

Discussion on Immuno-Nutrition in the Intensive Care Unit

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Facts (1)

- **Stress response**
- **Catabolism**
- **immune system dysfunction**
- **pro VS anti – inflammatory process**

are interrelated pathophysiological mechanisms that underlie critical illness after an intense physiological insult

Questions concerning nutritional support in the ICU

- A. Route of Nutritional Support (Total Parenteral Nutrition versus Total Enteral Nutrition)
- B. Timing of Nutritional Support (Early versus Late)
- C. Site of Nutritional Support (Gastric versus Jejunal)
- D. Macronutrient Formulation (How many calories and what proportion of protein, carbohydrate, and fat?)
- E. Monitoring of Nutritional Support (Which tests and how often?)
- F. Type of Nutritional Support (Standard versus Enhanced)

Answers Q(A)

A. Level I

Patients with *blunt and penetrating abdominal injuries* should, when feasible, be fed enterally because of the lower incidence of septic complications compared with parenterally fed patients.

B. Level II

Patients with *severe head injuries* should preferentially receive early enteral feeding, since outcomes are similar compared with parenterally-fed patients. If early enteral feeding is not feasible or not tolerated, parenteral feedings should be instituted.

(2003 Eastern Association for the Surgery of Trauma)

Answers Q(A)

C. Level III

1. In severely injured patients, TPN should be started by day 7 if enteral feeding is not successful.
2. Patients who fail to tolerate at least 50% of their goal rate of enteral feedings by post-injury day 7 should have TPN instituted but should be weaned when >50% of enteral feedings are tolerated.

(2003 Eastern Association for the Surgery of Trauma)

Answers Q(B)

Level I

In severely injured blunt/penetrating trauma patients, there appears to be no outcome advantage to initiating enteral feedings within 24 hours of admission as compared to 72 hours after admission.

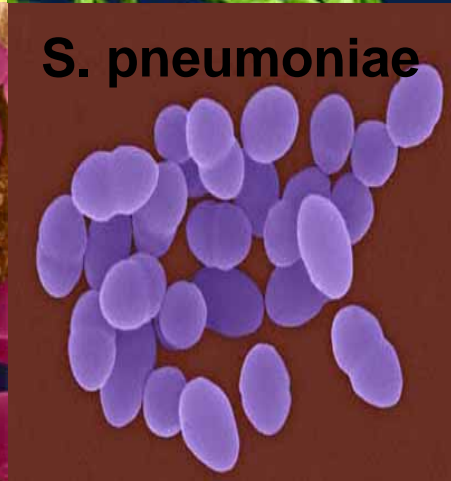
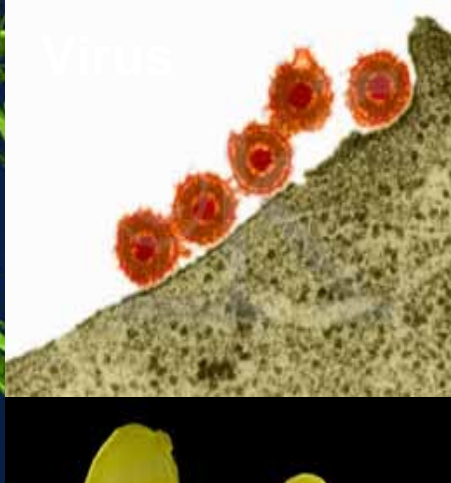
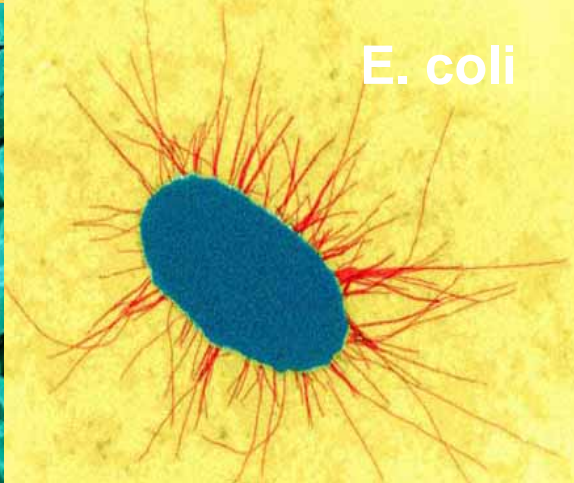
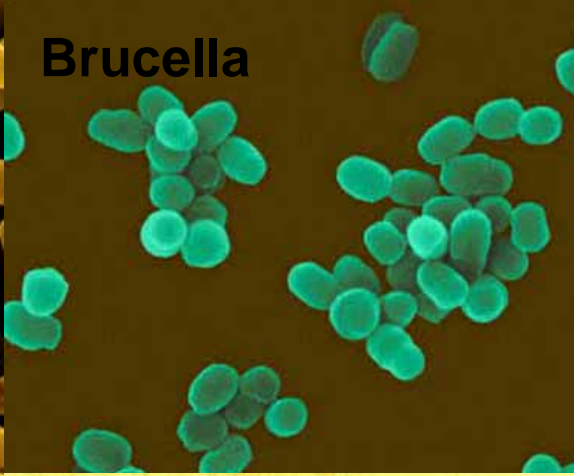
(2003 Eastern Association for the Surgery of Trauma)

Answers Q(B)

Level II

1. In burn patients, intragastric feedings should be started as soon after admission as possible, since delayed enteral feeding (>18 hours) results in a high rate of gastroparesis and need for intravenous nutrition.
2. Patients with severe head injury who do not tolerate gastric feedings within 48 hours of injury should be switched to postpyloric feedings, ideally beyond the ligament of Treitz, if feasible and safe for the patient.

(2003 Eastern Association for the Surgery of Trauma)



Answers Q(B)

Level III

1. Patients who are incompletely resuscitated should not have direct small bowel feedings instituted due to the risk of gastrointestinal intolerance and possible intestinal necrosis.
2. In patients undergoing laparotomy for blunt and penetrating abdominal injuries, direct small bowel access should be obtained (via nasojejunal feeding tube, gastrojejunal feeding tube, or feeding jejunostomy) and enteral feedings begun as soon as is feasible following resuscitation from shock.

(2003 Eastern Association for the Surgery of Trauma)

Answers Q(C)

A. Level I

No recommendations.

B. Level II

In critically injured patients, early gastric feeding, is feasible, and clinical outcome is equivalent to patients fed into the duodenum. For this reason and because access to the stomach can be obtained more quickly and easily than the duodenum, an initial attempt at gastric feedings appears warranted.

C. Level III

Patients at high risk for pulmonary aspiration due to gastric retention or gastroesophageal reflux should receive enteral feedings into the jejunum.

(2003 Eastern Association for the Surgery of Trauma)

Answers Q(D, E)

D. Macronutrient Formulation (How many calories and what proportion of protein, carbohydrate, and fat?)

E. Monitoring of Nutritional Support (Which tests and how often?)

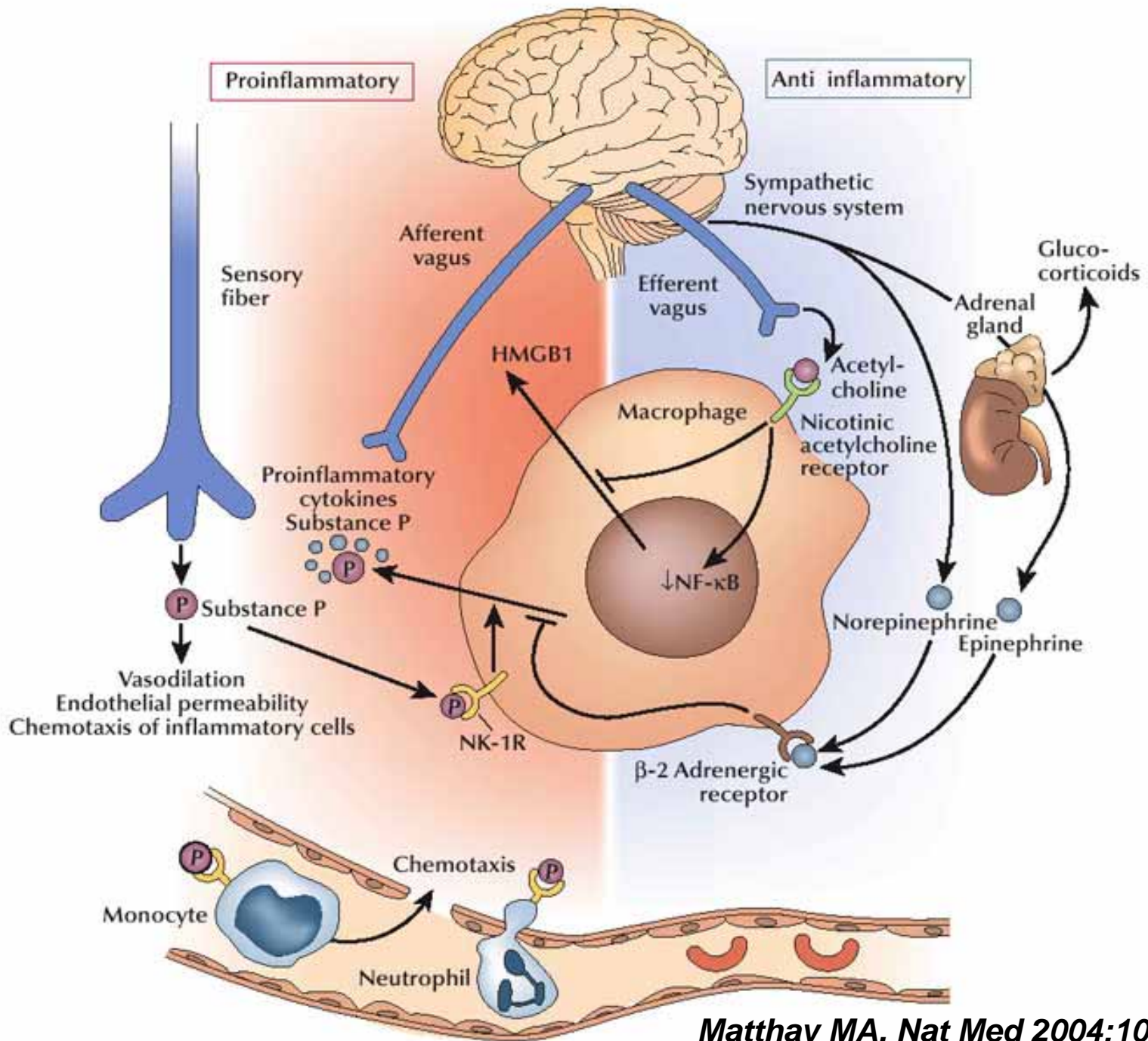
Answers Q(F)

Standard VS Enhanced feeding

Lack of uniformity in

- Population conditions
- Enhanced formulation composition
- Outcome parameters
- Enhanced enteral feeding initiation time
- Duration
- Supplemental TPN use
- Isocaloric / isonitrogenous feeding

Inadequate power (no of patients)



After an appropriately intense physiologic insult

interleukin-1, interleukin-2, interferon- γ and tumor necrosis factor- activate

interleukin-4, interleukin-10, and interleukin-13 deactivate

These two opposing responses can induce a state of imbalance

(Pierre Singer, Jonathan Cohen Nutrition 21 (2005) 282–283)

Lipids and Immune Function

High levels of PUFA (especially linoleic)

Suppressive on:

–Neutrophils

–Lymphocytes

–Monocytes

–Macrophage (*in vivo/ in vitro*)

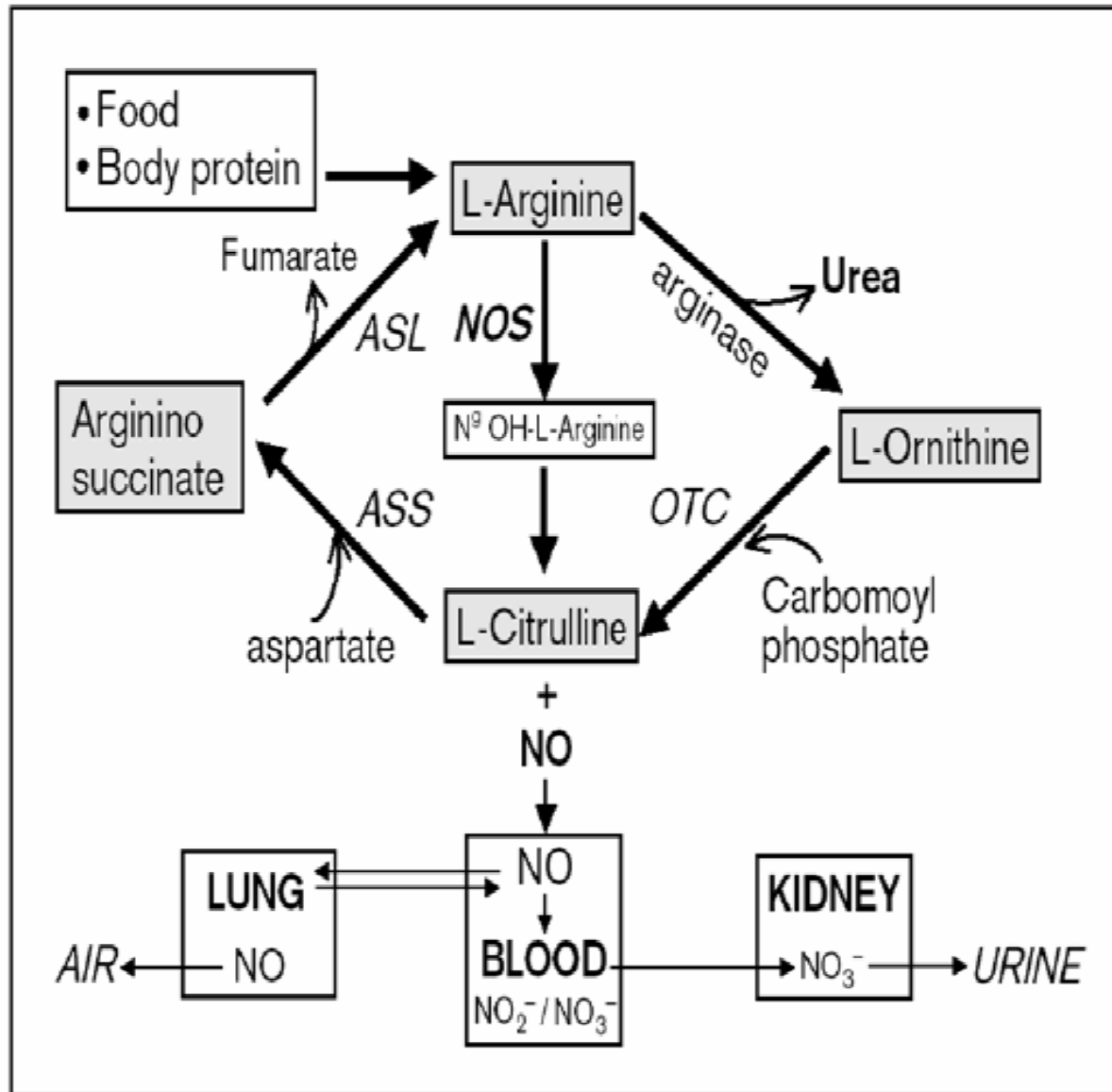
- Specific Immune suppressive effects
- Inhibition of lymphocyte proliferation
- Decrease in chemotaxis and migration
- Impairs RE system
- Decrease bactericidal capacity

Omega 3 Fatty Acids

Clinical Data

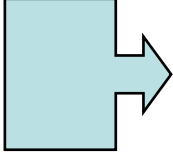
- ↓inflammatory response
 - ↓arrhythmia on vent patients
 - ↑tissue microperfusion
 - ↑graft function
 - Limits omega-6 immune suppression
 - Maturation of CNS
 - ↑clearance
-
- Biological regulators
 - Cell membrane structure and function
 - Influences membrane fluidity
 - Alters receptors activity
 - Eicosanoidmetabolism
 - Cytokine production
 - Gene expression

Arginine pathways



During stress or after major surgery, plasma and muscle glutamine concentrations are significantly decreased, reflecting the increased demand of these immune cells, which cannot always be met by protein breakdown

Immuno-nutrition

- Malnutrition  suppressed immune response
- Immune-enhancing nutrients -IEN

Most beneficial:

L-arginine, L-glutamine, nucleotides, ω -3 (EPA & DHA), zinc, vitamins A,E,C

Table 6—Complication Rates by BMI Category*

Variables	Underweight	Normal Weight	Overweight	Obese	Severely Obese
Central line infection	7 (12)	8 (10.5)	9 (10.7)	8 (16)	4 (17.4)
Pneumothorax	3 (5.2)	7 (9.2)	3 (3.6)	1 (2)	2 (8.7)
Vancomycin-resistant enterococci	3 (5.2)	3 (3.9)	4 (4.8)	1 (2)	2 (8.7)
Deep venous thrombosis	6 (10.3)	5 (6.6)	5 (6.0)	3 (6)	2 (8.7)
VAP	5 (8.6)	10 (13.2)	11 (13.1)	10 (20)	2 (8.7)
Catheter-related sepsis	4 (6.9)	8 (10.5)	7 (8.3)	3 (6)	0
Failed extubation	12 (20.7)	18 (23.7)	11 (13.1)	11 (22)	2 (8.7)
GI hemorrhage	2 (3.4)	5 (6.6)	12 (14.3)	5 (10)	4 (17.4)
Prolonged paralysis from NMB	1 (1.7)	1 (1.3)	3 (3.6)	0	1 (4.3)
Oxacillin-resistant <i>Staphylococcus aureus</i>	2 (3.4)	1 (1.3)	4 (4.8)	3 (6)	2 (8.7)
Self extubation	8 (13.8)	7 (9.2)	12 (14.3)	5 (10)	1 (4.3)
Aspiration	1 (1.7)	1 (1.3)	1 (1.2)	0	0
Complication percentage difference	2 (3.4)	2 (2.6)	1 (1.2)	0	0
Arterial line infection	0	0	0	0	1 (4.3)
Self extubation that needed to be reintubated	1 (1.7)	0	1 (1.2)	0	0
Pneumothorax by barotrauma	1 (1.7)	0	0	0	0
Total	58	76	84	50	23
Sample size	350	663	585	396	154

Immunonutrition formulas examples

Table 1. Main constituents of immunonutrition (IMN) formulae that have been most commonly used in clinical trials

Constituent	Impact (per L)	Immunaid (per L)	Abbott Diet (per L)	IMN formula (per L) ^a
Protein	56 g	80 g	66.7	75 g
Arginine	12.5 g (5.6% energy)	15 g (6% energy)	6.6–6.8 (2.5% energy)	9 g (2.8% energy)
Glutamine	—	12 g	—	13 g
Fat	28 g	22 g	37.3	42 g
n-3 Fatty acids	2 g as EPA and DHA	1.1 g as α -linolenic	1.3–1.5 g as α -linolenic	1.1 g as α -linolenic
Carbohydrate	134 g	120 g	180 g	145 g
Nucleic acid	1.2 g	1 g	0	0

Gadek JE, DeMichele SJ, Karlstad MD et al:
Crit Care Med 1999; 27:1409-1420

Effect of enteral feeding with
eicosapentaenoic acid, gamma-linolenic
acid, and antioxidants in patients with acute
respiratory distress syndrome

Enteral Nutrition in ARDS Study Group

Surgery 2002 Nov;132(5):805-14

Preoperative oral arginine and n-3 fatty acid supplementation improves the immunometabolic host response and outcome after colorectal resection for cancer.

Braga M, Gianotti L, Vignali A, Carlo VD.

Two hundred patients with colorectal neoplasm

- (a) oral intake for 5 days before surgery of a formula enriched with arginine and n-3 fatty acids (pre-op group; n = 50)
- (b) same preoperative treatment prolonged after surgery by jejunal infusion (peri-op group; n = 50)
- (c) oral intake for 5 days before surgery of a standard isoenergetic, isonitrogenous formula (control group; n = 50)
- (d) no supplementation before and after operation (conventional group; n = 50)

Montejo JC et al *Clin Nutr.* 2003 Jun;22(3):221-33
Immunonutrition in the intensive care unit. A systematic review and consensus statement

Lower incidence in abdominal abscesses

(OR: 0.26, CI: 0.12-0.55) (P=0.005)

Nosocomial pneumonia

(OR: 0.54, CI: 0.35-0.84) (P=0.007)

Bacteremia (OR: 0.45, CI: 0.35-0.84) (P=0.0002)

Reduction in time on mechanical ventilation

(mean 2.25 days, CI: 0.5-3.9) (P=0.009)

ICU length of stay

(mean reduction of 1.6 days, CI: 1.9-1.2) (P<0.0001)

Hospital length of stay

(mean reduction of 3.4 days, CI: 4.0-2.7) (P<0.0001)

No effects were appreciated on mortality

(OR: 1.10, CI: 0.85-1.42) (P=0.5)

Intensive Care Med. 2003

May;29(5):834-40. Epub 2003 Apr 09.

The primary endpoint for the subgroup analysis on patients with severe sepsis was mortality on Intensive Care Unit (ICU).

The ICU mortality of patients with severe sepsis given enteral nutrition (EN) was higher than for those given PN (44.4% vs 14.3%; $p=0.039$).

More patients given EN than patients given PN still had severe sepsis when they died (38.9% vs 9.5%, $p=0.055$). Recruitment of patients with severe sepsis was subsequently stopped.

Main immunonutrition studies in Intensive Care patients

Lead author	Reference	n	Population	Formula
Atkinson	41	390	ICU	Impact
Bower	42	296	Injury, surgery, or sepsis/in ICU	Impact
Brown	27	37	Trauma	Abbott diet
Galban	40	181	Septic ICU	Impact
Kieft	43	597	ICU	IMN formula (see Table 1)
Kudsk	39	35	Trauma	Immunaid
Mendez	28	42	Trauma	Abbott diet
Moore	38	98	Trauma	Immunaid
Weimann	66	32	Trauma	Impact

In What Populations Should We Attempt Immune Modulation

Clearly established benefit

- Elective GI surgery
 - Esophageal, pancreatic, gastric, hepatobiliary
- Blunt or Penetrating Torso Trauma
 - ISS > 18, Abdominal trauma index > 20

Probable benefit

- Elective major surgery
 - Aortic reconstruction with COPD
 - Expected post op ventilator
 - Major head and neck surgery
- Severe head injury
- Burns > 30 %
- Ventilator dependent, non-septic ICU patient

Consensus statement JPEN 2001

The immune system and the inflammation pathways in the critically ill patient are in a dynamic state and the use of these nutrients at different stages of the disease, in different dosages, for different durations, with different combinations of nutrients and in different populations may result in very different outcomes.







MEDICAL CARE

NURSING CARE

INTENSIVE CARE

PHYSIOTHERAPY

***NUTRITIONAL
SUPPORT***