

# TOP Journal Club

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### 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.

### 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.

### Enteral Immunonutrition During Sepsis Prevents Pulmonary Dysfunction in a Rat Model.

*J Gastrointest Surg.* 2007 Mar 30

**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.

## Fiber and magnesium intake and incidence of type 2 diabetes: a prospective study and meta-analysis.

*Arch Intern Med.* 2007 May 14;167(9):956-65.

BACKGROUND: Prospective studies on fiber and magnesium intake and risk of type 2 diabetes mellitus were inconsistent. We examined associations between fiber and magnesium intake and risk of type 2 diabetes and summarized existing prospective studies by meta-analysis. METHODS: We conducted a prospective cohort study of 9702 men and 15 365 women aged 35 to 65 years who were observed for incident diabetes from 1994 to 2005. Dietary intake of fiber and magnesium were measured with a validated food-frequency questionnaire. We estimated the relative risk (RR) by means of Cox proportional hazards analysis. We searched PubMed through May 2006 for prospective cohort studies of fiber and magnesium intake and risk of type 2 diabetes. We identified 9 cohort studies of fiber and 8 studies of magnesium intake and calculated summary RRs by means of a random-effects model. RESULTS: During 176 117 person-years of follow-up, we observed 844 incident cases of type 2 diabetes in the European Prospective Investigation Into Cancer and Nutrition-Potsdam. Higher cereal fiber intake was inversely associated with diabetes risk (RR for extreme quintiles, 0.72 [95% confidence interval [CI], 0.56-0.93]), while fruit fiber (0.89 [95% CI, 0.70-1.13]) and vegetable fiber (0.93 [95% CI, 0.74-1.17]) were not significantly associated. Meta-analyses showed a reduced diabetes risk with higher cereal fiber intake (RR for extreme categories, 0.67 [95% CI, 0.62-0.72]), but no significant associations for fruit (0.96 [95% CI, 0.88-1.04]) and vegetable fiber (1.04 [95% CI, 0.94-1.15]). Magnesium intake was not related to diabetes risk in the European Prospective Investigation Into Cancer and Nutrition-Potsdam (RR for extreme quintiles, 0.99 [95% CI, 0.78-1.26]); however, meta-analysis showed a significant inverse association (RR for extreme categories, 0.77 [95% CI, 0.72-0.84]). CONCLUSION: Higher cereal fiber and magnesium intakes may decrease diabetes risk.

## 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.

## Brain activation in uremic anorexia.

*J Ren Nutr.* 2007 Jan;17(1):57-61.

This article reviews current knowledge about mechanisms responsible for uremic events, especially those that involve the central nervous system (CNS). Anorexia is a frequent complication of the uremic syndrome that contributes to malnutrition in patients on dialysis. Uremic anorexia has been associated with many factors. Traditionally, anorexia in dialysis patients has been regarded as a sign of uremic toxicity; therefore, 2 hypotheses have been proposed: the "middle molecule" and "peak concentration" hypotheses; both of these remain unproved. Recently, our group has proposed the tryptophan-serotonin hypothesis, which is based on a disorder in the amino acid profile that may be acquired when the patient is in uremic status. It is characterized by low concentrations of large neutral and branched chain amino acids in the cerebrospinal fluid. This situation permits a high level of tryptophan transport across the blood-brain barrier and enhances the synthesis of serotonin (the final target responsible for inhibiting appetite). The role of inflammation in the genesis of anorexia-malnutrition is also emphasized. In summary, in the CNS, factors associated with uremic anorexia include high levels within the cerebrospinal fluid of proinflammatory cytokines, leptin, and free tryptophan and serotonin (hyperserotonergic-like syndrome), along with deficiency of neural nitric oxide (nNO) and disorders in various receptors such as melanocortin receptor-4 (MC4-R). Uremic anorexia is a complex complication associated with malnutrition and high levels of morbidity and mortality. Several uremia-acquired disorders in the CNS such as high cerebrospinal fluid levels of anorexigen substances and disorders in appetite regulator receptors may explain the lack of appetite.

## Meal pattern of male rats maintained on histidine-, leucine-, or tyrosine-supplemented diet.

*Obesity (Silver Spring).* 2007 Mar;15(3):616-23.

OBJECTIVE: Food intake is known to be affected by macronutrient composition of the diet, and protein manipulation has been reported to alter food intake, but the effect of individual amino acids on eating behavior has not been fully studied. This study investigated the effect of diet supplementation with three individual amino acids on meal pattern in male rats. RESEARCH METHODS AND PROCEDURES: Thirty-two Sprague-Dawley rats were randomly divided into four equal groups and fed control diet or histidine (5%)-, leucine (5%)-, or tyrosine (5%)-supplemented diet for 2 weeks and were monitored for their meal pattern. RESULTS: Total food intake and feeding rate of the different groups were not affected, although other components of meal pattern were altered. Histidine supplementation reduced diurnal meal size by 42% ( $p < 0.05$ ), whereas that of leucine increased nocturnal meal size by approximately 35% ( $p < 0.05$ ). Tyrosine supplementation increased food intake of the nocturnal period and decreased that of the diurnal period. Both histidine and tyrosine supplementation elevated fasting plasma insulin levels and suppressed fasting glucose significantly. DISCUSSION: Individual amino acids were found to alter meal pattern differently. Further investigations are required to dissect the involvement of central and peripheral factors in these alterations.

<http://www.thai-otsuka.co.th/pxnews>

Dr. Shwe Win <[shwewin@thai-otsuka.co.th](mailto:shwewin@thai-otsuka.co.th)>