Immunonutrition/pharmaconutrition

In this dynamic field of nutrition research, Prof P Déchelotte indicated that despite following the basics of nutrition support after injury, namely timely, appropriate route, and meeting nutrient requirements, some nutrients may play a beneficial role, in pharmacological quantities, by preserving lean body mass, reducing intestinal permeability, enhancing the immune response, reducing nosocomial infections, reducing length of stay (LOS) and costs, and ultimately reducing mortality in both malnourished and well-nourished patients.

Formulae enriched with n-3 fatty acids, arginine and nucleotides resulted in a significant reduction in LOS and infectious complications in surgical GI cancer patients. The data in head and neck surgical cancer patients is still controversial while the data in cardiac surgical patients require confirmation (Prof P Déchelotte).

In the same lecture Prof P Déchelotte summarised the advantages of glutamine in critically ill patients. Glutamine supplemented total parenteral nutrition (TPN) has been shown to be beneficial after major surgery for cancer in terms of LOS and infectious complications. Intravenous glutamine supplementation results in better outcomes after bone-marrow transplant, but the use of enteral glutamine in this patient population is still controversial. Glutamine supplemented TPN also reduced 6-month mortality in severely ill ICU patients. Indeed the available meta-analytic evidence indicated a significant reduction in mortality with intravenous glutamine in critically ill patients. Both enteral and parenteral glutamine have benefits in the burns patient namely reduced Gram negative bacteraemia, mortality, infectious morbidity. The results with enteral glutamine supplementation in mixed intensive care unit (ICU) populations ranged from no benefit to similar benefits as those documented for parenteral glutamine.

Both Prof Kreymann and Prof Laviano pointed out the advantages of the new lipid emulsion containing olive oil and/or fish oil in immune modulation. On the basis of the available evidence on the metabolic effects of lipid emulsions, it is now tempting to speculate if their use as “drugs” could provide an adequate amount of immunomodulating fatty acids on top of the calculated energy needs. In this context, omega-9 fatty acids could be provided as the energy source because of their “immuno-neutrality”, while omega-3 and omega-6 fatty acids could be provided as metabolic modulators. It was acknowledged that the available literature cannot yet support this approach, but it can also not be denied that such an approach would favourably exploit the potential clinical benefit of lipid emulsions. While waiting for clinical trials addressing the feasibility and relevance of this approach, it is important to be reminded that in matters concerning lipid emulsions “one size may not fit all (patients)”. 

Dr S Chetty highlighted the various potential benefits of arginine supplementation including, enhanced protein metabolism, improved microcirculation and organ function, enhanced immune and gut function , apart from its antioxidant role. He reiterated though that the safety of arginine supplementation during sepsis is still uncertain.

Ms J Visser drew attention to the association of critical illness with increased ROS production and low circulating levels of most antioxidant micronutrients. Although micronutrient supplementation in critical illness is thought to be beneficial, by providing basic requirements, preventing and correcting deficiences and modulating the acute phase and immune responses and reinforcing endogenous AO defences, uncertainty exists with regards to exact benefits, exact requirements, doses, route and timing as well as safety of such a practice. Meta-analytically, a significant reduction in overall mortality and 28-day mortality with micronutrient supplementation, but no effect on hospital mortality, ICU mortality or infectious complications was shown. Single, as well as cocktail supplements, had no effect on mortality. The review did not find a benefit of parenteral over enteral supplementation and highlighted the necessity of large randomised multicentre trials, as well as the necessity to assess the benefits in specific populations.

Clinical practice guidelines

During the last four years the The American Society of Enteral and Parenteral Nutrition (ASPEN), the European Society for Clinical Nutrition and Metabolism (ESPEN) and the Canadian Critical Care Clinical Practice Guidelines Committee (CCPG) practice guidelines were published. The guidelines are in agreement on most points with regards to the nutritional support of critically ill patients. Prof G Kreymann pointed out that the most important controversies concerned indications for parenteral nutrition in non-malnourished patients, supplemental parenteral nutrition and the use of lipids during the first week of TPN as part of the mixture. There are also smaller differences in recommendations with regards to fibre containing formulae in critically ill patients and supplementation of antioxidants.

The metabolic syndrome, blood glucose control and specialised enteral products for the diabetic patient

Ms A Till discussed the current controversy on the relevance of identifying the metabolic syndrome, a complex of interrelated risk factors for cardiovascular disease (CVD) and diabetes, and concluded that the primary advantage was the early identification of patients at risk for CVD and diabetes. Lifestyle and diet changes remain the mainstay of the treatment for the metabolic syndrome. More emphasis needs to be placed on diet quality and the intake of micronutrients, particularly those with antioxidant properties.
Prof R Blaauw discussed the role of specialised diabetic enteral products which are associated with better glycaemic control than standard products and their potential to reduce diabetic complications in the long-term. However, Prof Blaauw pointed out that in the critically ill patient there may be other considerations, such as the fibre content of the diabetes-specific products that may be contra-indicated, and concluded that in the critically ill patient the choice to use such specialised diabetic enteral products needs to be based on the individual situation and current condition of the patient.

Ms A Prins addressed the complex question whether tight glucose control improves morbidity and mortality in critically ill patients and concluded that the current controversy arising from the recent clinical trials could be attributed to differences in methodology and heterogeneous patient populations as well as the major obstacle, namely the increased risk for hypoglycaemia. Most of the recent guidelines suggest maintaining blood glucose between 7.7 and 9.9 mmol/L. It may well be that it is more important to avoid glucose variability than adhering to a strict control range. Other questions that still need to be addressed include timing and the effect of insulin per se versus blood glucose control.

Malnutrition and diarrhoea

Prof D Labadarios presented the emerging evidence and approach on the need to arrive at an aetiology-based definition of the diagnosis of malnutrition. Such an approach would include the patient’s nutritional risk and the influence of the presence/absence of inflammation, leading to three clinical states, namely marasmus, cachexia or protein-energy undernutrition. Although this approach needs further refinements, it has nevertheless been sufficiently developed to warrant the use of the currently proposed terminology, namely starvation-related malnutrition (SRM): chronic starvation without inflammation; chronic disease related malnutrition (CDRM): chronic inflammation of mild to moderate degree; and acute disease (or injury) related malnutrition (ADRM): acute inflammation of severe degree.

Ms C Schübl discussed the difficulties in addressing malnutrition to meet the Millennium Development Goals (MDG). Achievement of these goals has been varied, with some countries in sub-Saharan Africa actually recording an increased number of children who are underweight. South Africa is one of the countries where stunting prevalence has not decreased and an increased trend since 1990 in the mortality of children under the age of five years has been reported. In order to address the MDGs, Ms Schübl concluded, it is essential that malnutrition is addressed at the international and national levels.

Dr ED Nel referred to the well known association between diarrhoea and malnutrition and its detrimental effect on nutritional status. Dr Nel pointed out that there is actually little evidence to substantiate the hypothesis. Intake, absorption and digestion, nutrient losses and the inflammatory response are some of the factors that are thought to contribute to the detrimental effect of diarrhoea on nutritional status. Lactose and fat malabsorption are common complications in HIV infected children with diarrhoeal disease. Dr Nel recommended that the guidelines for the management of malnourished patients with diarrhoea should include: feeds should only be interrupted to correct severe dehydration and shock; diluted, low volume feeds are not necessary; and specialised feeds are indicated in malabsorption, such as lactose intolerance. Zinc supplementation may reduce severity and duration of diarrhoea and although preventive vitamin A supplementation reduce the number of severe episodes of diarrhoea, there was little evidence that supplementation was of any benefit once children already had diarrhoea. Glutamine and arginine supplementation were not well established in the management of acute infectious diarrhoea.

Diarrhoea remains a major cause of death in developing countries, and Dr ML Cooke highlighted its causes and prevention measures. Oral rehydration fluids (ORS) are the first line of management for gastro rather than intravenous fluids. Rice-based ORS are only effective in cholera, while there is improved efficacy of amylase-resistant starch or combinations with guar-gum, mixed non-digestible carbohydrates, probiotics, zinc and glutamine. The nutritional management of diarrhoeal disease includes: continue breastfeeding at all times, continue with normal foods in uncomplicated gastroenteritis within four hours, do not dilute products, no benefit of gradual reintroduction of formula or for special formula like soy or lactose-free formula, avoid beverages with a high sugar content and an extra meal a day for at least a week following the episode to allow for catch-up growth. Zinc supplementation reduces the severity and duration of acute as well as persistent diarrhoea. Probiotics are a useful adjunct in the treatment of diarrhoea, particularly Lactobacillus GG and Saccharomyces boulardii based products.

Intestinal failure and post-transplant nutrition support

Prof O Goulet discussed the causes of intestinal failure, namely short bowel syndrome (SBS), intestinal motility disorders and congenital enteropathies. Home parenteral nutrition was the mainstay of the treatment since very few patients received an intestinal transplant. Liver disease is a concern in these diseases due to factors related to the disease itself as well as TPN. Hepatic dysfunction can be ameliorated by the prevention and treatment of infections, prevention of bacterial overgrowth, improvement of digestive function, minimal/maximal oral or enteral feeding, balanced cyclic protein supply, use of paediatric amino acid solutions, appropriate use of lipid emulsions and early cyclic parenteral nutrition as well as by preventing excessive glucose intake. The use of fish oil can reverse Parenteral Nutrition Associated Liver Disease (PNALD) by providing less pro-inflammatory n-6 fatty acids in favour of the beneficial effects of n-3 fatty acids and the increased content of α-tocopherol. The new generation lipid emulsions containing fish oil as part of the fat supply as well as the amount of lipid supplied are known to influence the occurrence of PNALD.

Prof Goulet also pointed out that paediatric Crohn's disease results in growth failure in 30–70% of cases and the mechanism(s) underlying growth failure was multifactorial. Enteral nutrition or special formulae containing Transforming Growth Factor-beta (TGF-β) may control the disease activity by inducing remission and maintaining remission, through anabolic and metabolic responses and by manipulating the intestinal microbiota.
Although there is a paucity of data on nutrition post-transplantation in children, Dr L Goddard indicated that the following points are important: early oral or enteral feeding, aggressive post-transplant feeding improves outcomes and long-term nutritional follow-up is essential. Pre-transplant nutrition is equally important, since nutritional status is a known determinant of clinical outcome. Growth retardation and malnutrition are common in chronic liver disease and nutrition support is difficult. Nutrition support goals pre-transplant includes maintaining maximum growth potential, preventing further liver injury, promoting liver regeneration, minimising the risk for infection and avoiding vitamin and mineral deficiencies. The early post-transplant nutritional therapy should aim to provide adequate nutrition and to compensate for the stress of major abdominal surgery. The feeding route of choice is oral or enteral nutrition with parenteral nutrition reserved for prolonged ileus and GIT complications. Fluid, electrolytes, clotting time, full blood count should be monitored, and the patient's energy and protein intake should be closely evaluated for 2–3 years post-transplant to maximise growth and to prevent obesity. Obesity, growth retardation, diabetes and metabolic bone disease are complications post-transplant and the side effects of immunosuppressive agents need to be monitored and addressed.

**HIV**

Ms J Downs discussed gut function and HIV pathogenesis. GIT dysfunction is a major manifestation of HIV infection. The mucosal immune system and intestinal immune system are important in the pathogenesis of AIDS. HIV enteropathy is characterised by diarrhoea, increased GIT inflammation, increased intestinal permeability, malabsorption of bile acids and vitamin B12. The histological changes with GIT enteropathy in HIV occurs in the absence of any detectable bacterial, viral or fungal enteropathogens. The mechanisms that cause the abnormalities in HIV enteropathy are poorly understood, but it has been suggested that HIV has a “virotoxic” effect on the enterocytes. Structural changes to the villi and significant impact to lactose absorptive capacity also occur. The presentation of HIV-diarrhoea varies depending on the principal section of the GIT involved. Opportunistic infections further aggravate the HIV-associated enteropathy due to structural damage and/or immune sensitisation. It is thus difficult to assess whether the severity of the GIT symptoms is due to HIV progression or the severity of other opportunistic infections. In children advanced stages of HIV disease are associated with accelerated whole GIT transit time. Therefore measures should be taken to delay gastric transit time such as specialised low lactose feeds with a low osmolality to allow for better nutrient absorption. In a recent study, citruline has been shown to be a reliable marker of severe chronic infectious enteropathy in HIV disease.

**Cancer**

Ms Rene Smalberger recommended that patients with GIT malignancies should be screened to identify those at risk of malnutrition. Nutritional management included appropriate nutritional assessment and advice on meeting energy and protein goals. In post-operative, severely malnourished patients, who are anticipated to have inadequate intake for seven days or longer, TPN should be commenced within 48 hours post-surgery. Peripheral parenteral nutrition can be used where inadequate intake is anticipated to be less than seven days. Consequences of the GIT surgery such as early satiety, vitamin deficiencies, dumping syndrome and steatorrhoea must be addressed in the nutrition care plan.

**Food allergies**

An estimated 6–8% of children are affected by food allergies at some point in their childhood. Dr Harris Steinman emphasised that the nutritional implications of food allergy does not only include eliminating the essential food(s) from the diet, but undiagnosed or poorly managed conditions may result in decreased physical activity, and/or increased or decreased food intake with the consequent negative effects on growth or obesity respectively. Therefore, accurate diagnosis with appropriate tests, dietary intervention, annual nutritional assessment, supervised and monitored elimination diets and re-exposure are essential in the overall management of the child.

**Food for thought**

As always Prof D Labadarios left us with some food for thought. Snakes don’t eat for weeks, their gut atrophies, yet when they finally get a meal they can digest it. Prof Labadarios reminded us that gut atrophy is a normal adaptive and survival enabling response, but asked the question whether the gut becomes dysfunctional in the presence of the acute phase response. Furthermore, does early enteral feeding restore functionality from the final outcome point of view? Although early enteral feeding should be implemented, it should not be on the assumption that it will reverse any gut atrophy present, and it should be implemented bearing in mind the potential for doing harm. Current meta-analytic data are consistent in their conclusion that there is insufficient evidence to support so called early trophic feeding, at least in low birth weight infants. Enteral feeding is the preferred route, but not the automatic route. Any patient needs to be fully resuscitated, have a normal acid-base balance, electrolyte status and oxygenation before feeding, irrespective of its administration route, is initiated.

**Ethics**

Prof M Kruger addressed evidence-based medicine and the impact it has had on health care in the last 30 years. She pointed out that evidence-based medicine relied on a hierarchy of evidence, which is ranked from absolute proven interventions to the least reliable knowledge, and assisted in answering two questions, namely what is in the best interest of the patient and how should one allocate health care resources fairly. Prof Kruger emphasised that there should be genuine “therapeutic equipoise” which implied that there is a valid doubt about the value of the treatment modalities under investigation, which can only be answered by randomised control trials. In this regard, health care professionals should practise their profession by combining their individual clinical skills in conjunction with evidence-based medicine.

Ms Arina Prins