

TOP Journal Club

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Enteral immunonutrition during sepsis prevents pulmonary dysfunction in a rat model.

J Gastrointest Surg. 2007 Jun;11(6):719-24.

BACKGROUND: Sepsis often results in severe pulmonary dysfunction. Via the thoracic duct, the lung is the first organ exposed to gut-derived inflammatory mediators released into mesenteric lymph during sepsis. **AIM:** To investigate whether an enteral immunonutrition during sepsis improves pulmonary function. **METHODS:** Mesenteric lymph was obtained from lymph fistula donor rats after intra peritoneal (i.p.) saline (control lymph) or lipopolysaccharide (sepsis lymph) injection. Sepsis lymph was also collected during enteral immunonutrition with omega-3 enriched, long-chain fatty acids (SMOF lipid). Control, sepsis, or sepsis-SMOF lymph was reinfused into the jugular vein of separate recipient rats. The lungs were then harvested, stained with hematoxylin-eosin, and analyzed for: (1) perpendicular parenchyma thickness of the alveolar wall; (2) myeloperoxidase-positive cells; and (3) terminal deoxynucleotidyl transferase Biotin-dUTP nick end labeling (TUNEL)-positive cells. **RESULTS:** Enteral immunonutrition during sepsis reduced the release of TNFalpha into mesenteric lymph by about 4.5-fold within the first 2 h. Infusion of sepsis lymph into recipient rats induced thickening of alveolar walls, inflammatory reaction, and apoptosis. Infusion of sepsis lymph obtained during enteral immunonutrition did not cause anatomical changes, induced only a mild inflammatory reaction, and prevented apoptosis in the lungs of recipient rats. **CONCLUSIONS:** Mediators in sepsis lymph induce pulmonary dysfunction such as an increased distance for oxygen transport, inflammatory reaction, and apoptosis. The lung may be protected by an enteral immunonutrition containing long-chain fatty acids.

The scientific rationale for optimizing nutritional support in cancer.

Eur J Gastroenterol Hepatol. 2007 May;19(5):371-7.

Cancer patients lose weight as a result of the anorexia-cachexia syndrome, and this weight loss is associated with significant morbidity and mortality. Thus, nutritional support to arrest or reverse weight loss is of paramount importance in the management of Cachexia cancer patients. Persistent tumour-induced metabolic changes result, however, in a suboptimal response to such support, making nutritional maintenance or improvement difficult targets to achieve. Mechanisms involved in the blockade to anabolism in cancer cachexia include alterations in skeletal muscle and hepatic protein metabolism, and reduced physical activity. Mediators underlying these mechanisms of weight loss include proinflammatory cytokines, tumour-specific cachectic factors, and neuroendocrine mediators of muscle catabolism. The complex mix of different mediators renders unimodal nutritional intervention a strategy that is unlikely to succeed completely. Therefore, clinical trials using combination therapies or immunonutrition are required for future success.

Immunonutrition in elective gastrointestinal surgery patients.

Scand J Surg. 2007;96(1):46-50.

BACKGROUND: Previous trials have shown that perioperative immunonutrition could protect patients from infectious complications after gastrointestinal cancer operations. The purpose of this study was to determine whether perioperative immunonutrition decreases postoperative morbidity, especially infection complications, mortality and length of hospital stay in patients undergoing major gastrointestinal tract surgery. **METHODS:** One hundred patients with a planned elective operation for benign or malignant gastrointestinal illness were randomized into two groups: group 1) oral supplementation for five days before and five days after surgery with 900 mL/day of a formula enriched with arginine, gamma-3-fatty acid and RNA + liquid diet ad libitum on one and two postoperative day and then solid food (immunonutrition group; n = 50) or group 2) no artificial nutrition before and after surgery, on one and two postoperative day intravenous solution of 5% glucose and

electrolytes and then normal diet (conventional group; n = 50). RESULTS: The groups were comparable for all key baseline and surgical characteristics. There were nine (18%) infectious complications in both groups. Overall complication rates were 28% (n = 14) in the immunonutrition group and 24% (n = 12) in the conventional group. No significant difference between the groups was found in complication rates, mortality or length of hospital stay. CONCLUSION: Routine perioperative immunonutrition to the patients undergoing major gastrointestinal surgery is not beneficial.

Genes, diet and inflammatory bowel disease.

[Mutat Res.](#) 2007 Jun 2

Inflammatory bowel disease (IBD) arises in part from a genetic predisposition, through the inheritance of a number of contributory genetic polymorphisms. These variant forms of genes may be associated with an abnormal response to normal luminal bacteria. A consistent observation across most populations is that any of three polymorphisms of the Caspase-activated recruitment domain (CARD15) gene are more prevalent in IBD patients as compared with unaffected controls. Similar aberrant responses to bacteria are associated with variants in Autophagy-related 16-like 1 (ATG16L1) and human defensin (HBD-2, -3 and -4) genes. The defective bacterial signal in turn leads to an excessive immune response, presenting as chronic gut inflammation in susceptible individuals. Inconsistent population reports implicate the major histocompatibility complex (MHC), that encodes a number of human leukocyte antigens (HLA), MHC class I chain-related gene A (MICA) or cytokines, such as tumour necrosis factor-alpha (TNF-alpha). Toll-like receptors encoded by the TLR4 or TLR9 genes may also play a role. Recent whole genome scans suggest that a rare variant in the interleukin-23 receptor (IL23R) gene may actually protect against IBD. Other implicated genes may affect mucosal cell polarity (Drosophila discs large homologue 5, DLG5) or mucosal transporter function (sodium dependent organic cation transporters, SLC22A4 and SLC22A5). A variant in ABCB1 (ATP-binding cassette subfamily B member 1) may be especially associated with increased risk of UC. While pharmacogenetics is increasingly being used to predict and optimise clinical response to therapy, nutrigenetics may have even greater potential. In many cases, IBD can be controlled through prescribing an elemental diet, which appears to act through modulating cytokine response and changing the gut microbiota. More generally, no single group of dietary items is beneficial or detrimental to all patients, and elimination diets have been used to individualise dietary requirements. However, recognising the nature of the genes involved may suggest a more strategic approach. Pro- or prebiotics will directly influence the microbial flora, while immunonutrition, including omega-3 fatty acids and certain polyphenols, may reduce the symptoms of gut inflammation. The expression of gut transporters may be modulated through various herbal remedies including green tea polyphenols. Such approaches would require that the gene of interest is functioning normally, other than its expression being up or down-regulated. However, new approaches are being developed to overcome the effects of polymorphisms that affect the function of a gene. A combination of human correlation studies with experimental models could provide a rational strategy for optimising nutrigenetic approaches to IBD.

Preoperative Immunonutrition Suppresses Perioperative Inflammatory Response in Patients with Major Abdominal Surgery-A Randomized Controlled Pilot Study.

[Ann Surg Oncol.](#) 2007 Jul 15

BACKGROUND/AIM: Perioperative administration of immunoenriched diets attenuates the perioperative inflammatory response and reduces postoperative infection complications. However, many questions still remain unresolved in this area, such as the length of diet administration, diet composition, and the mechanisms involved. We performed an open, randomized, triple-arm study comparing the effect of two perioperative feeding regimens with a postoperative one. METHODS: 46 candidates for major elective surgery for malignancy in the upper gastrointestinal tract were randomized to drink preoperatively either 1 L of an immunoenriched formula (Impact) for 5 days (IEF group) or 1 L of Impact plus (Impact enriched with glycine) for 2 days (IEF plus group). The same product as the patient received preoperatively was given to both groups for 7 days postoperatively. In the control group (CON group), patients only received Impact for 7 days postoperatively; there was no preoperative treatment. The main outcome measures were postoperative C-reactive protein (CRP) serum levels. RESULTS: In the two preoperatively supplemented groups (treatment groups), perioperative endotoxin levels, CRP (postoperative day 7), and TNF-alpha (postoperative days 1 and

3) levels were significantly lower compared to the CON group ($p < .01$). Furthermore, the length of postoperative IMU/ICU stay (Impact 1.9 +/- 1.3 days; Impact plus 2.2 +/- 1.1 days; control group 5.9 +/- 0.8 days) and length of hospital stay (Impact 19.7 +/- 2.3 days; Impact plus 20.1 +/- 1.3 days; control group 29.1 +/- 3.6 days) were both reduced in the treatment groups compared to the control group. Infectious complications (Impact 2/14 (14%); Impact plus 5/17 (29%); control group 10/15 (67%)) also showed a trend toward reduction in the treatment groups. CONCLUSIONS: Perioperative administration of an immunoenriched diet significantly reduces systemic perioperative inflammation and postoperative complications in patients undergoing major abdominal cancer surgery, when compared with postoperative diet administration alone. A shortened preoperative feeding regimen of 2 days with Impact enriched with glycine (Impact plus) was as effective as Impact administered for 5 days preoperatively.

Role of branched-chain amino acids in liver disease: the evidence for and against.

Curr Opin Clin Nutr Metab Care. 2007 May;10(3):297-303

PURPOSE OF REVIEW: There is ample evidence that patients with liver disease have an ongoing energy and protein catabolism. Nutritional management in these patients must receive high priority. The administration of branched-chain amino acids to patients with liver disease has been a controversial subject. This review is an update on the data available from various studies involving branched-chain amino acids supplementation in patients with chronic liver disease and associated complications. **RECENT FINDINGS:** This review summarizes the results of nutritional interventions involving branched-chain amino acids supplementation carried out in different centres around the world. It is interesting to note that no toxic effects of branched-chain amino acids supplementation have been reported in any of these trials. **SUMMARY:** Administration of branched-chain amino acids stimulates hepatic protein synthesis in patients with chronic liver disease and this could contribute significantly to improving their nutritional status, and result in a better quality of life. The beneficial role of branched-chain amino acids supplementation in patients with chronic hepatic encephalopathy has been clearly documented in some studies but the exact mechanism of action is still not clear.

Metabolic effects of amino acid mixtures and whey protein in healthy subjects: studies using glucose-equivalent drinks.

Am J Clin Nutr. 2007 Apr;85(4):996-1004.

BACKGROUND: Milk protein, in particular the whey fraction, has been shown to display insulinotropic properties in healthy persons and persons with type 2 diabetes. In parallel to the hyperinsulinemia, a pronounced postprandial rise of certain amino acids and of glucose-dependent insulinotropic polypeptide (GIP) was observed in plasma. **OBJECTIVE:** The objective of the study was to determine to what extent the insulinotropic properties of whey could be simulated by specific amino acid mixtures. **DESIGN:** Twelve healthy volunteers were served drinks consisting of pure glucose (reference drink) or glucose supplemented with free amino acids or whey proteins (test drinks). **RESULTS:** A test drink with the branched-chain amino acids isoleucine, leucine, and valine resulted in significantly higher insulin responses than did the glucose reference. A drink containing glucose and leucine, isoleucine, valine, lysine, and threonine mimicked the glycemic and insulinemic responses seen after whey ingestion. With consumption of this drink, the glucose area under the curve (AUC) was 44% smaller ($P < 0.05$) and the insulin AUC was 31% larger (NS) than with consumption of the reference drink. With consumption of the whey drink, the AUCs were 56% smaller (glucose; $P < 0.05$) and 60% larger (insulin; $P < 0.05$), respectively, than with the reference drink. The whey drink was accompanied by an 80% greater GIP response ($P < 0.05$), whereas the drinks containing free amino acids did not significantly affect GIP secretion. **CONCLUSION:** A mixture of leucine, isoleucine, valine, lysine, and threonine resulted in glycemic and insulinemic responses closely mimicking those seen after whey ingestion in the absence of an additional effect of GIP and glucagon-like peptide 1.

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