

# CLINICAL NUTRITION HIGHLIGHTS

Science supporting  
better nutrition

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## **Prebiotics: Diet–bacterial–gut interactions and their impact on health**

Clinical nutrition abstracts  
Highlights of the 27<sup>th</sup> ESPEN Congress

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# Prebiotics: Diet–bacterial–gut interactions and their impact on health

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Over the last few decades, it has become clear that our diet has a profound effect on intestinal and general health in ways other than the delivery of digestible and absorbable nutrients. In fact, the importance of *components that are not digested by human enzymes and are not absorbed* has become increasingly recognized.

The best example of this is non-digestible plant components that fall under the general category of dietary fiber. Dietary fiber, in its multiple forms, is part of a healthy diet, and is naturally present or added to foods (Table 1). It is associated with a number of health benefits, relative to bowel function, as well as being beneficial in chronic conditions, including cancer, cardiovascular disease and type 2 diabetes. It is generally established that some of these benefits are in turn associated with the physicochemical changes that dietary fiber can bring about in its interaction with intestinal luminal contents (eg, effects on viscosity of gastric and intestinal contents, gel formation, and water-holding capacity). These changes can modify gastric emptying, alter availability

of absorbable nutrients, and modulate colonic motility, usually helping to regulate bowel habits.

However, some of the most important effects and ultimate benefits that derive from dietary non-digestible substances relate to their capacity to serve as an energy substrate for intestinal flora or microbiota (the complex ecosystem that inhabits the gut lumen), and the subsequent effects of this biomass on gut mucosal structure and immune function.

The study of these interactions has led to a better understanding and identification of the specific dietary components that can best deliver the benefits associated with diet–microbe–gut interactions in the intestinal lumen.<sup>1,2</sup>

## Intestinal microbiota: Composition, evolution and function

The gastrointestinal (GI) tract is essentially sterile at the time of birth, with colonization by microflora upon exposure to the environment. Enterobacteria, bifidobacteria and lactobacilli are typically acquired in the first few days of life. In breastfed infants, bifidobacteria counts increase dramatically and account for 80% to 90% of the total fecal flora. The increase in bifidobacteria counts is mostly due to the presence of human milk oligosaccharides, which are not digestible by human enzymes (functionally behaving as the 'fiber' of breast milk), providing a selective substrate to bifidobacteria in the distal gut. Breast milk thus favors the growth of these non-pathogens, leading to a desirable bacterial profile, with predominance of bifidobacteria and lactobacilli,<sup>3,4</sup> rather than potential pathogenic species, as will be discussed below.

With the introduction of weaning foods, the fecal flora of infants begins to change, and by the age of 1 year, is similar to that of adults. In healthy adults, the intestinal microbiota comprises more than 400 species of bacteria with a population of  $10^{12}$  –  $10^{14}$  colony-forming units (CFU)/g, of which more than 98% reside in the colon.

The type and number of microorganisms varies greatly along the GI tract. In the stomach, gastric acid limits the

**Table 1. Soluble fibers in the food supply considered most abundant, commonly added to foods, or provided as nutritional supplements**

- Beta-glucans
  - Gums
  - Mucilages
  - Hemicelluloses – certain hemicelluloses are soluble
  - Inulin, oligofructose and fructo-oligosaccharides (FOS)
  - Pectin
  - Polydextrose and polyols
  - Psyllium
  - Resistant dextrins
- 
- Other fibers identified as most abundant in the food supply are insoluble. These include cellulose, chitin and chitosan, lignin and resistant starch.

number of bacteria to very low levels ( $10^3$  CFU/mL) of mostly gram-positive and aerobic bacteria. Bacterial concentrations in the small intestine range between  $10^3$  and  $10^4$  CFU/mL. In the colon, bacterial counts dramatically increase to  $10^{11}$  to  $10^{12}$  CFU/g, with predominant organisms being *Bacteroides*, *Enterobacter*, coliforms, bifidobacteria, lactobacilli, and other facultative anaerobes, staphylococci and *Candida* species.

## Role of intestinal microbiota

Intestinal microbiota serve a number of systemic and gut health-related functions, including synthesis of vitamins (biotin, folate, B<sub>12</sub> and vitamin K). Colonic bacteria deconjugate bile acids to allow enterohepatic recirculation and maintenance of bile acid pools in the liver. They also transform excess cholesterol found in the large intestine to coprostanol, thus reducing available cholesterol and increasing cholesterol excretion in the stools.<sup>5</sup>

In addition, maintenance of an adequate intestinal microbiota is vital to normal immunologic gut development, structure and function.<sup>6,7</sup> In a germ-free murine model, lack of microflora leads to a hypotrophic or atrophic mucosa, with loss of adequate nutrient handling and barrier function. Germ-free mice reared in a sterile environment do not survive exposure to 'normal' bacterial flora later in life. Since the intestinal biomass includes both non-pathogens that are metabolically active and a large number of potentially pathogenic agents, including invasive, infective and toxin-producing bacteria, the maintenance of a 'healthy' and stable intestinal biomass is critical and can have profound health implications.

## Modulating intestinal microbiota: Probiotics and prebiotics

The concept of manipulating microflora to enhance the positive effects on the GI tract is not new. The suggestion that ingesting bacteria with fermented foods offered health benefits dates back to the early 1900s. Eli Metchnikoff first proposed this effect having observed the long lives and good health of Bulgarian peasants who consumed great amounts of milk soured (fermented) with live, non-pathogenic, lactic acid-producing bacteria.<sup>8</sup>

The study of orally supplemented live bacteria for the purposes of improving health led to the concept of probiotics. Various strains of bifidobacteria and lactobacilli have been the most studied, because of their history of safe use in the food supply, and ability to survive the upper GI tract and transiently proliferate in the gut. The health benefits associated with modulation of intestinal bacterial populations by directly consuming probiotic agents include prevention and treatment of diarrhea (particularly rotavirus- and antibiotic-associated), improved lactose digestion and, most recently, prevention and

treatment of food allergy and its systemic effects (eg, atopic dermatitis, allergic disease), as well as inflammatory bowel disease (IBD).<sup>9-12</sup> A discussion on probiotics is beyond the scope of this review.

This progress, in turn, brought about significant interest in the possibility of modulating the composition and activity of intestinal microbiota by dietary means. It is well recognized that there are certain dietary substrates (typically carbohydrates and fibers) that are not digested in the upper GI tract. These substrates appear to selectively promote the growth of specific, non-pathogenic, potentially desirable bacterial species in the gut, including bacteria used as probiotic agents, namely bifidobacteria and lactobacilli.

These are called prebiotics: "nondigestible food ingredients that beneficially affect host health by selectively stimulating the growth and/or activity of one, or a limited number of, bacteria in the colon".<sup>13,14</sup>

## Prebiotics: A closer look

Conceptually, prebiotic substances behave just as other soluble fibers, reaching the colon and becoming available for bacterial fermentation. However, they are unique in that they selectively serve as substrate to specific non-pathogenic bacteria, particularly bifidobacteria and lactobacilli.<sup>15</sup>

A number of substances have been suggested to have this effect. However, fructans (inulin and fructo-oligosaccharides [FOS]) have been the most studied and a prebiotic effect has been conclusively demonstrated in multiple human intervention trials.<sup>16-18</sup>

## Fructans: Composition, characteristics and bifidogenicity

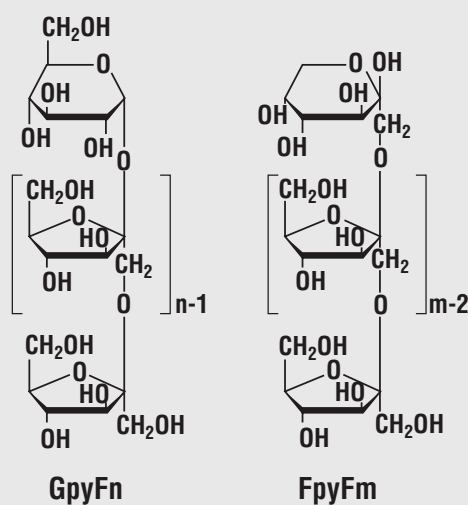
Fructans are a family of substances, in essence polymers of fructose, with varying chain lengths or degrees of polymerization (DP). The number of individual simple sugar units that make up the molecule defines the DP of a polymer. Most nomenclature distinguishes inulin-derived FOS (with a DP range of 3-60) from shorter-chain FOS with a lower DP range from 3-5 (Figure 1).

Fructans are naturally present in relatively low concentrations in many edible fruits and vegetables, such as onion, garlic, the roots of Jerusalem artichoke, asparagus, chicory root, wheat and banana.<sup>19-21</sup> Recently, methods to obtain concentrated and purified dietary fructans have allowed these compounds to be studied and to be incorporated into the diet, alone or in nutritional products. Dietary fructans can be derived from naturally occurring oligosaccharides or synthesized artificially.

Both inulin-derived and synthesized FOS are known to resist digestion in the upper GI tract. They are not recovered in stool, indicating that they are almost completely fermented in the colon; thus, they behave as soluble fiber. The carbohydrate



Figure 1. Structure of dietary fructans



G = glucose; F = fructose; py = pyranosyl; n or m equals the number of fructose units.

polymers of fructans are principally joined by (2→1) glycosidic linkages between their sugars. Bifidobacteria have high beta-fructosidase activity, which is selective for the beta (2→1) glycosidic bond. Thus, inulin and FOS act as a preferential energy source for bifidobacteria, thereby selectively enhancing their growth over that of other species.<sup>22-27</sup>

In general, prebiotics are assessed based on their capacity to increase bifidobacteria populations in the gut (bifidogenicity), particularly in the colon and stool. This effect has been demonstrated with inulin and shorter-chain FOS in multiple clinical trials. The lower amount of FOS required for bifidogenesis appears to be 4 g/d.<sup>28</sup> The greatest increases appear to occur in individuals with lower bifidobacterial counts, and continued administration appears to be necessary to maintain this effect.<sup>29</sup>

A number of trials in pediatric, as well as adult, individuals have demonstrated the bifidogenicity of fructans given in various forms.<sup>13,30-33</sup> Results consistently demonstrated the ability of fructans to modulate microbiota by significantly increasing concentrations of bifidobacteria and/or lactobacilli in stool, in some studies in a dose-dependent manner,<sup>31,34</sup> with increases of as much as 28% to 35%.<sup>30,35</sup> Combinations of longer-chain inulin with shorter-chain FOS result in significant increases in mucosal-associated bifidobacteria and lactobacilli.<sup>36</sup>

In addition to bifidogenicity, several trials have demonstrated associated decreases in *Bacteroides*<sup>37</sup> and *Clostridium* species.<sup>38-40</sup>

In summary, results from several in vitro, animal and controlled human trials indicate that dietary fructans are prebiotics that have the capacity to modulate intestinal ecology, generally increasing the number of bifidobacteria and decreasing potential pathogens, resulting in a 'more desirable' gut microbiota.<sup>41</sup>

## Beneficial effects of fructans

Fructan-stimulated growth of bifidobacteria and lactobacilli has the ability to specifically and non-specifically modulate gut and host response to physiologic and pathologic conditions.<sup>17,41-43</sup>

In general, non-specific or innate resistance in the GI tract primarily prevents opportunistic pathogens already resident in the gut, as well as invading pathogenic organisms, from translocating through the gut wall into the systemic circulation. Mechanisms include entrapping pathogens, increasing their movement through the gut, and/or providing an inhibitory environment for preventing the proliferation of less desirable microbiota. The effect of fructans on these aspects of gut health has been increasingly demonstrated in studies.

### 1) Increasing short-chain fatty acids and improving mucosal trophism

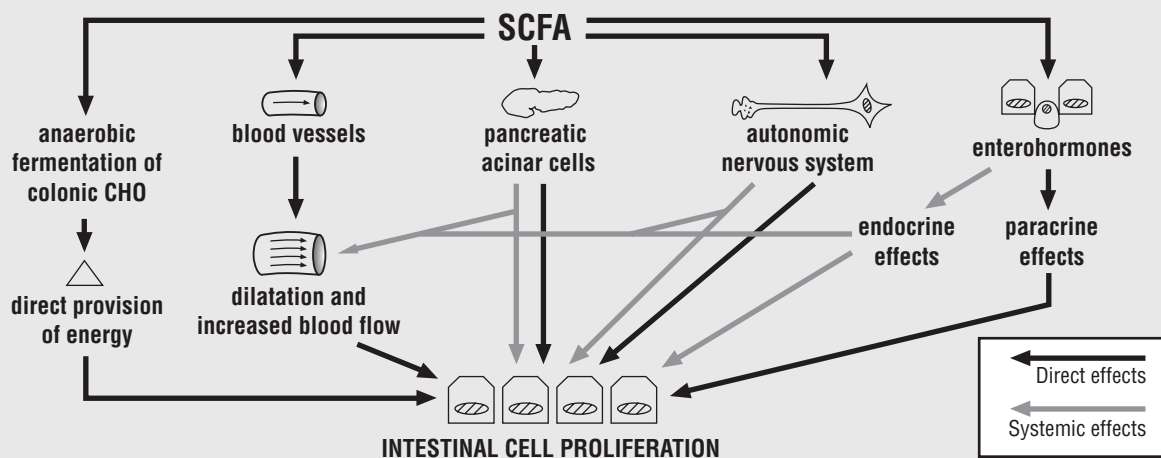
Since the gut mucosa is a first line of defense against pathogenic luminal inhabitants, its integrity and trophism is critical in performing as a protective barrier. Soluble fibers, including inulin and FOS, are fermented by colonic bacteria to produce short-chain fatty acids (SCFA; acetate, propionate and butyrate). All three predominant SCFA stimulate epithelial cell growth and differentiation in the colon and small intestine. The various mechanisms by which SCFA can support gut function are shown in Figure 2.<sup>44</sup> SCFA in the large bowel account for approximately 80% of the SCFA produced by humans and more than 70% of the metabolic energy supply for the colonocyte, with butyrate serving as the most important oxidative fuel. Defective SCFA metabolism appears to be a factor in the etiology of inflammatory bowel conditions, and the direct administration of SCFA to patients with ulcerative colitis and diversion colitis has been shown to ameliorate inflammation.<sup>45-47</sup> Fructans and specifically inulin appear to be more butyrogenic than most fibers,<sup>48</sup> and both inulin and FOS have been shown to increase mucosal villus height, crypt depth and number of goblet cells,<sup>49,50</sup> thus reinforcing and stabilizing the gut mucosal barrier.

In addition, animal studies have shown SCFA can enhance mesenteric and colonic blood flow through a vasodilatory effect, enhance gut hormone production and stimulate the autonomic nervous system.<sup>44</sup>

### 2) Decreasing luminal pH

Consumption of fermentable fiber, including fructans, decreases colonic luminal pH mainly through an increased concentration of SCFA, most markedly in the cecum.<sup>51</sup> This creates a very unfavorable environment for a number of pathogenic species, as only a limited number of pathogenic bacteria can survive in an acid environment.<sup>52</sup> The distal colon, a region with a slower rate of fermentation, may

**Figure 2. Mechanisms by which short-chain fatty acids (SCFA) can modulate trophism of the intestinal mucosa**



SCFA result from bacterial fermentation of undigested carbohydrates and fiber, including inulin and fructo-oligosaccharides.

Adapted from reference 44.

benefit from the provision of longer-chain fructans, which can be more slowly fermented and provide substrate for bacteria in this region of the large bowel. Enhanced secretion of acid-type mucins associated with fructan feeding<sup>49</sup> could be further responsible for decreasing the lumen pH to one incompatible with the growth of some pathogens.

### 3) Enhancing the mucous and mucin-gut barrier

Mucus is continuously produced by goblet cells to lubricate and protect the GI epithelium. The primary gene identified in mucosal cells that is responsible for the production and secretion of mucus and its resulting sugar, mucin, is the MUC2 gene. Mucin forms a viscous gel that coats the epithelial surface of the intestine, protecting it from chemical and mechanical stress. Increasing mucin glycoprotein provides potential sites for both indigenous and pathogenic bacteria to bind, and constitutes a significant line of defense against pathogens. Probiotic agents have been shown in vitro to stimulate MUC genes and mucin production.<sup>53,54</sup> Inulin and FOS have also been shown in animal studies to increase thickness of the epithelial mucous layer.<sup>42,49,55</sup> Indigenous bacteria also utilize the carbohydrate component of mucins as fuel, encouraging the growth of bifidobacteria and lactobacilli, increasing the likelihood that pathogens become trapped in the lumen.

### 4) Supporting motility and intestinal luminal flow

Increasing the bacterial biomass of bifidobacteria and lactobacillus through fermentation of inulin and FOS provides some bulk to enhance the effects of peristalsis.<sup>56</sup> Accompanying the growth of lactic acid bacteria, SCFA are produced and may have an independent effect on stimulating peristalsis. Although the effect of the numerically and volumetrically dominant bifidobacteria and lactobacilli

associated with inulin and FOS intake may be minor in terms of laxation, their presence may also limit the number of binding sites and receptors on the mucosa to which pathogens can attach. Decreased counts of potentially pathogenic strains of microbes with concomitant bifidogenesis may be explained, in part, by this exclusion phenomenon.<sup>50</sup>

SCFA can stimulate colonic blood flow, fluid and electrolyte uptake,<sup>57</sup> and mediate sodium and water absorption in the colon.<sup>44</sup> Furthermore, dietary fructans have been used with some success to ameliorate diarrhea and improve cell proliferation in animal studies.<sup>58-60</sup>

### 5) Directly decreasing potential pathogens

Prebiotics have been associated not only with the increase in desirable species, but with decreases in potentially pathogenic organisms, including *Bacteroides* and *Clostridia*. The mechanisms are probably multiple, and include the effects mentioned above (eg, SCFA formation and lowering of pH, enhancement of the mucin barrier, decrease in available receptor sites). In addition to this, several trials have demonstrated associated decreases in *Bacteroides*<sup>37</sup> and *Clostridium* species.<sup>38-40</sup>

Lactobacilli and bifidobacteria, enhanced by fructan ingestion, excrete endogenous substances, such as lactocins, helveticins, lactacins, curvacins and bifidocin.<sup>2</sup> These substances exert antimicrobial effects on various gram-positive and gram-negative intestinal pathogens, including *Escherichia coli*, salmonellae and campylobacters.<sup>24</sup>

### 6) Modulating gut-associated immunity

The importance of the intestinal flora in modulating gut and systemic immunologic response has received great attention over the last few years, and is beyond the scope of this article. However, it is clear that the intestinal microbiota have a

profound influence on mucosal and systemic immunity and their relevance to human disease.<sup>6,61,62</sup> Thus, in this regard, dietary influences on intestinal flora may be of great significance. There is limited but increasing evidence of the role of fructans in modulating gut-associated lymphoid tissue (GALT) immune response.<sup>55,63</sup>

In animals (mice and dogs), FOS have been shown to upregulate IgA secretion in a dose-dependent fashion.<sup>63-65</sup> In mice, fructans can have an immunostimulatory effect on T cells, as well as CD4+ and B lymphocytes, improving survival of pathogens (*Listeria* and *Salmonella* species).<sup>42,66,67</sup> In chickens, FOS can reduce *Salmonella* concentrations.<sup>68,69</sup> Mechanisms to explain improved immune function in animals are still speculative and their application to humans is conjectural.

### Calcium bioavailability

In animal models, FOS and, particularly, inulin have been shown to increase calcium absorption, bone density and volume,<sup>70,71</sup> and prevent bone loss in gastrectomized<sup>72</sup> and estrogen-deficient animals.<sup>73,74</sup> At least one well-designed study has demonstrated daily fructan supplementation improves calcium absorption in young girls.<sup>75</sup> Although the mechanism is not fully understood, lower pH in the distal gut from SCFA formation may help solubilize calcium salts and improve absorption.

### Prebiotics in the compromised gut

The recognition that prebiotic agents, such as fructans, can support gut structure and function has led to their inclusion in formulations of enteral feeding regimens, as part of standard nutrition provision, and, more importantly, in enteral formulations for those with compromised GI function.

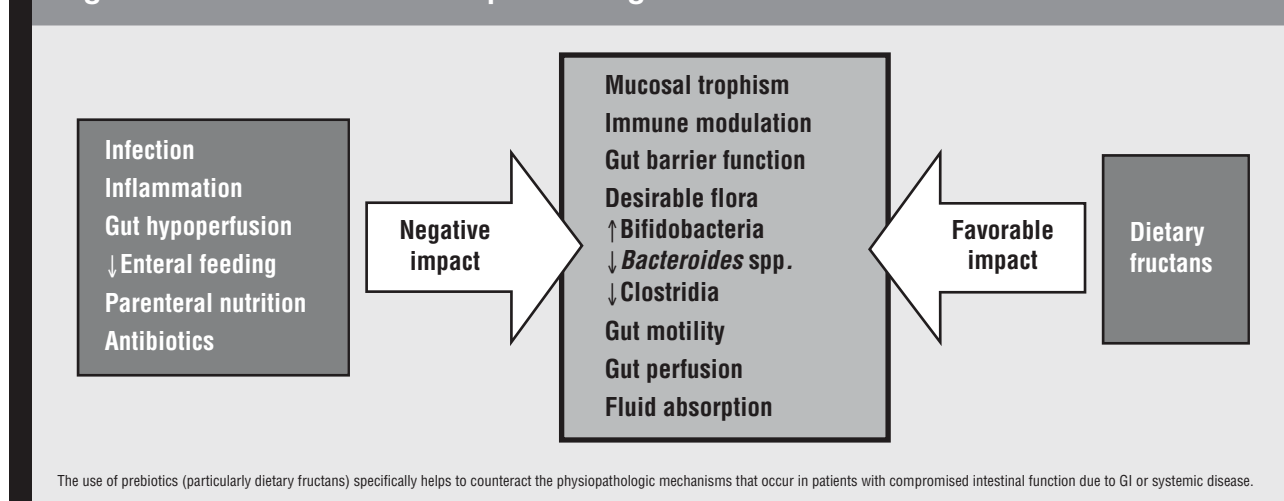
Gastrointestinal disease in its various forms can be associated with gut changes (inflammation, infection,

hypoperfusion) and therapeutic practices (no enteral feedings, parenteral nutrition, antibiotics) that are detrimental to gut trophism, permeability and barrier function, and favor growth of undesirable intestinal microbiota. Support of intestinal health and of a desirable microbiota are actually of greater relevance and highly desirable in these circumstances. The benefits of prebiotics provide a sound argument for including specific types of fiber and fiber-like substances, particularly fructans, in the diets of these compromised patients (Figure 3).

For example, preliminary trials have documented the potential benefits of dietary fructans as an adjuvant to the management of patients with IBD. There is significant evidence that intestinal microbiota composition and function play a role in the development and course of IBD,<sup>76,77</sup> so the microbiota is postulated as a potential target for management of IBD.<sup>78</sup> In animal models, FOS have been shown to attenuate trinitrobenzene sulfonic acid (TNBS)-induced colitis,<sup>79</sup> and patients receiving FOS or combinations of short- and long-chain fructans, as part of a nutritional formulation, have shown various degrees of decreased inflammatory markers, disease activity and requirement for steroid use.<sup>80,81</sup> Fructan supplementation alone has also been shown to improve pouchitis in a similar patient population.<sup>82</sup>

Unfortunately, many enteral products commonly used in compromised patients to maximize nutrient absorption, including 'elemental' or 'semi-elemental' diets, have traditionally excluded fiber and fiber-like substances. Part of the rationale for this exclusion came from inappropriately equating any fiber addition to the adverse effects seen with fibrous and particulate dietary components (such as unprocessed grains or seeds) in patients with intestinal strictures. Excluding all fiber from the diet of these patients actually deprives the gut mucosa of major dietary components needed to support trophism, barrier function and a

**Figure 3. Prebiotics in the compromised gut**



more desirable microbiota. Today, the forms of fiber used in enteral feeding products, including fructans, are a safe and reliable way to support gut structure and function in these patients.

## Safety and tolerance

Dietary fructans have been thoroughly studied in vitro as well as in human and animal trials, which found a lack of morbidity, mortality, toxicity, carcinogenicity, and mutagenic and genotoxic effects.<sup>83-85</sup> Fructans have been used as animal feed additives, approved as a food ingredient, and have been granted 'generally recognized as safe' (GRAS) status.

Like any other fermentable substrate, excessive amounts of distal fermentation of fructans by colonic bacteria can lead to increased gas formation, loose stools and abdominal cramps. The effect is strictly dose-related. Some adults may develop mild symptoms at a dose of 15 g/d, other trials in adults have reported that up to 20 g/d of inulin and/or FOS

can be generally well tolerated.<sup>84</sup> However, doses necessary to elicit signs and symptoms of intolerance vary among individuals and are influenced by other dietary components ingested with the dose of inulin or FOS. As with other non-absorbable carbohydrates, intake with other foods or as part of a nutritional supplement, or in divided daily doses, can decrease symptoms compared with a large once-daily dose.

## Conclusions

The use of dietary fiber, including soluble fermentable fibers, such as fructans, can support intestinal mucosal trophism and function, improve gut barrier function and modulate intestinal microbiota in a positive manner. The use of prebiotic agents in health and, more significantly, in cases of compromised intestinal function can be a major adjuvant in the adequate delivery of enteral nutrition. The complete understanding of the mechanisms, as well as of the full potential, of these agents requires further study.

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# CLINICAL NUTRITION ABSTRACTS

## CANCER

### Early enteral feeding compared with parenteral nutrition after oesophageal or oesophagogastric resection and reconstruction

*Br J Nutr* 2005 Apr;93(4):509-513.

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After resective and reconstructive surgery in the gastrointestinal tract, oral feeding is traditionally avoided in order to minimize strain to the anastomoses and to reduce the inherent risks of the postoperatively impaired gastrointestinal motility. However, studies have given evidence that the small bowel recovers its ability to absorb nutrients almost immediately following surgery, even in the absence of peristalsis, and that early enteral feeding would preserve both the integrity of gut mucosa and its immunological function. The aim of this study was to investigate the impact of early enteral feeding on the postoperative course following oesophagectomy or oesophagogastric resection and reconstruction. Between May 1999 and November 2002, forty-four consecutive patients (thirty-eight males and six females; mean age 62, range 30-82) with oesophageal carcinoma (stages I-III), who had undergone radical resection and reconstruction, entered this study (early enteral feeding group; EEF). A historical group of forty-four patients (thirty-seven males and seven females; mean age 64, range 41-79; stages I-III) resected between January 1997 and March 1999 served as control (parenteral feeding group; PF). The duration of both postoperative stay in the Intensive Care Unit (ICU) and the total hospital stay, perioperative complications and the overall mortality were compared. Early enteral feeding was administered over the jejunal line of a Dobhoff tube. It started 6 h postoperatively at a rate of 10 mL/h for 6 h with stepwise increase until total enteral nutrition was achieved on day 6. In the controls oral enteral feeding was begun on day 7. If compared to the PF group, EEF patients recovered faster considering the duration of both stay in the ICU and in the hospital. There was a significant difference in the interval until the first bowel movements. No difference in overall 30 d mortality was identified. A poor nutritional status was a significant prognostic factor for an increased mortality. Early enteral feeding significantly reduces the duration of ICU treatment and total hospital stay in patients who undergo oesophagectomy or oesophagogastric resection for oesophageal carcinoma. The mortality rate is not affected.

## CRITICAL CARE NUTRITION

### The role of macronutrients in gastrointestinal blood flow

*Curr Opin Clin Nutr Metab Care* 2005 Sep;8(5):552-556.

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**PURPOSE OF REVIEW:** The presence of luminal nutrients after a meal increases gastrointestinal blood flow in a phenomenon called postprandial hyperemia. In many conditions related to splanchnic hypoperfusion, enteral nutrition may play a role in counterbalancing the installed splanchnic low-flow state by producing intestinal hyperemia. However, when the gut is hypoperfused there is a chance of enteral nutrition producing a mismatch of the oxygen demand:supply ratio with subsequent gut ischemia. This article aims to review the effects of macronutrients on gastrointestinal blood flow in both healthy and critical conditions, especially those related to hepatosplanchnic hypoperfusion. **RECENT FINDINGS:** Splanchnic blood flow is related not only to the route (intravenous or enteral) and timing of nutritional support (during the course of the insult) but also to the composition of the formula. Critically ill patients with gut hypoperfusion may tolerate enteral nutrition, but this effect may be restricted to the early post-injury phase. During ischemia reperfusion injury, immune nutrients may promote different outcomes: glutamine may protect whereas arginine may deteriorate the mucosal barrier and enhance permeability. **SUMMARY:** Understanding the relationship between macronutrients and gastrointestinal blood flow is a major challenge. Ongoing research in nutritional support in hypoperfused, catecholamine-dependent patients will open the door to optimize the recovery of patients in critical care.

### Negative impact of hypocaloric feeding and energy balance on clinical outcome in ICU patients

*Clin Nutr* 2005 Aug;24(4):502-509.

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**BACKGROUND AND AIMS:** Critically ill patients with complicated evolution are frequently hypermetabolic, catabolic, and at risk of underfeeding. The study aimed at assessing the relationship between energy balance and

outcome in critically ill patients. **METHODS:** Prospective observational study conducted in consecutive patients staying  $\geq 5$  days in the surgical ICU of a University hospital. Demographic data, time to feeding, route, energy delivery, and outcome were recorded. Energy balance was calculated as energy delivery minus target. Data in means  $\pm$  SD, linear regressions between energy balance and outcome variables. **RESULTS:** Forty-eight patients aged  $57 \pm 16$  years were investigated; complete data are available in 669 days. Mechanical ventilation lasted  $11 \pm 8$  days, ICU stay was  $15 \pm 9$  days, and 30-day mortality was 38%. Time to feeding was  $3.1 \pm 2.2$  days. Enteral nutrition was the most frequent route with 433 days. Mean daily energy delivery was  $1,090 \pm 930$  kcal. Combining enteral and parenteral nutrition achieved highest energy delivery. Cumulated energy balance was between  $-12,600 \pm 10,520$  kcal, and correlated with complications ( $p < 0.001$ ), already after 1 week. **CONCLUSION:** Negative energy balances were correlated with increasing number of complications, particularly infections. Energy debt appears as a promising tool for nutritional follow-up, which should be further tested. Delaying initiation of nutritional support exposes the patients to energy deficits that cannot be compensated later on.

### Nutritional care of the obese intensive care unit patient

*Curr Opin Crit Care* 2005 Aug;11(4):300-303.

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**PURPOSE OF REVIEW:** This review discusses the unique metabolic changes in critically ill obese patients and the challenges in estimating and providing them with nutritional support while in the intensive care unit. It provides some of the scientific data in support of and against hypocaloric, high-protein nutritional support in critically ill obese patients. **RECENT FINDINGS:** The growing prevalence of obesity worldwide and particularly in the developed countries has resulted in concerns regarding the implementation of effective and specialized nutritional support for critically ill obese patients. The concerns arise from the limited data regarding the obese individual's response to various metabolic stresses, especially trauma and burns. There is continuous debate about the most appropriate method of calculating the critically ill obese patient's basic energy and calorie needs. **SUMMARY:** Nutritional support of the critically ill obese represents a unique challenge but early administration of protein followed by carbohydrates and finally lipids can result in net protein anabolism and better glycemic control.

### Variation in enteral nutrition delivery in mechanically ventilated patients

*Nutrition* 2005 Jul-Aug;21(7-8):786-792.

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**OBJECTIVE:** We determined the variability in enteral feeding practices in mechanically ventilated patients in four

adult intensive care units of a tertiary-care, referral hospital. **METHODS:** Patients who had been mechanically ventilated for at least 48 h and received enteral nutrition were prospectively followed. **RESULTS:** Fifty-five of 101 consecutive mechanically ventilated patients received enteral nutrition; in 93% of patients, feedings were infused into the stomach. Patients who were cared for in the medical intensive care unit, where a nutritional protocol was operational, received enteral nutrition earlier in their ventilatory course ( $p = 0.004$ ) and feedings were advanced to target rates faster ( $p = 0.043$ ) than those who received care in other units. The number ( $p = 0.243$ ) and duration ( $p = 0.668$ ) of interruptions in feeding did not differ by patient location. On average, patients received only 50% to 70% of their targeted caloric goals during the first 6 days of enteral nutrition. Most feeding discontinuations (41%) were secondary to procedures. Gastrointestinal intolerances, including vomiting, aspiration, abdominal distention, and increased gastric residuals, were uncommon despite allowing gastric residuals up to 300 mL. **CONCLUSIONS:** The practice of providing enteral feeds to mechanically ventilated patients varies widely, even within one hospital. A protocol enhanced early initiation of enteral feeds and advancement to target feeding rates but did not alter the number or duration of interruptions in enteral feedings. Procedures represented the most common reason for stopping enteral feeds, and gastrointestinal intolerances (vomiting, aspiration, and increased gastric residuals) caused few feeding interruptions. The gastric route was safe and well tolerated for early enteral feeding in most mechanically ventilated patients.

### Nutritional support in sepsis [article in Spanish]

*Nutr Hosp* 2005 Jun;20(suppl 2):51-53.

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Although it is considered that metabolic and nutritional support must be part of the management of septic patients, it has not been conclusively shown that nutritional support will improve survival or complications from sepsis. Specific data on this issue are scarce since there are few studies that have investigated specialized nutritional support in septic patients. Thus, most of the recommendations are based on outcomes obtained in severely ill patients with different pathologies. It is assumed that nutritional support should be carried out through the enteral route whenever possible, as in other critically ill patients. The energetic waste in these patients is highly variable, although in general terms the hypermetabolic situation may be classified as moderate. An adjustment factor of 1.25-1.30 is recommended for the Harris-Benedict's equation to calculate the caloric intake. Septic patients should receive a hyperproteic intake. The amount of glucose administered should not exceed 70% of non-protein calories, and lipids intake should not exceed 40%. With regards to micronutrients, it is recommended to increase the supply of those with antioxidant properties (vitamin E, carotenes, vitamin C, selenium). There are data to consider that the use of diets enriched with pharmaconutrients (both with parenteral and enteral routes) may be beneficial in septic patients, although there is some controversy when interpreting the outcomes.

## Artificial nutrition in acute pancreatitis [article in Spanish]

*Nutr Hosp* 2005 Jun;20(suppl 2):25-27.

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Metabolic changes that occur in acute pancreatitis result, as with other critically ill patients, in a metabolic stress situation that many times requires the application of a specialized nutritional support. Patients presenting the highest severity indexes (defined as Ranson's index = 3 or an APACHE II = 10) are candidates to receive nutritional support. Enteral nutrition must be the first route to consider for nutrients supply and must be maintained except for patients that have intolerance or develop pain, ascites, or increased serum amylase levels. Transpyloric enteral nutrition, through a nasojejunal tube or by means of a jejunostomy catheter, is a safe access in severe acute pancreatitis, and it may even be accompanied by advantages in the patients' clinical course as compared with parenteral nutrition. The indication for parenteral nutrition would be conditioned by the inability to obtain an appropriate enteral (jejunal) approach, intolerance to enteral nutrition, or disease exacerbation after the onset of enteral nutrition support. With current data, no recommendations can be established in relation to the ideal characteristics that nutrients composition received by acute pancreatitis patients should meet.

## Requirements of macronutrients and micronutrients [article in Spanish]

*Nutr Hosp* 2005 Jun;20(suppl 2):13-17.

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Critically ill patients have important modifications in their energetic requirements, in which the clinical situation, treatment applied and the time course take part. Thus, the most appropriate method to calculate the caloric intake is indirect calorimetry. When this test is not available, calculations such as Harris-Benedict's may be used, although not using the so high correction factors as previously recommended in order to avoid hypercaloric intakes. The intake of a fixed caloric amount (comprised between 25-30 kcal/kg/min) is adequate for most critically ill patients. Carbohydrates intake must be of 5 g/kg/d maximum. Glucose plasma levels must be controlled in order to avoid hyperglycemia. With regards to fat intake, the maximum limit should be 1.5 g/kg/d. The recommended protein intake is 1.0-1.5 g/kg/d, according to the clinical situation characteristics. Special care must be taken with micronutrients intake, an issue that is many times undervalued. In this sense, there are data to consider some micronutrients such as Zn, Cu, Mn, Cr, Se, Mo and some vitamins (A, B, C, and E) of great importance for patients in a critical condition, although specific requirements for each one of them have not been established.

## Contemporary strategies for the prevention of stress-related mucosal bleeding

*Am J Health Syst Pharm* 2005 May 15;62(10 suppl 2):S11-S17.

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**PURPOSE:** The purpose of this review is to describe the clinical presentation and pathophysiology of stress-related

mucosal bleeding and review the strategies to prevent bleeding. **SUMMARY:** The mortality rate associated with clinically significant stress-related mucosal bleeding is high. Respiratory failure requiring mechanical ventilation for more than 48 hours and coagulopathy are two strong, independent risk factors for bleeding. Splanchnic hypoperfusion is the underlying etiology of stress-related mucosal injury and bleeding. Mucosal damage typically manifests as multiple superficial lesions without perforation, and bleeding often originates in superficial capillaries after the patient is admitted to the intensive care unit. Providing adequate visceral perfusion is vital to preventing bleeding. Gastrointestinal function should be taken into consideration before using enteral nutrition, and enteral nutrition should not be the sole stress ulcer prophylactic therapy. Acid-suppression therapy should be used to raise the intragastric pH above 3.5 because it reduces the incidence of stress-related mucosal bleeding. Proton pump inhibitors are at least as effective, and may be more effective than histamine H<sub>2</sub>-receptor antagonists in achieving this pH goal and preventing bleeding. **CONCLUSION:** The key to reducing mortality from stress-related bleeding in critically ill patients is to prevent mucosal damage. Providing adequate visceral perfusion and acid-suppression therapy can reduce the risk of stress-related mucosal damage and bleeding.

## Nutritional adequacy in patients receiving mechanical ventilation who are fed enterally

*Am J Crit Care* 2005 May;14(3):222-231.

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**BACKGROUND:** Inadequate nutritional intake in critically ill patients can lead to complications resulting in increased mortality and healthcare costs. Several factors limit adequate nutritional intake in intensive care unit patients given enteral feedings. **OBJECTIVE:** To examine the adequacy of enteral nutritional intake and the factors that affect its delivery in patients receiving mechanical ventilation. **METHODS:** A prospective, descriptive design was used to study 60 patients receiving enteral feedings at target or goal rate. Energy requirements were determined for the entire sample by using the Harris-Benedict equation; energy requirements for a subset of 25 patients were also determined by using indirect calorimetry. Energy received via enteral feeding and reason and duration of interruptions in feedings were recorded for 3 consecutive days. **RESULTS:** Mean estimated energy requirements (8,996 kJ, SD 1,326 kJ) and mean energy intake received (5,899 kJ, SD 3,058 kJ) differed significantly (95% CI 3,297-3,787;  $p < 0.001$ ). A total of 41 patients (68.3%) received less than 90% of their required energy intake, 18 (30.0%) received within  $\pm 10\%$ , and 1 (1.7%) received more than 110%. Episodes of diarrhea, emesis, large residual volumes, feeding tube replacements, and interruptions for procedures accounted for 70% of the variance in energy received ( $p < 0.001$ ). Procedural interruptions alone accounted for 45% of the total variance. Estimated energy requirements determined via indirect calorimetry and mean energy received did not differ. **CONCLUSIONS:** Most critically ill patients receiving mechanical ventilation

who are fed enterally do not receive their energy requirements, primarily because of frequent interruptions in enteral feedings.

### **Antioxidant nutrients: a systematic review of trace elements and vitamins in the critically ill patient**

*Intensive Care Med* 2005 Mar;31(3):327-337.

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**OBJECTIVE:** Critical illness is associated with the generation of oxygen free radicals and low endogenous antioxidant capacity leading to a condition of oxidative stress. We investigated whether supplementing critically ill patients with antioxidants, trace elements, and vitamins improves their survival. **METHODS:** We searched four bibliographic databases from 1980 to 2003 and included studies that were randomized, reported clinically important endpoints in critically ill patients, and compared various trace elements and vitamins to placebo. **RESULTS:** Eleven articles met the inclusion criteria. When the results of all the trials were aggregated, overall antioxidants were associated with a significant reduction in mortality [Risk Ratio (RR) 0.65, 95% confidence intervals (CI) 0.44-0.97,  $p = 0.03$ ] but had no effect on infectious complications. Studies that utilized a single trace element were associated with a significant reduction in mortality [RR 0.52, 95% CI 0.27-0.98,  $p = 0.04$ ] whereas combined antioxidants had no effect. Studies using parenteral antioxidants were associated with a significant reduction in mortality [RR 0.56, 95% CI 0.34-0.92,  $p = 0.02$ ] whereas studies of enteral antioxidants were not. Selenium supplementation (alone and in combination with other antioxidants) may be associated with a reduction in mortality [RR 0.59, 95% CI 0.32-1.08,  $p = 0.09$ ] while non-selenium antioxidants had no effect on mortality. **CONCLUSIONS:** Trace elements and vitamins that support antioxidant function, particularly high-dose parenteral selenium either alone or in combination with other antioxidants, are safe and may be associated with a reduction in mortality in critically ill patients.

## **DIABETES**

### **Artificial nutrition in hyperglycemia and diabetes mellitus in critically ill patients [article in Spanish]**

*Nutr Hosp* 2005 Jun;20(suppl 2):34-37.

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The need to strictly control glucose levels, even in non-diabetic patients, has recently emerged following the publication of the results that indicate the possibility of reducing the morbidity and mortality in critically ill patients. Since hyperglycemia is one of the most frequent metabolic impairments in these patients, insulin therapy is a necessity in most of the cases. In order to prevent hyperglycemia and its associated complications, nutritional support must be adjusted to the patient's requirements, avoiding hyponutrition. Whenever possible, nutrients supply should be done through the digestive route.

Parenteral nutrition is more often accompanied by hyperglycemia and requires an increase in insulin dosage to control it. There are two types of enteral diets designed to help controlling hyperglycemic conditions: carbohydrates rich diets, and fat rich diets. In general terms, carbohydrates rich diets may be recommended in type 1 diabetic patients who are in a stable condition, and fat rich diets in type 2 diabetes and in stress hyperglycemia. In both cases, the use of low glycemic index carbohydrates is recommended. Protein intake should be adjusted to the patients' metabolic stress level. In diabetic patients with acute disease, an increase in antioxidants intake is recommended.

## **GASTROINTESTINAL TRACT DISORDERS**

### **Control of systemic and local inflammation with transforming growth factor $\beta$ containing formulas**

*JPEN J Parenter Enteral Nutr* 2005 Jul-Aug;29(4 suppl):S126-S133.

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Enteral nutrition therapy with liquid diet has been shown to be effective in achieving clinical remission in intestinal Crohn's disease. The mechanism of action of this therapy, however, is still poorly understood. As part of our assessment of the action of 3 related polymeric enteral therapies, we have used a variety of techniques to document the histological and cytokine responses, in the mucosa and, systemically, to these treatments. The feeds studied (AL110, Modulen IBD and ACD004 [Nestlé, Vevey, Switzerland]) all have casein as the protein source, are lactose-free and are rich in transforming growth factor  $\beta$  (TGF- $\beta$ ). They have all been shown to induce clinical remission associated with mucosal healing. In the case of Modulen IBD, as well as mucosal macroscopic and histological healing there was a fall in mucosal proinflammatory cytokines: interleukin-1 mRNA in colonic and ileal, interleukin-8 mRNA in the colon and interferon  $\gamma$  mRNA in the ileum, but a rise in the regulatory cytokine TGF- $\beta$  mRNA in the ileum. These results indicate that these formulas are influencing the disease process itself, and thus suggest that the clinical remission achieved is a result of a reduction in inflammation, rather than a consequence of some other nutrition effect.

### **The anti-inflammatory effects of enteral nutrition**

*JPEN J Parenter Enteral Nutr* 2005 Jul-Aug;29(4 suppl):S134-S140.

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Enteral nutrition has a positive effect on growth in children with active Crohn's disease. The question arises: is this due only to improved nutrition? Enteral formulas may also directly reduce inflammation, lowering the expression of cytokines like interleukin (IL)-6 that inhibit growth. Four lines of evidence support the hypothesis that enteral formulas directly lessen inflammation: enteral nutrition directly



affects the inflamed intestine; changes in inflammatory markers precede repletion of nutrition status; molecular pathways exist linking changes in luminal contents to the expression of class II MHC genes in intestinal epithelium in animal studies; and enteral formulas have a direct effect on cytokine expression by intestinal epithelial cells.

### The use of enteral nutrition in the management of Crohn's disease in adults

*JPEN J Parenter Enteral Nutr* 2005 Jul-Aug;29(4 suppl):S166-S172.

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Crohn's disease is a chronic, relapsing disease and none of the treatments developed so far can cure it. Artificial nutrition is effective to both treat malnutrition when present and induce remission. However, striking advances in anti-inflammatory and immunomodulating therapies (including infliximab) and low compliance to treatment in the first trials have limited its place in the management of adults to drug-resistant patients. Randomized controlled trials show that artificial nutrition is effective in >50% of the cases in this selected population. Significant progress has recently been made to improve the palatability (and thus acceptability) of some enteral solutions, which can be consumed by the oral route and as pharmaconutrition. We reviewed the literature on enteral nutrition in adults with Crohn's disease. We present herein the results of the studies performed with antioxidants, glutamine, short-chain fatty acids, prebiotics, probiotics, low microparticle diets, and a TGF- $\beta_2$  enriched formulation.

### Nutritional therapy for Crohn's disease in Japan

*J Gastroenterol* 2005 Mar;40(suppl 16):25-31.

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In Japan, nutritional therapy as both a primary and as a secondary treatment is widely used for Crohn's disease (CD). The rationale for its use is based on a variety of reasons. The first is its ability to induce remission and to ameliorate the activity of intestinal lesions in the short term by enteral (EN) or by parenteral nutritional therapy in which overexpression of chemokine receptors in an active stage are decreased significantly in the remission stage. Second is its ability to maintain remission over the long term through home-based enteral nutrition in which tube feeding during the nighttime is encouraged. Third is its ability to reduce the steroid dosage over the period of a long-term treatment course. However, several disadvantages of this therapy such as unpalatability and sluggish effect have been pointed out. Several studies have attempted to resolve this issue and determine the best components of EN, especially in fat composition. Some data have been suggestive of too much long-chained fatty acid having a hazardous effect on EN's clinical efficacy because it works as a precursor of inflammatory prostaglandins. Our recent data show that medium-chained triglyceride did not have such a hazardous effect on clinical efficacy. Several studies suggested that the patient factors that were resistant to inducing remission in the short term were a long period of suffering CD, a high activity (on Crohn's Disease Activity Index, CDAI), hemor-

rhagic colitis, and colitis with marked cobblestoning. Japanese guidelines for the treatment of CD recommended nutritional therapy as a first-line therapy and as a maintenance therapy after inducing remission. This treatment policy has led to Japanese CD patients having lower mortality rates than that of patients who do not receive EN. If this therapy could be combined with other drug therapies, including strong immunosuppressants, treatment strategies would be improved over those we have at present.

## GENERAL (ENTERAL AND PARENTERAL) NUTRITION

### Enteral nutrition via percutaneous endoscopic gastrostomy and nutritional status of patients: five-year prospective study

*J Gastroenterol Hepatol* 2005 Jul;20(7):1002-1007.

Erdil A, Saka M, Ates Y, Tuzun A, Bagci S, Uygun A, Yesilova Z, Gulsen M, Karaeren N, Dagalp K.

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**BACKGROUND:** Since it was described in 1980, percutaneous endoscopic gastrostomy (PEG) has been a widely used method for insertion of a gastrostomy tube in patients who are unable to swallow or maintain adequate nutrition. The aim of the present paper was to determine the complications of PEG insertion and to study pre- and post-procedural nutritional status. **METHODS:** During the period of March 1999-September 2004, placement of PEG tube was performed in 85 patients (22 women and 63 men). Patient nutritional status was assessed before and after PEG insertion via anthropometric measurements. **RESULTS:** The most frequent indication for PEG insertion was neurological disorders (65.9%). Thirty patients died due to primary disease and two patients due to PEG-related complications within 5 years. There were 14 early complications in 10 patients (15.2%; <30 days), and 18 late complications in 12 patients (19.6%). Total mortality was 37.6%. All complications other than four were minor. Before PEG insertion, patients were assessed with subjective global assessment and it was determined that 43.2% of them had severe, and 41.9% of them had mild malnutrition. After PEG insertion, significant improvements on patient nutrition levels was observed. **CONCLUSION:** Percutaneous endoscopic gastrostomy is a minimally invasive gastrostomy method with low morbidity and mortality rates, is easy to follow up and easy to replace when clogged.

### Continuous enteral nutrition versus single bolus: effects on urine C peptide and nitrogen balance [article in Spanish]

*Med Clin (Barc)* 2005 Apr;124(16):613-615.

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**BACKGROUND AND OBJECTIVE:** Our study was designed to assess the impact on nitrogen and glucose metabolism when it is administered either as discontinuous or as continuous infusion. **PATIENTS AND METHOD:** We assessed the nutritional efficacy (nitrogen balance) and

hyperinsulinism risk (urine C peptide excretion) of enteral nutrition in 23 patients hospitalized because of acute stroke. **RESULTS:** The feeding tolerance of our enteral nutrition protocol (nasogastric catheter) was full in every patient. The nitrogen balance was positive in both patterns, but the balance in the continuous feeding pattern was better than in the bolus feeding one. On the contrary, the urine C peptide excretion was increased when enteral nutrition was administered intermittently as compared with continuous feeding. Calciuria was greater in the continuous fed pattern than in the bolus feeding. **CONCLUSIONS:** Continuous feeding is associated with better nitrogen balance and less urine C peptide excretion than intermittent feeding. These results suggest that continuous feeding would be an interesting choice to improve glucose control in diabetic patients with enteral nutrition.

## HEALTH OUTCOMES AND HEALTH ECONOMICS

### Enteral nutritional support in prevention and treatment of pressure ulcers: A systematic review and meta-analysis

*Ageing Res Rev* 2005 Aug;4(3):422-450.

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**BACKGROUND:** There have been few systematic reviews and no meta-analyses of the clinical benefits of nutritional support in patients with, or at risk of developing, pressure ulcers. Therefore, this systematic review and meta-analysis was undertaken to address the impact of enteral nutritional support on pressure ulcer incidence and healing and a range of other clinically relevant outcome measures in this group. **METHODS:** Fifteen studies (including eight randomized controlled trials (RCTs) of oral nutritional supplements (ONS) or enteral tube feeding (ETF), identified using electronic databases (including PubMed and Cochrane) and bibliography searches, were included in the systematic review. Outcomes including pressure ulcer incidence, pressure ulcer healing, quality of life, complications, mortality, anthropometry and dietary intake were recorded, with the aim of comparing nutritional support versus routine care (eg, usual diet and pressure ulcer care) and nutritional formulas of different composition. Of these 15 studies, 5 RCTs comparing ONS (4 RCTs) and ETF (1 RCT) with routine care could be included in a meta-analysis of pressure ulcer incidence. **RESULTS:** Meta-analysis showed that ONS (250-500 kcal, 2-26 weeks) were associated with a significantly lower incidence of pressure ulcer development in at-risk patients compared to routine care (odds ratio 0.75, 95% CI 0.62-0.89, 4 RCTs, n = 1,224, elderly, post-surgical, chronically hospitalized patients). Similar results were obtained when a combined meta-analysis of ONS (4 RCT) and ETF (1 RCT) trials was performed (OR 0.74, 95% CI 0.62-0.88, 5 RCTs, n = 1,325). Individual studies showed a trend towards improved healing of existing pressure ulcers with disease-specific (including high protein) versus stan-

dard formulas, although robust RCTs are required to confirm this. Although some studies indicate that total nutritional intake is improved, data on other outcome measures (quality of life) are lacking. **CONCLUSIONS:** This systematic review shows enteral nutritional support, particularly high protein ONS, can significantly reduce the risk of developing pressure ulcers (by 25%). Although studies suggest ONS and ETF may improve healing of PU, further research to confirm this trend is required.

### Evidence-based strategies for the use of oral nutritional supplements

*Br J Community Nurs* 2005 Apr;10(4):158,160,162-164.

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Prescribable oral nutritional supplements are commonly used as a method of nutritional support in the prevention and treatment of malnutrition in adults. There is growing evidence to suggest that when used appropriately in treatment plans, individuals receiving them will benefit from functional and clinical improvements. The use of supplements in the community has increased over the last decade and questions about the increasing costs and efficacy of the products are often raised within health-care communities. The development of guidelines and protocols for the use of supplements in the community that are based on evidence of need and indicate a clear pathway of care, together with intended benefit, should help to address the issues of costly, inappropriate prescribing.

## IMMUNONUTRITION

### Preoperative oral supplementation with long-chain $\omega$ -3 fatty acids beneficially alters phospholipid fatty acid patterns in liver, gut mucosa, and tumor tissue

*JPEN J Parenter Enteral Nutr* 2005 Jul-Aug;29(4):236-240.

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**BACKGROUND:** The uptake of  $\omega$ -3 polyunsaturated fatty acids (PUFAs) into the liver, gut mucosa, and tumor tissue and plasma levels after preoperative administration of supplemented enteral nutrition was investigated in patients with malignancies of the upper gastrointestinal tract. The objective of the study was to evaluate the incorporation of preoperatively administered PUFAs, eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA) into cell phospholipids. **METHODS:** Patients undergoing major gastrointestinal surgery (n = 40) were prospectively randomized to receive a PUFA-supplemented liquid oral diet 5 days preoperatively or an isocaloric control diet. The planned diet intake was 1,000 mL/d providing 3.7 g of PUFA. The diet was given in addition to the usual hospital diet. The phospholipid fractions in plasma were analyzed on the day of surgery. Tissue samples of liver, gut mucosa (small intestine), and tumor

were taken during surgery and homogenized. EPA and DHA content was analyzed using liquid gas chromatography. **RESULTS:** Both patient groups (PUFA group:  $n = 20$ ; control group:  $n = 20$ ) were similar in age, weight, and surgical procedures. As compared with the control group, the PUFA group had significantly increased levels of EPA in liver tissue (0.4 vs 1.3 weight %), gut mucosa (0.3 vs 1.0 weight %), and tumor tissue (0.3 vs 0.8 weight %). Also, the DHA levels in the PUFA group were significantly higher than the control group: liver tissue (4.1 vs 7.5 weight %), gut mucosa (2.1 vs 3.7 weight %) and tumor tissue (1.9 vs 4.2 weight %). **CONCLUSIONS:** This study suggests that administration of PUFA-enriched diets leads to increased incorporation of EPA and DHA not only in liver and gut mucosa tissue, but also in tumor tissue in patients with solid gastrointestinal tumors. Thus, pre-operative administration of oral PUFA-enriched diets could have an impact on the postoperative inflammatory response after major abdominal surgery.

### Role of enteral immunonutrition in patients with gastric carcinoma undergoing major surgery

*Asian J Surg* 2005 Apr;28(2):121-124.

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**OBJECTIVE:** To evaluate the influence of postoperative immunonutrition on immune and nutritional parameters in patients with gastric carcinoma. **METHODS:** From September 2002 to August 2003, 40 patients with gastric carcinoma who had undergone major surgery were randomly divided into an immunonutrition group and standard nutrition group, each of 20 patients. On post-operative Day 2, patients in the standard nutrition group received a standard enteral formula, while those in the immunonutrition group received an enteral formula enriched with glutamine, arginine and omega-3 fatty acids. Nutritional support was continued for 7 days. Blood samples were obtained to determine plasma albumin, prealbumin and transferrin on Days 0, 5 and 9. On Days 0, 1 and 9, blood samples were collected to detect immunoglobulin (Ig) A, IgG, IgM, CD4 and CD8 cell counts, the ratio of CD4/CD8, interleukin (IL)-2, IL-6 and tumour necrosis factor (TNF)-alpha, respectively. **RESULTS:** There were no significant differences between the two groups in protein and immune parameters pre-operatively and no significant differences in management perioperatively. No serious adverse effects were recorded with the two formulas. Postoperative procedures were smooth in both groups. On Day 9, serum levels of prealbumin and transferrin were higher in the immunonutrition group than in the standard nutrition group ( $p < 0.01$ ). After 7 days' nutritional support, patients in the immunonutrition group had higher levels of immunoglobulin, CD4 cell counts, CD4/CD8 ratio and IL-2 than those in the control group, whereas IL-6 and TNF-alpha levels were significantly lower in the immunonutrition group. **CONCLUSION:** Compared with standard enteral nutrition, enteral immunonutrition can improve defence mechanisms and modulate inflammatory action after major elective surgery for gastric carcinoma.

## OBESITY

### Severe obesity: a growing health concern A.S.P.E.N. should not ignore

*JPEN J Parenter Enteral Nutr* 2005 Jul-Aug;29(4):288-297.

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The definition of malnutrition in the published standards of the American Society of Parenteral and Enteral Nutrition (A.S.P.E.N.) is any derangement in the normal nutrition status and includes overnutrition, commonly referred to as obesity. The incidence of obesity is increasing and reaching epidemic proportions in the United States and even worldwide. This has significant financial impact as our society spends billions of dollars on fad diets, commercial weight-loss programs, nutrition and dietary supplements, prescription and over-the-counter medications, and health clubs. Another approximately \$100 billion are spent to treat the medical consequences of obesity. Currently, for those patients with intractable morbid obesity, defined as having a body mass index  $>40 \text{ kg/m}^2$ , surgery offers the only option for achieving meaningful and sustainable weight loss. The resultant weight loss dramatically improves health and decreases the cost of health care for these patients. Years of refinement in technology and the introduction of safer and less invasive procedures have dramatically reduced the short-term morbidities and long-term metabolic consequences of these procedures. This address will review the field of weight loss (bariatric) surgery and will offer a compelling request for A.S.P.E.N. to include obesity in its fabric.

## PEDIATRICS

### Nutritional treatment in childhood Crohn's disease [article in French]

*Arch Pediatr* 2005 Aug;12(8):1255-1266.

Comité de Nutrition de la Société Française de Pédiatrie

Unité de Gastroentérologie, Hépatologie et Nutrition, Clinique de Pédiatrie, Hôpital Jeanne-de-Flandre et Faculté de Médecine, Université de Lille-II, Lille Cedex, France.

Growth retardation and delay in sexual maturation are the major complications of child-onset Crohn's disease (CD). Nutritional assessment and monitoring should comprise: weight and height measurement with calculation of respective velocities (growth velocity should be  $\geq 4\text{-}5 \text{ cm/year}$  during the prepubertal period); pubertal staging; dietetic evaluation; laboratory analysis for mineral, vitamin and trace element deficiencies; bone age. At diagnosis, weight loss and growth delay are present in 80-90% and one third of cases, respectively. In case of an acute flare-up in a CD child with normal nutritional status, nutritional therapy is limited to oral feeding, with a caloric intake at least equal to recommended dietary allowances for age and sex. A low-fiber diet is advised in case of small bowel stenosis. No diet has been shown as efficient in the long-term maintenance of remission. Exclusive enteral nutrition (EN) is an alternative

to corticosteroids for the treatment of an acute flare-up of CD, especially in case of malnutrition. Prolonged nocturnal EN is of great interest for the treatment of growth retardation and delay of sexual maturation and in case of steroid-dependent or steroid-refractory CD. In case of steroid-dependent CD with no delay of growth and/or sexual maturation, immunomodulating agents are nowadays an alternative to long-term EN. Efficacy of polymeric solutions is identical to that of semi-elemental or elemental solutions. Parenteral nutrition is limited to an acute flare-up with resistance to medical treatment and/or EN, and contraindications to surgery; occlusion or fistula; short bowel syndrome.

## Enteral nutrition and microflora in pediatric Crohn's disease

*JPEN J Parenter Enteral Nutr* 2005 Jul-Aug;29(4 suppl):S173-S178.

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**BACKGROUND:** Exclusive enteral nutrition (EN) is an established primary therapy for pediatric Crohn's disease (CD). The mechanism of action of such treatment is still conjectural. The aim of the present study was to investigate if EN-induced remission is associated with modification of the fecal microflora in CD. **METHODS:** Stool samples were collected from 5 healthy children and adolescents over a period of 3 months, and from 9 children and adolescents with active CD. To induce disease remission, children with CD received a course of exclusive EN for 8 weeks with a polymeric formula (Modulen IBD, Nestlé). At the end of the course of exclusive EN, children returned to a free diet but continued to take 40% of the daily caloric intake as polymeric formula. Fecal microflora was analyzed by 16S ribosomal DNA polymerase chain reaction and temperature gradient gel electrophoresis (TGGE) with direct visual comparison of band profiles of PCR products. **RESULTS:** In 8 of 9 children, the exclusive EN alone induced disease remission. In 1 child, it was necessary to add steroids to the exclusive EN course to achieve remission. In all children with CD, analysis of gel band distribution revealed profound modification of the fecal microflora after exclusive EN. Variations of band distribution corresponding to different bacterial species were observed also in children on partial EN and required time to achieve stability of the band profile. In contrast, control healthy children showed a host-specific and stable TGGE profile over time. **CONCLUSION:** These data suggest that a possible mechanism of action of EN in inducing disease remission in CD is the capacity of modification of gut microflora. Possible explanations of such capacity are both low residue and prebiotic properties of the polymeric liquid formula.

## Interventions for growth failure in childhood Crohn's disease

*Cochrane Database Syst Rev* 2005 Jul 20;(3):CD003873.

Newby E, Sawczenko A, Thomas A, Wilson D.

**BACKGROUND:** Crohn's disease in childhood is a chronic relapsing condition. Fifteen to forty per cent of children

with Crohn's disease have growth retardation (Griffiths 1993a). Some treatment modalities including corticosteroids have been implicated in growth failure but it is thought mainly to be secondary to uncontrolled disease activity (Motil 1993; Markowitz 1993). Growth is fundamental to the practice of pediatrics, so by taking growth as the primary outcome measure we address issues important to both patients, their families and pediatricians. **OBJECTIVES:** To evaluate the effectiveness of the different modalities available for the treatment of childhood Crohn's disease with regard to the reversal of growth failure and the promotion of normal growth. **SEARCH STRATEGY:** Searches were made of the following databases using the Collaborative Review Group Search Strategy: EMBASE (1984-2004), MEDLINE (1966-2004), The Cochrane Central Register of Controlled Trials, The Cochrane Inflammatory Bowel Disease and Functional Bowel Disorders Group Specialized Trials Register and the Science Citation Index. Abstracts from the major gastrointestinal research meetings and references from published articles were also reviewed. **SELECTION CRITERIA:** Randomized controlled trials pertaining to children less than 18 years of age with Crohn's disease were selected. Those with growth as an outcome measure were included in the review. **DATA COLLECTION AND ANALYSIS:** Data extraction and assessment of the methodological quality of each trial was independently reviewed by two reviewers. Only one good quality randomized controlled trial was included in the review and therefore no statistical analysis was possible. **MAIN RESULTS:** Three randomized controlled trials were identified. One was of good methodological quality (Markowitz 2000). This study looked at the use of 6-mercaptopurine (6-MP) as a steroid sparing agent. No difference in linear growth was observed between the intervention and placebo groups, although the total steroid dose received over the 18 month follow up period was reduced in the group receiving 6-MP. The two remaining randomized controlled trials (Sanderson 1987; Thomas 1993a) consider the use of enteral feeding versus corticosteroids for induction of remission, with height velocity standard deviation score at 6 months as an outcome measure. Although of less rigorous methodological quality, the results of these studies are discussed in detail in the review. In both studies height velocity standard deviation scores were significantly increased in the enteral feeding group compared with the corticosteroid group. **AUTHORS' CONCLUSIONS:** In addition to these randomized controlled trials, a body of lower quality evidence does exist relevant to two other important interventions; the use of supplemental enteral nutrition (Morin 1980; Belli 1988; Israel 1995) and the judicious use of surgical interventions in pre-pubertal children with refractory disease (Alperstein 1985; Lipson 1990; McLain 1990). Newer treatments, such as infliximab, are now becoming more widely used and may offer advantages in promoting growth. These effects are as yet unstudied. This review highlights the need for large, multicentre studies of the different treatment options in pediatric Crohn's disease and the importance of standardized measurements of growth, such as height velocity standard deviation scores and height standard deviation scores as outcome measures.



## Synergy between immunosuppressive therapy and enteral nutrition in the management of childhood Crohn's disease

*JPEN J Parenter Enteral Nutr* 2005 Jul-Aug;29(4 suppl):S160-S165.

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Induction of a remission in children with Crohn's disease is increasingly successful. However this success is dependent on what measure we use to define "remission". Achieving a clinical remission is possible in >70% of children with Crohn's disease at diagnosis, while a mucosal or even immunological remission may occur in <50%. The importance of what "degree of remission" should be achieved during maintenance therapy is discussed. Does early aggressive management with immunomodulators or biological agents indeed alter the natural history of the disease, and is it possible to give a prognosis based on either a snap-shot of endoscopic appearance, or a mucosal cytokine profile? The potential benefits of using a 6-8 week course of exclusive enteral nutrition as an induction therapy in combination with azathioprine/6-mercaptopurine are discussed. Whole protein formulae are safe and effective at achieving a clinical remission, however they are not a long-term maintenance strategy. Given the relative safety of these immunosuppressants and their efficacy in children treated at diagnosis, it is now more important than ever to predict which individuals will benefit from use of immunomodulators very early in the disease process. There is brief mention of enteral nutrition as maintenance therapy. Given the very limited data available, it is still not possible to recommend long-term nutrition supplementation as a maintenance therapy in all children. However, some children may respond to repeated shorter cycles of exclusive enteral nutrition in the absence of other therapeutic options.

## The need for nutrition support teams in pediatric units: a commentary by the ESPGHAN Committee on Nutrition

*J Pediatr Gastroenterol Nutr* 2005 Jul;41(1):8-11.

Agostoni C, Axelson I, Colomb V, Goulet O, Koletzko B, Michaelsen KF, Puntis JW, Rigo J, Shamir R, Szajewska H, Turck D; ESPGHAN Committee on Nutrition; European Society for Paediatric Gastroenterology.  
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The reported prevalence of malnutrition in pediatric hospitals ranges from 15% to 30% of patients, with an impact on growth, morbidity and mortality. Major deficits in nutrition care have been highlighted in European hospitals, and the implementation of nutrition support teams (NSTs) has been suggested as a means to improve malnutrition diagnosis and nutrition care for hospitalized patients. This comment by the ESPGHAN Committee on Nutrition reviews disease-related mechanisms causing malnutrition and consequences of malnutrition and suggests a framework for implementation of NSTs in pediatric units. The recommendations by the Committee on Nutrition include: 1) Implementation of NSTs in hospitals is recommended to improve nutritional management of sick children; 2) The main tasks of the NST should include screening for nutritional risk, identification of patients who require nutritional support, provision of adequate nutritional management, education and training of

hospital staff and audit of practice; 3) The NST should be multidisciplinary, with expertise in all aspects of clinical nutrition care; 4) The funds needed to support NSTs should be raised from the healthcare system; and 5) Further research is needed to evaluate the effects of NSTs in prevention and management of pediatric nutritional disorders, including cost effectiveness in different settings.

## Enteral nutrition as primary therapy in childhood Crohn's disease: control of intestinal inflammation and anabolic response

*JPEN J Parenter Enteral Nutr* 2005 Jul-Aug;29(4 suppl):S151-S159.

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Crohn's disease in childhood is a chronic relapsing and remitting condition that can significantly impact normal growth and development. This influences choice of both initial and ongoing management. The goal of therapy is to induce and maintain remission with minimal side effects. Enteral nutrition is effective in active disease and will induce disease remission in most cases avoiding corticosteroid use. The high frequency of relapse means additional immunosuppressive therapies are usually required but nutrition remains a key priority as part of the subsequent management strategy.

## Long-term outcome of nutritional therapy in paediatric Crohn's disease

*Clin Nutr* 2005 Oct;24(5):775-779.

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**BACKGROUND & AIMS:** Long-term effects of using enteral feed therapy to induce remission in pediatric Crohn's disease are poorly documented. The aim of this study is to examine the short and long-term impact of enteral nutrition as primary therapy for children with newly diagnosed Crohn's disease. **METHODS:** Since 1994, a database was set up in Bristol for all children with inflammatory bowel diseases. The data of newly diagnosed patients with Crohn's disease in whom enteral nutrition was used as the primary therapy (44 children) was analyzed, with particular reference to time to remission, to first and subsequent relapse, and to first steroid usage. **RESULTS:** Forty out of 44 patients (90%) responded to enteral nutrition, with a median time to remission of 6 weeks. 25 of these 40 (62%) relapsed, with a median duration of remission of 54.5 weeks (range 4-312). 15 (38%) have not relapsed. 21 of the 44 (47%) have not received steroids. In those who eventually required steroids, their use was postponed for a median 68 weeks (range 6-190). Site of disease activity had no impact on response to enteral nutrition, but there was a trend towards earlier relapse in those with isolated colonic involvement. **CONCLUSIONS:** This data suggests that there are long-term benefits to the use of enteral nutrition to induce remission in children with Crohn's disease. Steroids may be avoided in nearly half the cases and, in others, their use postponed by 68 weeks.

## Effect of gastrostomy on growth in children with neurodevelopmental disabilities

*Can J Diet Pract Res* 2005 Spring;66(1):19-24.

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Chronic malnutrition and growth failure are frequent consequences of feeding difficulties in neurodevelopmentally disabled children. Gastrostomy feeding has been used successfully to alleviate chronic malnutrition as well as distress and frustration associated with feeding. Unfortunately, caregivers are often resistant to gastrostomy placement. In order to determine the impact of gastrostomies in 20 children with neurodevelopmental disability (NDD), a questionnaire was used to collect caregivers' perceptions both before and after gastrostomy. The questionnaire assessed caregivers' retrospective perceptions of quality of life, feeding difficulties, and the burdens and benefits of gastrostomies. To determine impact on growth, height and weight were measured once before and three times after gastrostomy (at six, 12, and 24 months). The number of times a child was fed and the amount of time spent feeding decreased significantly following gastrostomy ( $p < 0.001$  and  $p < 0.05$ , respectively). Growth for all children improved following gastrostomy ( $p < 0.001$ ). Pre-gastrostomy problems improved significantly following gastrostomy, as did caregivers' perceptions of quality of life for both themselves and their child ( $p < 0.001$ ). These results indicate that gastrostomy has a positive impact on growth for neurodevelopmentally disabled children, and on quality of life for both children and caregivers. Caregivers may find these results encouraging if they are faced with a decision about gastrostomy placement for their child.

## PRE- AND PROBIOTICS

### Bio-ecological control of acute pancreatitis: the role of enteral nutrition, pro and synbiotics

*Curr Opin Clin Nutr Metab Care* 2005 Sep;8(5):557-561.

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**PURPOSE OF REVIEW:** Increasing knowledge, both experimental and clinical, supports the fact that early and aggressive enteral nutrition has the capacity to reduce superinflammation and prevent infections in severe acute pancreatitis. Clearly, the main role of enteral nutrition is to boost the immune system, and not, at least initially, to provide calories. Whereas enteral nutrition improves, parenteral nutrition reduces immune functions. **RECENT FINDINGS:** The content of enteral nutrition solutions is more important than the route of administration per se. Antioxidants, plant fibres and live lactic acid bacteria are especially important for boosting the immune system. Recent studies support the fact that enteral nutrition and the supply of fibres and live lactic acid bacteria may significantly reduce the rate of infections. So far none of the

treatments has been able to reduce the incidence of the systemic inflammatory response syndrome and multiorgan dysfunction syndrome. A recent unpublished study indicates, however, that the systemic inflammatory response syndrome and multiorgan dysfunction syndrome can also be reduced if much higher doses of lactic acid bacteria and a combination of several bioactive lactic acid bacteria are used (synbiotics). **SUMMARY:** Immunosupporting enteral nutrition with synbiotics is an important tool to control superinflammation and infection, and might also reduce the multiorgan dysfunction syndrome and systemic inflammatory response syndrome. It is essential that it is supplied early, if possible in the emergency room. New autopositioning regurgitation-resistant feeding tubes are available to facilitate such a policy.

## PULMONARY DISEASE

### Optimizing oral nutritional drink supplementation in patients with chronic obstructive pulmonary disease

*Br J Nutr* 2005 Jun;93(6):965-971.

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Nutritional support is indicated in some patients with chronic obstructive pulmonary disease to restore nutritional status and improve functional capacity. However, the efficacy of nutritional supplements is sometimes disappointing, partly owing to a compensatory drop in habitual food intake. We retrospectively studied the effect of nutritional drink supplements, differing in portion size and energy content, on weight gain and body composition. Thirty-nine patients with stable chronic obstructive pulmonary disease, participating in an 8-week pulmonary rehabilitation program and eligible for nutritional support, were studied. Group A ( $n = 19$ ) received three portions of 125 mL (2,380 kJ), whereas group B ( $n = 20$ ) received three portions of 200 mL (3,350 kJ) daily. The macronutrient composition of the regimens was similar (20% protein, 60% carbohydrates and 20% fat). Lung function, body weight, body composition (by bio-electrical impedance analysis), habitual dietary intake (by dietary history) and resting energy expenditure (by ventilated hood) were determined. Weight gain was compared with expected weight as predicted by a computer simulation model. Although patients in both groups significantly increased in weight, this increase was higher in group A (A, 3.3 [sd 1.9] kg; B, 2.0 [sd 1.2] kg;  $p = 0.019$ ), while receiving less energy. The observed weight gain in group A was similar to that expected, but in group B it was lower than expected ( $p < 0.001$ ). In both groups, fat-free mass and fat mass were gained in a ratio of 2:1, fat-free mass increasing primarily during the first 4 weeks. This study illustrates that there might be an optimum for the portion size of nutritional drink supplements in chronic obstructive pulmonary disease and that more is not always better.

# Highlights of the 27<sup>th</sup> ESPEN Congress

European Society for Clinical Nutrition and Metabolism

27 – 30 August 2005  
Brussels, Belgium

## Glutathione metabolism in critical illness

F Hammarqvist, MD  
Sweden

Glutathione (GSH) is the body's principal scavenger of reactive oxygen species (ROS) and is used to reduce oxidative stress. GSH, a tripeptide of glutamate, cysteine and glycine, is found in the blood, muscle and liver, and in highest concentration in the duodenal mucosa. GSH acts with the enzyme glutathione peroxidase and the trace element selenium (Se) to neutralize ROS. Another enzyme, glutathione reductase, recycles the oxidized glutathione for further use.

Mitochondrial malfunction in critical illness was discussed throughout the congress, with a focus in this session on the inhibitory effects of ROS and the corresponding decrease in GSH production (Brealey D, et al. *Lancet* 2002;360:219-223). Lower GSH levels have also been measured in malnutrition and in Crohn's disease (CD).

A number of trials support the use of glutamine in attenuating post-traumatic GSH depletion. It was also noted that cysteine is a rate-limiting constituent of GSH. Compounds high in cysteine may enhance GSH synthesis and thereby decrease oxidative stress associated with cellular and organ damage.

## Life-saving effects of tight blood glucose control in the critically ill

G Van den Berghe, MD  
Belgium

Dr Van den Berghe shared the results of her latest randomized controlled trial (RCT), which assessed blood glucose (BG) control in surgical and medical intensive care unit (ICU) patients (n = 1,200). ICU and total hospital mortality rates were lower in patients with tight BG control (80-110 mg/dL) than those with poorer BG control (180-200 mg/dL).

A question was raised to ask whether the positive outcomes are due to decreased BG or increased insulin levels. Despite the contribution of both insulin and BG,

it appears that the reduction in BG is the more important factor.

Discussion followed about animal studies that have shown lactic acidosis develops when insulin drives large amounts of glucose from the blood into cells. This observation may support a need to limit overall carbohydrate intake to control BG levels and, ultimately, lower insulin requirements.

## The effects of severe chronic malnutrition and refeeding on metabolism, protein synthesis and digestive function

T Winter, MD  
USA

Research has shown that secretion of gastric acid and pancreatic enzymes is impaired in the severely undernourished, as well as those with malnutrition secondary to CD (Winter TA, et al. *Inflamm Bowel Dis* 2004;10:618-625; Winter TA, et al. *Nutrition* 2001;17:230-235). Severe chronic malnutrition also decreases gastrointestinal (GI) motility and increases intestinal permeability. In the severely malnourished, refeeding has a trophic effect on the gut and resolves pancreatic atrophy. Successful refeeding has been observed in patients given semi-elemental diets for 1-2 weeks, with subsequent transition to polymeric feeds. People with malnutrition secondary to anorexia are a notable exception, as it appears that protein synthesis and intestinal permeability are not impacted in these patients as is the case in severe chronic malnutrition.

## Physiological response of the pancreas to enteral and parenteral nutrition

S O'Keefe, MD  
USA

Several studies in healthy volunteers examined the effect of different enteral formulations and total parenteral nutrition

(TPN) on pancreatic secretion. TPN did not stimulate the pancreas, while elemental formula fed orally or duodenally decreased pancreatic secretion by 50% compared with a standard whole protein formula. An additional study in 8 healthy volunteers (Vu MK, et al. *Eur J Clin Invest* 1999;29:1053-1059) showed that placing the feeding tube 40 cm distal to the ligament of Treitz was most effective in avoiding pancreatic stimulation. Mid-distal jejunal feeding tube placement in severe acute pancreatitis is feasible, even in those with ileus (Kaushik N, et al. *Pancreas* 2005 [in press]). However, there are conflicting views as to the correct position of the tip of the feeding tube for patients with severe acute pancreatitis. Dr O'Keefe challenged a recent study in patients with pancreatitis (Eatock FC, et al. *Am J Gastroenterol* 2005;100:432-439) that found no difference between feeding via the nasogastric vs the nasojejunal route. Dr O'Keefe questioned the conclusions of the study, suggesting that the data reflect an inconsistent use of feeding tubes that are small enough to be placed jejunally.

## Diet therapy and pharmacological therapy in chronic intestinal failure

B Messing, MD  
France

Patients with intestinal failure may be classified into one of two groups: those with a jejunostomy and those with a preserved colon. Absorptive adaptation is more likely to occur in the latter group, although both are dependent upon the length of the remaining small intestine. Recommended nutritional intervention for both groups includes hyperphagia ( $>1.5 \times$  resting energy expenditure [REE]) (Crenn P, et al. *Gut* 2004;53:1279-1286), a low oxalate diet, and the following dietary recommendations:

JEJUNOSTOMY	JEJUNO-COLON ANASTOMOSIS
Avoid hyperosmolar liquids	Avoid liquid intake outside of meal times
Fat not restricted	Restrict fat to $<33\%$ of total Kcal and utilize medium-chain triglycerides (MCT)

A study done by Joly F, et al, compared a standard oral diet, tube feeding (TF) and a combination of TF and oral diet, which were given for 7 days. The combination of TF and oral diet resulted in a 20% increase in measured absorption (proteins and lipids,  $p < 0.001$ ) relative to oral diet alone.

Pharmacological interventions concentrate on supplementing hormonal peptides that regulate motility. After short bowel resection, physiological adaptive processes and pharmacological therapy can be optimized only in the absence of malnutrition.

## Pre- and probiotics before and after liver transplantation

N Rayes, MD  
Germany

A recent, prospective, randomized, double-blind trial (Rayes N, et al. *Am J Transplant* 2005;5:125-130) compared the effect of two enteral nutrition (EN) formulas on the incidence of postoperative bacterial infections after liver transplant ( $n = 66$ ). One group of patients received four lactic acid bacteria (LAB) in combination with four fibers (beta-glucan, inulin, pectin and resistant starch), while the second group received only the addition of supplemental fibers. Treatment was commenced the day before surgery and continued for 14 days. Thirty-day infection rate, length of stay (LOS), duration of antibiotic therapy, non-infectious complications and side effects of EN were recorded. The infection rates were markedly different between groups; the incidence was 48% in those receiving fibers alone compared with 3% in those receiving LABs and fibers. However, the infections were considered mainly mild or moderate across groups, with a large percentage of urinary tract infections (UTIs). The duration of antibiotic therapy was significantly shorter in the group receiving LABs and fibers.

It was concluded that early EN combined with prebiotic fibers was associated with a low incidence of severe infections and may have a protective effect. Early EN with both LABs and fibers was found to reduce bacterial infection rates following liver transplantation. A possible mechanism for the protective effects of prebiotic fiber is the associated bifidogenic effect on healthy gut microbiota and supplemented probiotic bacteria. LABs are also known to induce heat-shock proteins (HSP).

The question of the safety of using probiotics in immunocompromised patients was raised. Dr Rayes noted one positive blood culture associated with the use of probiotics in the study, but it did not have clinical consequences for the patient.

## Glutamine: role of heat-shock protein expression

P Wischmeyer, MD  
USA

HSPs are a family of highly conserved proteins that are present in all cells. HSPs are induced by a variety of stressors, and serve to stabilize cells and prevent cell death. Data were presented that showed pharmacological doses of alanyl-glutamine are associated with enhanced HSP expression in both cellular media and in animal models. Earlier induction of HSP may help to better attenuate end-organ injury related to trauma or stress. Enhanced pulmonary HSP expression is associated with a lessening of sepsis/systemic inflammatory response syndrome (SIRS), lung injury and intestinal epithelial cell injury. New data were presented from a 7-day study in critically ill patients given pharmacological doses of intravenous (IV) alanyl-glutamine that showed a 4-fold increase in HSP, and a decrease in LOS and time on the ventilator.

In the future, HSPs may be a useful marker to study outcomes in critically ill patients.



## Nestlé Nutrition Institute Satellite Symposium – Wound Healing: Does Nutrition Make a Difference?

### Wound physiology overview

L Télet, MD, PhD  
France

The complex aspects of the normal wound healing process were reviewed, with an emphasis on growth factors that spur the cascade of intracellular reactions that result in the synthesis of collagen. One such growth factor, nerve growth factor, is important in nerve development following angiogenesis that occurs with normal wound healing. A deficiency in this growth factor is considered one explanation for the impaired wound healing that occurs in patients with spinal cord injury. Under normal conditions, healing is promoted by neuropeptides that are released from newly generated nerve endings.

In addition to malnutrition, a number of other barriers to normal wound healing that may be present in patients were described:

- Necrotic tissue
- Infection
- Age, neurological status and general physical condition
- Pressure as a causal factor
- Local treatment, ie, type of dressings

While evidence-based medicine is ideal, RCTs in this field are prohibitively expensive, and would require too large a number of patients to be conducted within Western Europe. Thus, nutritional guidelines, based on smaller studies and meta-analyses, were discussed as a compromise to scientifically support the role of nutrition in wound healing and to scientifically evaluate the most appropriate practice.

### The role of nutrition in wound healing

C Collins, SRD  
United Kingdom

Independent risk factors for impaired wound healing include presence of infection, inadequate tissue perfusion, older age, poor glycemic control and suboptimal nutrition. The National Pressure Ulcer Long-Term Care Study (Horn SD, et al. *J Am Geriatr Soc* 2004;53:359-367) retrospectively evaluated 1,524 nursing home residents and found that the incidence of pressure ulcer (PU) was 29%. Furthermore, the risk of PU was increased by 74% and 42% in those with involuntary weight loss and dehydration, respectively. Disease-specific and high protein/energy TE, as well as oral nutritional supplements (ONS), statistically significantly lowered the risk of PU.

A range of nutrients can help to improve wound healing, and data were presented on the role of supplemental vitamin C. While an RCT (ter Riet G, et al. *J Clin Epidemiol* 1995;48:1453-1460) demonstrated no difference in pressure sore wound healing between patients receiving vitamin C supplements of 1,000 mg or 20 mg, the results have more

recently been disputed because the wound dressings used in this study disrupted the granulation process, making any differences in healing unobservable.

The need to critically review research on micronutrient supplementation and wound healing was emphasized. Studies show that healing is impaired in patients with micronutrient deficiencies, but limited data are available supporting the benefit of supplementation beyond 100% of normal requirements. In practical terms, the challenge is to determine which patients are most at risk of deficiency and then implement supplementation as early as possible within current guidelines.

### Pressure ulcers: How big is the problem?

M Clark, PhD  
United Kingdom

A recent pilot study from the European Pressure Ulcer Advisory Panel (EPUAP) looked at PU prevalence in hospitals across five European countries and found that 20% of patients may experience some form of pressure lesion or injury.

Data on cost is difficult to obtain, as there is little data outside the acute sector. Within the acute sector, Stage I PUs are not always recorded. An ongoing study of the EPUAP may concentrate on identifying Stage II, III and IV PU, all of which involve a wound with broken skin. Stage I does not involve broken skin and, thus, would be excluded.

Cost data from the United Kingdom (UK) in 2004 predicts the cost of treatment for each Stage IV PU to be £10,551 (US \$19,427) and data from Allman RM and colleagues (*Adv Wound Care* 1999;12:22-30) showed large increases in cost associated with a longer LOS for patients with PU. In general, up to 4% of Western healthcare budgets are currently spent on the treatment and complications of PU.

### Can enteral nutrition prevent and treat pressure ulcers?

RJ Stratton, PhD  
United Kingdom

A recent meta-analysis (Stratton RJ, et al. *Ageing Res Rev* 2005;4:422-450) of 15 studies involving patients on TE, ONS or a combination of the two (n = 3,216) considered two questions:

- Can EN decrease the incidence of PU?
- Can EN improve healing of PU?

It was concluded that high protein EN could reduce the risk of developing PU by 25% in those at high risk compared with those receiving routine care (odds ratio 0.75, 95% confidence interval [CI] 0.62-0.89). Proposed mechanisms for the role of improved nutrition in preventing PU include:

- Increased soft tissue padding
- Increased well-being and energy
- Improved skin condition from increased blood flow associated with the use of arginine
- Decrease in other treatments needed

EN may also improve PU healing (Benati G, et al. *Arch Gerontol Geriatr Suppl* 2001;7:43-47). However, the number of RCTs on this subject is presently inadequate. Thus, the current meta-analysis could not definitively address this question.

## Is there evidence for enteral nutrition in cancer patients?

G Nitenberg, MD  
France

A recent meta-analysis of 62 studies involving the use of EN or PN in cancer patients addressed two questions:

- Is EN better than PN in cancer patients?
- Does supplementation with eicosapentaenoic acid (EPA) show benefit?

Studies were categorized according to three patient populations:

- Radiation/chemotherapy/bone marrow transplant (BMT)
- Cancer surgery
- Palliative care

No studies utilizing IEDs (immune-enhancing diets) were included.

Although there were no significant differences in survival, it was concluded that EN vs PN in cancer surgery patients was associated with:

- Decreased hospital LOS by 1.72 days (95% CI 0.9-2.8)
- Reduced incidence of infectious complications
- Lower sepsis scores

There was some discussion about the comparative PN studies being dated and perhaps reflective of practice that is now classified as overfeeding.

Analysis of three RCTs in radiation/chemotherapy/BMT patients showed an improvement in energy intake (381 Kcal/d) with the use of ONS. Conclusions could not be drawn on the use of EN vs PN in either this or the palliative care population, as insufficient RCTs exist. The same was true regarding EPA supplementation in cancer patients. It was noted that certain patient populations, often those of greatest concern, are often excluded from studies and that data from RCTs is only one component of the relevant information that must be evaluated to determine appropriate management in these patients.

## Scientific Abstracts

### Systematic review and meta-analysis of the effects of standard versus diabetes-specific enteral formulas for patients with diabetes mellitus

Stratton RJ, Ceriello A, Laube H, et al.  
United Kingdom

A systematic review was undertaken to investigate the effects of standard enteral formulas compared with diabetes-specific enteral formulas given orally or via tube in patients with type 1 or 2 diabetes. The review identified 20 studies (n = 744) of which 14 (n = 437) compared ONS and 6 (n = 307)

compared enteral TF formulas. Meta-analyses were performed, where possible, to measure the following outcomes: BG, blood lipids, medication requirements and complications.

Diabetes-specific formulas significantly reduced postprandial rise in BG, peak BG concentration and glucose area under the curve compared with standard formulas. No significant differences were noted in fasting glucose, high-density lipoprotein (HDL), low-density lipoprotein (LDL), total cholesterol or triglyceride concentrations.

The use of diabetes-specific enteral oral supplements and TF can improve glycemic control compared with standard supplements and TF. Accordingly, diabetes-specific enteral oral supplements and TF may assist management and improve outcomes in patients with diabetes.

### If the gut works, use it! But how well does it work? A study on malabsorption in the ICU

Wierdsma NJ, Van Heijningen EB, De Groot SDW, et al.  
The Netherlands

This pilot study evaluated energy loss via feces collected from stable, fully enterally-fed ICU patients (n = 13) with loose stools. Stools were collected for 3 days; the energy value was determined using bomb calorimetry and fecal fat content was also analyzed. The total amount of TF during the 3-day collection period was recorded, and energy expenditure was measured by indirect calorimetry. Malabsorption was arbitrarily defined as an energy absorption capacity of 85% or less.

Mean energy absorption capacity was found to be  $84 \pm 14\%$ . Forty-six percent of subjects met the criteria to be considered malabsorbers. Mean fecal fat loss was  $8.0 \pm 8.3$  g/d, resulting in a mean fat absorption capacity of  $90 \pm 16\%$ . A daily fecal output of  $>250$  g was a good predictor of malabsorption.

Malabsorption contributed to negative energy balances in 30% of patients, and is a previously unrecognized, but significant, problem in ICU patients with loose stools.

### Selenium supplements reduce the incidence of nosocomial pneumonia after major burns

Berger MM, Eggimann P, Revelly JP, et al.  
Switzerland

A previous trial in 20 patients found that the incidence of pneumonia was lower when Se, copper (Cu) and zinc (Zn) supplements were provided for 8 days after major burns. The present study examined the same outcome, but in a larger patient population (n = 41, Body Surface Area Burn [BSAB] =  $46 \pm 19\%$ ). Two consecutive prospective, randomized, placebo-controlled trials delivered Cu  $59 \mu\text{mol}$ , Se  $4.8 \mu\text{mol}$  (370 mg) and Zn  $574 \mu\text{mol}$ , or placebo IV for 8-21 days depending on burn size.

Data were collected over 30 days and showed plasma Se and glutathione peroxidase concentrations were significantly higher in the supplemented group (TE) after day 5.

The total number of infectious complications was lower in the TE group (2.0 vs 3.5 episodes,  $p = 0.0002$ ) as were the number of cases of pneumonia (0.6 vs 1.7 episodes,  $p = 0.0005$ ). Trace element supplementation was associated with a 30% risk of developing nosocomial pneumonia over a 30-day period compared with a risk of 80% in the placebo group. The length of ICU stay per % BSAB was also shorter in the TE group (0.64 vs 1.03 days/%,  $p = 0.008$ ).

Trace element supplements, including Se, were associated with a significant reduction in the incidence of nosocomial pneumonia and duration of ICU stay. The authors concluded that a possible mechanism is the reinforcement of antioxidant defenses by the trace elements.

### Plasma amino acid profiles in critically ill children: Relationship with underlying disorder and severity of inflammation

Waardenburg DA, Luiking YC, Deutz NEP, et al.  
The Netherlands

This study aimed to investigate changes in arterial amino acid (AA) profiles in children (aged 3 months to 16 years,  $n = 60$ ) admitted to the pediatric ICU with a variety of acute conditions: sepsis, trauma, major surgery and viral airway disease. Plasma AA levels were studied in the fasted state and within 24 hours of admission.

Glutamine, arginine and citrulline levels were lower while phenylalanine levels were higher in children with sepsis and trauma compared with those with viral disease. C-reactive protein (CRP) levels were significantly negatively correlated with total AA levels, plasma glutamine ( $p < 0.001$ ), citrulline ( $p < 0.001$ ) and arginine ( $p < 0.001$ ).

It was concluded that critical illness in children is associated with low arterial AA concentrations. The severity of inflammation, as defined by CRP and underlying acute illness, rather than severity of illness per se was correlated with alterations in plasma glutamine, arginine, citrulline and phenylalanine levels.

### Continuous L-arginine infusion does not cause deterioration in the hemodynamic condition of patients with severe sepsis

Luiking YC, Poeze M, Hendriks M, et al.  
The Netherlands

Arginine is the precursor of nitric oxide, a known vasodilator. Although patients with sepsis have reduced plasma arginine levels, use of arginine in this population has been of concern because of the vasodilatory properties of nitric oxide. This study was performed to measure the dose-response of continuous intravenous arginine supplementation in patients with severe sepsis.

Eight ICU patients who had severe sepsis/septic shock (APACHE II scores 27-43) for less than 48 hours were studied. Norepinephrine dose ranged between 0.05 and 0.8  $\mu\text{g/kg/min}$ . Arginine levels were measured at baseline

and every 2 hours as the dose of IV arginine was increased in a step-wise fashion (0.6, 1.2 and 1.8  $\mu\text{mol/kg/min}$ ). Hemodynamics were recorded at 30-minute intervals.

No significant changes in systemic blood pressure were observed, while arginine levels were found to be significantly lower ( $p < 0.05$ ) than those of healthy age-matched controls. Heart rate decreased and stroke volume increased during arginine supplementation.

The authors concluded that arginine infusion does not affect blood pressure, but increases cardiac stroke volume. Continuous IV arginine supplementation was not associated with deterioration in hemodynamics in patients with severe sepsis, despite its vasodilatory effect.

### Reduced circulating TNF receptor p75 after enriching enteral nutrition with glutamine and antioxidants following major upper GI surgery

Boelens PG, Melis GC, Diks J, et al.  
The Netherlands

This study evaluated the effect of EN enriched with glutamine and antioxidants on inflammatory markers following major upper GI surgery ( $n = 20$ ). All patients had undergone surgery for at least 3 hours and were fed postoperatively via jejunostomy with either standard EN (Sondalis ISO) or EN enriched with glutamine, cysteine, Zn, Se,  $\alpha$ -tocopherol,  $\beta$ -carotene and vitamin C. CRP, interleukin (IL)-6, IL-1, IL-8 and soluble tumor necrosis factor (TNF) receptor p75 were measured before surgery and postoperatively on days 1, 3, 5 and 7.

CRP levels were lower in the first 5 and 7 days in patients receiving enriched EN ( $p = 0.084$ ). Soluble TNF receptor p75 decreased significantly in the first 3 days ( $p < 0.05$ ), with a trend for a reduction in the first 5 days ( $p = 0.072$ ). IL-1 and IL-6 levels were not significantly different between groups.

EN enriched with glutamine and antioxidants blunted the inflammatory response in patients after major GI surgery.

### Protein undernutrition in quiescent Crohn's disease: An unrecognized problem?

Suibhne Nic T, O'Morain C, O'Sullivan M, et al.  
Ireland

Undernutrition may be well studied in active CD, but the problem is poorly defined in patients who are in remission. This study examined the nature and prevalence of malnutrition in non-hospitalized CD patients ( $n = 70$ ) vs healthy controls ( $n = 23$ ). Protein stores were measured by midarm muscle circumference (MAMC) and grip strength (GS), and fat stores by triceps skin-fold thickness (TSF). Undernutrition was defined as MAMC and TSF  $< 15^{\text{th}}$  centile, GS  $<$  population standard and BMI (body mass index)  $< 20 \text{ kg/m}^2$ . Remission was defined as a Crohn's Disease Activity Index (CDAI)  $< 150$ .

Low MAMC and GS values were significantly more prevalent in CD compared with controls. Additional study of the CD participants with factors suggestive of muscle depletion found the majority had normal BMI, serum albumin and fat stores.

The data suggest a 47% prevalence of undetected muscle protein depletion among CD patients in remission with normal BMI.

## High prevalence of sarcopenia in patients with Crohn's disease: Association with osteopenia

Al-Jaouni R, Filippi J, Wiroth J, et al.  
France

The presence of sarcopenia and an association between sarcopenia and osteopenia were examined in adult patients ( $37 \pm 13$  years) with CD in remission ( $n = 67$ ) and healthy volunteers ( $n = 39$ ). CD patients had a CDAI  $<150$  and CRP  $<10$  mg/L. Appendicular muscle mass (AMM) and bone mineral density (BMD) were measured using DEXA (Hologic) and osteopenia assessed according to the World Health Organization (WHO) classification.

AMM was lower in CD patients than controls ( $p = 0.02$ ) and a positive correlation was found between AMM and BMD ( $r = 0.50$ ;  $p = 0.0001$ ). The prevalence of sarcopenia was 61% in patients and 20% in controls ( $p < 0.001$ ), while prevalence of osteopenia was 30% in patients and 5% in controls. Further, the prevalence of osteopenia was 43% in patients with sarcopenia, and 8% in patients without sarcopenia ( $p < 0.001$ ).

Sarcopenia is strongly associated with osteopenia and the prevalence of sarcopenia is high in patients with CD. These two phenomena may have synergistic deleterious effects and may share similar mechanisms. Findings suggest that the routine determination of BMD and AMM may be helpful in CD patients.

## Energy intake of hospitalized elderly people according to nutritional status

Hengstermann S, Nagel A, Azzaro M, et al.  
Germany

The aim of this study was to evaluate energy intake both in malnourished elderly patients with multiple comorbidities as well as those at risk of malnutrition ( $n = 232$ ). Three-day nutritional intakes were recorded and nutritional status was assessed with Mini Nutritional Assessment (MNA®), BMI, bioelectrical impedance analysis (BIA), GS and laboratory tests.

Daily energy intake was significantly lower than the recommended intake of 25 Kcal/kg ( $p = 0.001$ ).

This geriatric institution found that energy intake of elderly persons was 62% lower than recommended, highlighting the importance of considering nutritional supplementation to prevent the consequences of malnutrition.

## Mini Nutritional Assessment (MNA®): Preferable nutritional assessment tool

Hengstermann S, Nagel A, Azzaro M, et al  
Germany

The aim of this study was to identify a rapid and efficient assessment tool to diagnose malnutrition in geriatric institutions. Three established assessment tools (MNA®, subjective global assessment [SGA] and the malnutrition universal screening tool [MUST]) were compared in geriatric patients with multiple comorbidities ( $n = 520$ ). BMI and BIA were also assessed.

The most efficient assessment tool was found to be the MNA®, which was subsequently modified and termed the M-MNA®.

The MNA® was comparable to the M-MNA® and identified 11% of patients as well nourished, 76% with a risk of malnutrition and 13% malnourished. In comparison, the SGA found 42% well nourished and 5% malnourished while the MUST indicated the highest proportion of malnutrition (43%).

The MNA® was found to be the most sensitive parameter to identify malnutrition due to dietary issues, mobility and dementia.

## A cost-benefit analysis of oral nutritional supplements in preventing pressure ulcers in hospital

Elia M, Stratton RJ.  
United Kingdom

A systematic review of four RCTs examining the effect of liquid ONS (200-400 mL/d; 1-1.5 Kcal/mL, 2-26 weeks) on the incidence of PUs in high-risk hospitalized elderly patients was performed to conduct a cost-benefit analysis. A 25% increase in PU incidence was found in controls (39%;  $n = 712$ ) compared with ONS patients (32%;  $n = 613$ ). However, information on the stage of PU was lacking, and the cost analysis used full hospital costs from the UK for each PU stage (£1,064, £4,402, £7,313 and £10,551 for Stages I, II, III and IV, respectively.) The ONS cost was also based on UK hospital practice (£0.20/200 mL).

A net cost saving in favor of ONS was observed for all stages of PU; however, these cost savings were only statistically significant for Stage III ( $p = 0.04$ ) and IV ( $p = 0.04$ ) PU. This corresponds to a net cost saving of £5 (Stage I) to £460 (Stage IV) per patient, suggesting that use of ONS in older patients at high risk of PU produces a net cost-benefit, the magnitude of which depends on the stage of ulcer.

*The views expressed in this newsletter are of the presenters and participants, not Nestlé.*

**The next ESPEN congress will be held from 25-28 August 2006 in Istanbul, Turkey. Further information may be found at [www.espen.org](http://www.espen.org).**



## Conference Calendar

### **British Association for Parenteral and Enteral Nutrition (BAPEN)**

16-17 November 2005  
Telford, United Kingdom

Organizer:

Sovereign Conference  
Tel: +44 (0) 1527 518 777  
Fax: +44 (0) 1527 518 718  
E-mail: enquiries@sovereignconference.co.uk  
Web site: www.bapen.org.uk

### **3<sup>rd</sup> Cachexia Conference**

8-10 December 2005  
Rome, Italy

Organizer:

LMS Group  
Tel: +33 1 4253 0303  
Fax: +33 1 4253 0302  
E-mail: info@lms-group.com  
Web site: www.cachexia.org

### **35<sup>th</sup> Critical Care Congress**

7-11 January 2006  
San Francisco, California, USA

Organizer:

Society of Critical Care Medicine  
Tel: +1 847 827 6888  
Fax: +1 847 827 6886  
E-mail: info@sccm.org  
Web site: www.sccm.org

### **International Symposium on Obesity in the Elderly**

26-28 January 2006  
Rome, Italy

Organizer:

Organizing Secretariat FASI  
Tel: +39 06 9760 5610  
Fax: +39 06 841 4495  
E-mail: info@fasiweb.com  
Web site: w3.uniroma1.it/scialim/e\_index.html

### **Clinical Nutrition Week**

12-15 February 2006  
Dallas, Texas, USA

Organizer:

American Society for Parenteral and Enteral Nutrition  
Tel: +1 301 587 6315  
E-mail: aspen@nutr.org  
Web site: www.nutritionweek.org

### **27<sup>th</sup> American Overseas Dietetic Association Conference**

23-25 March 2006  
Dublin, Ireland

Organizer:

Conference Partners Ltd.  
Tel: +353 1 667 7188  
Fax: +353 1 664 3701  
E-mail: sinead@conferencepartners.ie  
Web site: www.eatrightoverseas.org/AODA

### **15<sup>th</sup> Chinese International Symposium for PN and EN (CISPEN)**

4-7 April 2006  
Macau, China

Contact:

E-mail: jiangzm@ms.imicams.ac.cn

### **4<sup>th</sup> Asian Congress of Dietetics**

23-26 April 2006  
Manila, Philippines

Organizer:

Nutritionist-Dietitians' Association of the Philippines  
Tel: +63 2 845 1651  
Fax: +63 2 753 3598  
E-mail: ndap@i-next.net  
Web site: www.asiancongressofdietetics.com

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