of severity should be established .with very different or even opposing metabolic responses,

so overall recommendations cannot be established .





polymorphonuclear leukocytes (PMNs) play a key role in host defence against infection
PMNs enhanced a Th١-type immune response (IFN-gamma, TNF-alpha), down-regulated the expression of the Th٢-type cytokine interleukin-١٠ (IL-١٠), and was associated with protection against

Polymorphonuclear leukocytes, or granulocyte

- Polymorphonuclear neutrophil, the most abundant white blood cells in the peripheral blood of humans, and many (though not all) mammals

general, harmful effects of reactive oxygen species on the cell are most often:[٤]

١. damage of DNA
٢. oxidations of polyunsaturated fatty acids in lipids (lipid peroxidation)
٣. oxidations of amino acids in proteins
٤. oxidatively inactivate specific enzymes by oxidation of co-factors

DNA Lesions Caused by ROS and RNOS: A Review of Interactions and Reactions Involving Guanine

RNOS Reactive Nitrogen Oxide Species *(aka Reactive Nitrogen Oxide Species)*

How can Nutrients help the critically ill?

- Provide nutritional substrates to meet protein and energy requirements
- Help protect vital organs and reduce break down of skeletal muscle
- To provide nutrients needed for repair and healing of wounds and injuries
- To maintain gut barrier function
- Modulate underlying pathphysiological processes in critically ill to improve outcome .

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When to start and how to give?

Critically-ill patients who are not expected to receive a complete oral diet for at least 3 consecutive days should receive specialized nutritional support (C).

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Early administration, ranging from 24 to 72 h from admission to the ICU.

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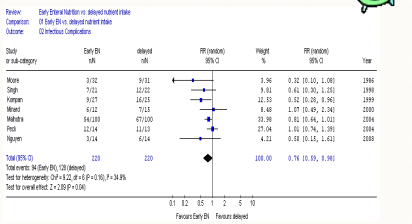
- in critically-ill patients have shown that the cumulative deficit in calorie intake is associated with more complications, both infectious and noninfectious, and a longer period of mechanical ventilation than with complete nutritional intake ٥.
- Combating malnutrition is more important than the route of nutritional support itself
- In critically-ill patients who will not receive a complete oral diet for ٣ days, specialized nutritional support should be started, both enteral٦(IV) and parenteral٧

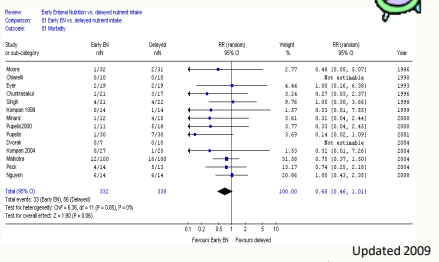
malnutrition is an independent risk factor for morbidity, with an increased rate of infections, ICU and hospital stay, days of mechanical ventilation, difficulty for wound healing and increased mortality

Early vs. Delayed EN: Effect on Infectious Complications



Updated 2009
www.criticalcarenutrition.com

Early vs. Delayed EN: Effect on Mortality



Updated 2009
www.criticalcarenutrition.com

Routes of Nutrients supply critically ill patient

Enteral route
1. Nasogastric tube
2. Gastrostomy tube
3. jejunostomy

❑ Routine or standard use of the naso-jejunal tube in critically-ill patients is not associated with increased efficacy in provision of enteral nutrition or a lower rate of infectious complications **(A)**.

❑ Severe acute pancreatitis, Elevated gastric output. can be considered (C).

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What if you can't provide adequate early enteral nutrition?

… to PN or not to PN, that is the question!

Complementary parenteral nutrition should be started when 60% of nutritional requirements are not met at the fourth day of admission, or for at least 2 consecutive days during the hospital stay (C).

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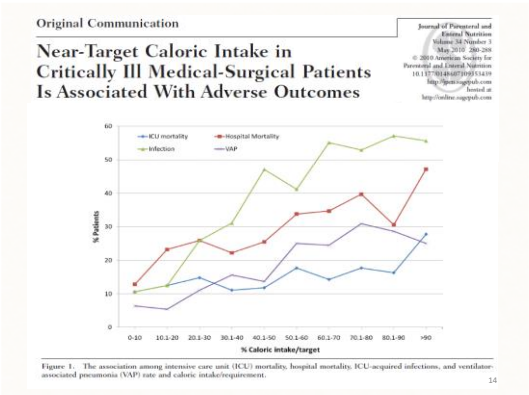
increased knowledge of PN in terms of calorie and protein needs, improved control of glucose levels and improved management of central catheters ---lead to that the complications associated with malnutrition for not starting nutrition early were greater than the complications from parenteral administration

What are the indications for postpyloric enteral nutrition

In specific conditions, such as severe acute pancreatitis, or in patients with elevated gastric output, their use may be considered for the purpose of reducing the use of PN in these patients٢٨

In a situation of persistent increase in gastric output with a high risk of bronchial aspiration or severe pancreatitis, its use can be considered (C).

•critically-ill patients do not appear to benefit from the complete provision, suggesting that it is more appropriate to administer ٣٣-٦٦٪ of nutritional objectives



Original Communication

Near-Target Caloric Intake in Critically Ill Medical-Surgical Patients Is Associated With Adverse Outcomes

Journal of Parenteral and Enteral Nutrition

ICU mortality — Hospital Mortality — Infection — VAP

% Patients

% Caloric intake/target

Figure 1. The association among intensive care unit (ICU) mortality, hospital mortality, ICU-acquired infections, and ventilator-associated pneumonia (VAP) rate and caloric intake/requirement.

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The role of carbohydrates critically-ill ,
What type &amount should be supplied

➢Stores are depleted in less than 24 hrs of fasting
➢skeletal muscle protein breakdown-- AA convert to glucose in the liver

Glucose → 4 g/kg/day
Glucose → 50% of the global energy requirements,

maintaining blood sugar 140 and 180 mg/dL

insulin → It is recommended, as most appropriate, to maintain glycemia levels below 150 mg/dl **(C).**

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•Excess CHO will cause: **at the higher infusion rate.**

(١) Steatosis of the liver Glucose → glycogen

Glucose → fat (lipogenesis , CO_2 production)

(٢) hyperglycemia – exacerbated by insulin resistance

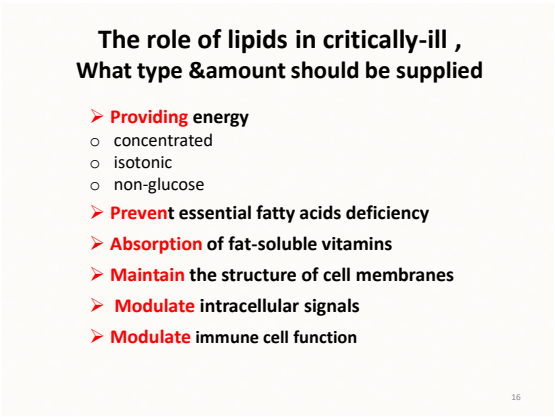
(٣) delayed weaning off the ventilator

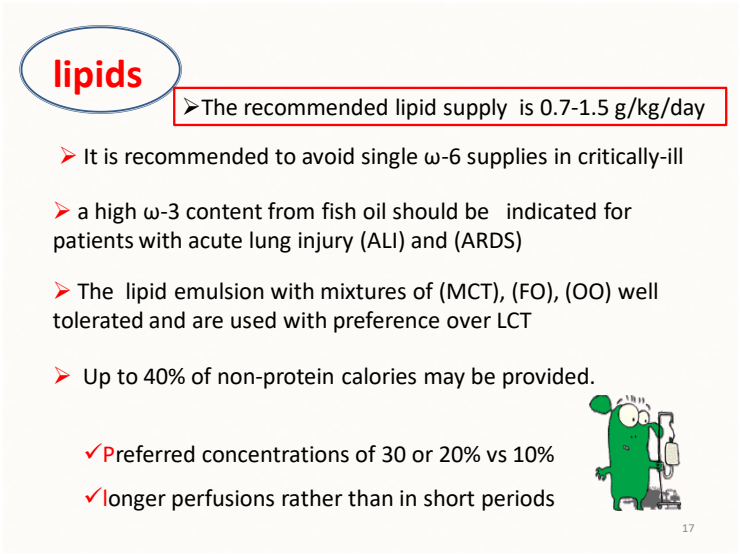
•

•The amount of CHO is related to the amount that can be oxidized by the liver.

•٦٠ –٧٠ % of energy
•Parenteral nutrition

Glucose is still the main calorie substrate in critically-ill patients. it is recommended never to administer a glucose supply greater than ٤ g/kg/day.attempting to maintain lower values would be associated with a higher incidence of severe hypoglycemia, without achieving beneficial effects on mortality





Lipid intake must be a fundamental part of nutritional support since, in addition to providing energy in a small volume, it is essential to prevent essential fatty acids deficiency and to maintain the structure of cell membranes, and also to modulate intracellular signals

Compared to carbohydrates, lipid supply causes a lower effect on thermogenesis, lipogenesis, stimulation of insulin release, CO production and glycemia values. It is generally considered that ω-٣ fatty acids may counteract the proinflammatory effects of ω-٦

It should be administered at concentrations of ٣٠ or ٢٠٪ vs ١٠٪, resulting from a decreased supply of phospholipids and longer perfusions rather than in short periods to prevent changes in pulmonary ventilation/perfusion

currently the mixtures with middle-chain triglycerides (MCT), fish oil, or olive oil have been shown to be well tolerated and are used with preference over LCT. However, it is difficult to make a specific choice on the type to be used as non of them has shown significant advantages over the other . They must not be administered, or their supply should be reduced, when plasma triglyceride levels are greater than ٤٠٠ mg/dL . Up to ٤٠٪ of non-protein calories may be provided. With regard to EN, diets with a high ω-٣ content from fish oil should be particularly indicated for patients with acute lung injury (ALI) and acute respiratory distress syndrome (ARDS)

What lipid emulsions must be used in sepsis?

As regards their use in PN, the results are somewhat more conclusive and are related to the dose of ω-٣ provided. The most favorable effects were obtained at doses of ٠,١-٠,٢ g/kg/day for survival, infection rates and length of stay. In addition, antimicrobial requirements decreased ٢٦٪A recent randomized, single-blind study ٢٧ including ٢٥ patients with sepsis receiving PN with MCT/LCTversus MCT/LCT/fish oil did not show significant differences in terms of mortality, days on mechanical ventilation or length of stay in ICUs Heller AR, Rossler S, Litz RJ, Stehr SN, Heller SC, Koch R et

The role of protein in critically-ill , What type &amount should be supplied.

In critically-ill patients, no specific formulation of amino acids has been defined for generic use (C).

Branched chain amino acid's – support immune cell functions.

The there is not sufficient evidence to justify the use of formula with excess branched chain amino acids in critically ill specially in septic patients.

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In general, the supply must be adjusted to an amount of **1-1.8 g/kg/day (B).**

1.5 g/kg/day decreases protein catabolism by 70%,

Estimate protein requirement

UUN : 5- 10 **level 1 stress** (1.2 –1.3 g protein/ kg BW)
UUN : 10- 25 **level 2 stress** (2 g protein/ kg BW)

very high supplies are not recommended,

- 2 g/kg/day causes an increase in net protein degradation, drive urea genesis .
- **No improvement in overall balance**
- will not likely promote better nitrogen retention,

Kcal : N ratio
150: 1 (moderate stress) 80 –100 : 1 (severe stress)

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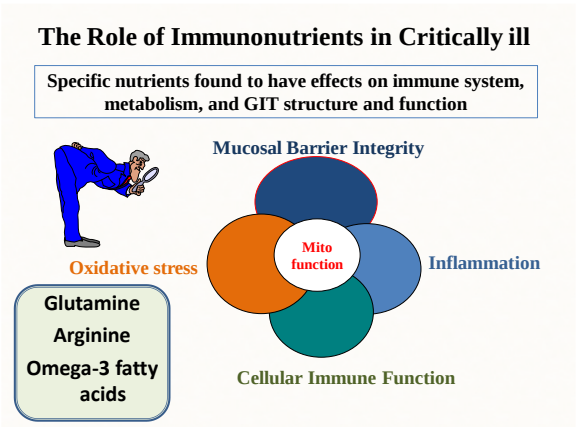
UUN > Assess the degree of hypermetabolism (stress)

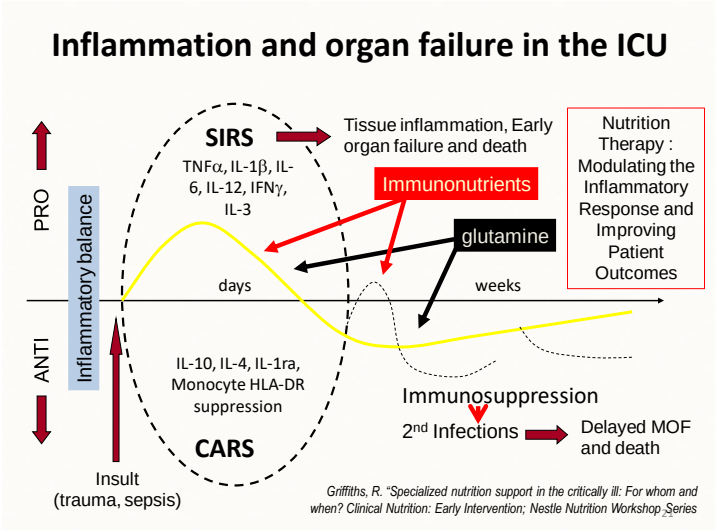
> If N excretion exceeds the protein equivalent of approximately ٢ g/kg , higher protein intakes will not likely promote better nitrogen retention, but will instead drive ureagenesis.

Estimation of nitrogen requirements per kg actual BW/day

- Normal ٠,١٧g (١,٠٦٢٥ g)
- Hypermetabolic ٥-٢٥ % ٠,٢ g (١,٢٥ g)
  ٢٥ –٥٠٪ ٠,٢٥ g (١,٥٦٢٥g)
  > ٥٠ % ٠,٣ g (١,٨٧٥ g)

Note: The maximum amount of nitrogen that can be metabolized by any individual is 18 g /day (112.5 g protein).





. **Immunonutrition**

Nutrients most often studied:

- Arginine - can enhance wound healing and improve immune function. Conditionally essential amino acid.
- Glutamine – Precursor for rapidly dividing immune cells, thus aiding in immune function. Conditionally essential.
- Branched chain amino acid's – support immune cell functions.

Omega ٣ fatty acids – lowers magnitude of inflammatory response, modulate immune response

Pathophysiology

•Slide-Modulation of dysfunctional inflammation by immunonutrition

Let me talk about modulation of dysfunctional inflammation by immunonutrition.

An initial insult such as sepsis, trauma and major operation induces an early systemic inflammatory response syndrome. The amplitude and duration depends on the magnitude of insult and inherent factors. The greater the insult, the larger the systemic inflammatory responses.

Severe systemic inflammatory response syndrome can precipitate early MOF.

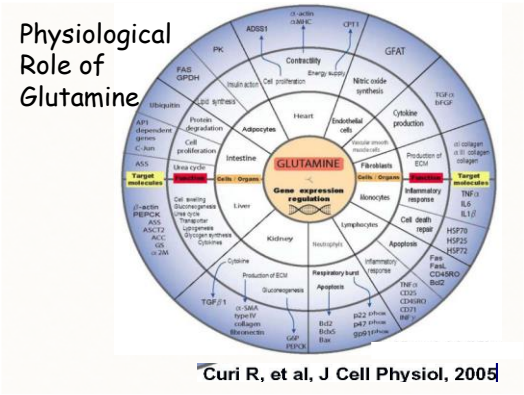
On the other hand, to counter-regulate the severe inflammatory response, systemic immunosuppression may occur. In addition, malnutrition induced by surgical stress also leads to systemic immunosuppression. The severe immunosuppression may contribute to the occurrence of infection. The resulting infection triggers late MOF.

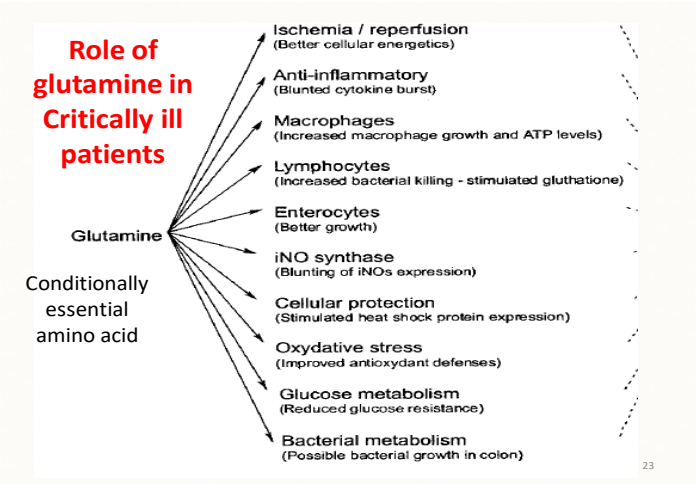
•Therefore, both severe inflammatory response and severe immunosuppression are needed to be moderated. Immunonutrition can modulate these dysfunctional responses to well-regulated inflammatory responses. Patients die early from single organ failure

- Due to primary pathology/ insult/ infection (brain, or heart, or liver or lung)

•Patients die later from multi-organ failure

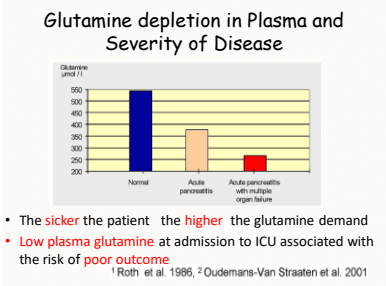
- Due to secondary infections (combined organ failure (e.g. lung, liver, and kidney)





After aggression, glutamine plays a major role in inducing mechanisms of cell protection mainly through increasing production of heat shock proteins, as their expression protects against cell damage and against ischemia/reperfusion mechanisms

which gives it a potential role to prevent progression to multiple organ failure.



Is glutamine administration of choice in Critically ill patients or sepsis?

In critically-ill patients intravenous administration of glutamine dipeptide (Ala-Gln) of 0.5 g/kg/day is recommended, complementing parenteral nutrition (A).

Although no studies have been performed in humans to evaluate the effect of glutamine on septic patients receiving PN When parenteral nutrition is indicated, it is recommended to use glutamine supplements (B).

When the patient is receiving EN It is recommend to give IV glutamine , as a supplement,

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CLINICAL NUTRITION WEEK 2013
February 9-12, 2013

•Do not exceed Glutamine recommended dose (up to 0.5 g/ kg IBW) in critically ill patients
•A combined enteral and intravenous administration of glutamine can be used as long as the total does not exceed 0.5 g/ kg IBW

i.v. glutamine-containing product should not be given in patients with

- renal insufficiency
- multi-organ failure incl. metabolic acidosis
- insufficient clinical nutrition

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Although no studies have been performed in humans to evaluate the effect of glutamine on septic patients receiving PN, there is sufficient evidence to the routine use of glutamine in all critically-ill patients receivingPN[٢]

its *intravenous use, as a supplement, when the patient is receiving EN.*

- Do not exceed Glutamine recommended dose (up to ٠,٥ g/ kg IBW) in critically ill patients
- A combined enteral and intravenous administration of glutamine can be used as long as the total does not exceed ٠,٥ g/ kg IBW

Role of Arginine in Critically ill patients

It is a non essential amino acid

It is reduced in trauma and sepsis.

- an increase in acute phase reactants,
- It gives rise to an increase in nitrogenous compounds such as NO. with antibacterial activity
- It can increase substrates necessary for the synthesis of connective tissue (leads to wound healing).
- action as bowel neurotransmitter
- activity in insulin stimulation,
- regulator of microcirculation
- improve immune function. And promoting cell growth and cell differentiation
- modulation of cell signals

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Arginine is considered a non essential amino acid although its availability is reduced in trauma and sepsis. There is a considerable body of literature that suggests that argnine effect **hormone release and polyamine release- these growth factors increase substrates necessary for the synthesis of connective tissue (leads to wound healing).** However, arginine also gives rise to an increase in nitrogenous compounds such as NO.

As arginine is an amino acid that is decreased in sepsis and it is considered necessary to restore its values, new pathways are under research to restore this deficit supplying citrulline[٢٠]

It is known that sepsis is a condition associated with arginine deficit and arginine has been associated with benefits for sepsis, such as an increase in acute phase reactants, genesis of nitric oxide (NO) with antibacterial activity, action as bowel neurotransmitter and regulator of microcirculation, production of ornithine promoting cell growth and cell differentiation and activity in insulin stimulation, as well as modulation of cell signals from its metabolite, agmatin

Are diets with mixtures of Pharmaconutrients indicated in critically ill (IMD)

There is a controversy about the outcomes and recommendations of the different meta analyses about (IMD)

(arginine,ω-3, nucleotides, antioxidants)

➢In Sepsis; It may be associated with increased mortality.

Montejo JC,et al .Clin Nutr 2003

➢there is sufficient evidence to use IMD in critically-ill patients, considering the benefits associated with their use and the lack of harmful effects Marik PE, et al Intensive Care Med 2008

➢A randomized, controlled, prospective study on PN vs EN enriched with Pharmaconutrients (mixture of arginine, ω -3 and antioxidants) in septic patients reported a greater intra-ICU mortality in the enteral group

Bertolini G, et al Intensive Care Med 2003 28

❑ Enteral diets with mixtures of substrates with different Pharmaconutrients capacity can provide outcome benefits in septic patients (C). SEMICYUC:& SENPE Nutr Hosp 2011

❑ Administration of diets enriched with arginine in severe sepsis and septic shock is not Cleary associated with deleterious effects in patient outcomes (C).

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❑ Immune modulating formula beneficial in the following patient groups:

- upper GI surgery
- mild sepsis
- trauma

If unable to tolerate <700ml/d immune modulating formula should be stopped. Espen guidelines (2006):

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known controversy about the outcomes and recommendations of the different metaanalyses.

Espen guidelines (٢٠٠٦):

•Immune modulating formula beneficial in the following patient groups:

- upper GI surgery
- mild sepsis
- trauma

If unable to tolerate <٧٠٠ml/d immune modulating formula should be stopped

in the last metaanalysis published, concluded that only in the group of patients with sepsis, septic shock, or acute respiratory distress syndrome (ARDS), the use of IMD was associated with a significant decrease of mortality, secondary infections, and stay at the ICU, but provided this formula contained fish oil.

• diets enriched with "immunomodulating"pharmaconutrients (arginine, ω-٣, nucleotides, antioxidants) in septic patients in a critical condition. is associated with lower mortality compared with the use of a control diet

IMD: Acute lung injury (ALI) or ARDS

multicenter study in patients undergoing mechanical ventilation with severe sepsis and septic shock reported:

- A 19.4% reduction in the absolute risk of mortality,
- Improved oxygenation,
- More days free from mechanical ventilation,
- Decreased stay at the ICU
- Less development of new organic dysfunctions

in the group receiving the study diet.

Pontes-Arruda A, Crit Care Med 2006;

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Omega-٣ fatty acids improve the diagnosis-related clinical outcome, Heller AR Crit Care Med ٢٠٠٦.

Other formulations enriched with pharmaconutrients, initially designed for acute lung injury (ALI) orARDS A

Antioxidants , vitamins and trace elements

The plasma concentration of micronutrients with antioxidant capacity decreases in critically-ill, particularly in septic patients

special attention should be paid to the supply of trace elements (particularly selenium, zinc and copper) and vitamins

The need for supplying micronutrients (vitamins and trace elements) **is set (A),**

But the amount cannot be established.

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❖ Meta-analysis of 15 randomized studies a combination of antioxidant vitamins and trace elements(selenium, zinc and copper)

> Reduces mortality and the duration of mechanical ventilation

> Does not improve infectious complications or length of stay

Canadian Clinical Practice Guidelines 2011

❖ The REDOX study,2013 on the potential beneficial effect of selenium for critically ill patients, Supplementation with antioxidants: selenium (i.v.) **plus** selenium, Vit. C+E, zinc, ß-carotene (enterally)

No significant difference found for 28-day mortality in any statistical analysis

High-dose selenium supplements alone may not be recommended routinely critically ill patients

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Summary

The main Role of Nutrients is Improve Survival of Critically Ill Patients

- Energy: Carbohydrate and fat intake frees up protein (essential amino acids and nitrogen) so that it can be used for tissue building.
- Antioxidants, Vitamins and minerals: Control protein and energy metabolism through their coenzyme roles.
- Immunonutrients : Modulate underlying pathphysiological processes

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SEPSIS

Recommendations

– *In patients with septic shock and hemodynamic instability it is recommended to delay the start of spcialized nutritional support until the patient has been adequately resuscitated and is in a stable condition (C).*

Splachnic infusion may be compromised in hypotensive patients with inadequate perfusion pressure fatal consequences of intestinal ischemia, to start EN after patient resuscitation or at least when a stable shock stage has been reached, with an adequate perfusion pressure n any case, particularly in the early stages of shock, close monitoring for signs of intestinal intolerance (abdominal distension, increased gastric residue, etc.)is necessary to early identify signs of subclinical intestinal ischemia Parenteral nutrition is a safe route in sepsis when there is no other option for feeding patients (C). Complementary parenteral nutrition could be used when calorie supply requirements may not be reached by the enteral route (C).