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The Nutrition Society Scottish Section Meeting was held at the Royal College of Physicians and Surgeons, Glasgow on 26–27th March 2018

Editorial

Conference on 'Nutrient–nutrient interaction'

Nutrient–nutrient interactions: competition, bioavailability, mechanism and function in health and diseases

The Nutrition Society Spring Conference 2018, held in Glasgow, brought together experts focusing on the interaction between different nutrients and how this impacts absorption, metabolism and health from biochemical and physiological perspectives. This cross-cutting theme was examined from a range of perspectives, bringing together experts on topics ranging from food processing to the impact of inflammation on nutrient status. Two plenary lectures provided a food landscape and lifecourse background to the proceedings, with on the first day a focus on processed/ultra-processed foods and their nutrient composition and, on the second day, a plenary lecture exploring the role that nutrient–nutrient interactions within the maternal diet have for the lifelong health of the offspring. The meeting was framed around three symposia, examining the competition and bioavailability of dietary components, nutrient–nutrient interactions and their role in protection from chronic diseases and the mechanisms of nutrient–nutrient interactions. The meeting ended with a round table, and an overall conclusion highlighting the opportunities to derive further understanding of the short- and long-term implications of diets through the study of nutrient–nutrient interactions.

Nutrient: Interaction: Diet: Metabolism: Biochemistry

With nutritional recommendations focusing mostly on single nutrients, nutrient–nutrient interactions are sometimes overlooked. There is, however, a long-standing recognition that nutrients interact at a chemical, biochemical and physiological level. As such, the Nutrition Society Spring conference 2018, hosted at the Royal College of Physicians and Surgeons in Glasgow, acknowledged the growing research focus on understanding not only the effects of single nutrients, but also their interactions and relevance for physiological function and ultimately health.

The conference, which attracted scientists, nutrition educators, healthcare professionals, clinicians and students from the UK, Europe, North America and South America, explored the complex ways in which nutrient–nutrient interactions impact on absorption and metabolism, from biochemical and physiological perspectives. As nutrient–nutrient interactions are relevant to scientists, food industry partners, clinicians and health care practitioners, the conference emphasised the translational value that research findings in this field hold for stakeholders, with a broad stance covering topics from food and food formulation to mechanisms of nutrient–nutrient interaction at the molecular level.

Modern diets provide a broad spectrum of nutrients, and the relative proportion of nutrients in foods, plus how these foods are combined into meals are important factors determining the fate of each nutrient in the body. Opening the conference, Professor Julie Miller Jones (St. Catherine University, St Paul, USA) addressed the recent concerns in the popular and scientific press related to the nutritional contribution of processed and ultra-processed foods[1]. Highlighting that there is no strong consensus on the definition of what is and what is not a processed food, Professor Miller Jones established how this lack of strong definition contributes to the controversies surrounding the effects of food processing on health. Using the NOVA definition[2], she highlighted how processed foods can make substantial contributions to dietary intakes of whole grains, cereal fibre, minerals and B vitamins.

This is particularly relevant in a dietary landscape where micronutrients come from a variety of foods, with a sizeable proportion of vitamins and minerals secured through fortified foods and supplements. It is therefore important to assess total nutrient exposure, as this is directly pertinent to the evaluation of risk and toxicity. Dr Marleen Lentjes (University of Cambridge, UK) used examples from observational cohort studies to illustrate these points, reflecting on the use of biomarkers and diurnal variations in the concentration of selected micronutrients, to discuss the concepts of adequacy and toxicity.

With 27% of women aged 19–64 years having an iron intake below the lower reference nutrient intake, and 12% with low iron stores (ferritin <15 μg/l)[3], oral iron

supplementation is commonly prescribed in the UK or obtained over the counter. Adequate absorption of iron (as a ferrous salt supplement, or from food as haem or non-haem iron) is essential for repletion of iron stores, and the role of ascorbic acid and phytates in the modulation of iron bioavailability are well known[4]. Beside iron, phytates may also impact on zinc bioavailability[5]. Taking into consideration both host-related factors (including growth, obligatory losses) and diet composition factors affecting bioavailability, Professor Susan Fairweather-Tait (University of East Anglia, UK) outlined the factorial approach taken to determine dietary reference values (DRV) when suitable biomarkers are not available[6]. While these DRV are applicable to the healthy UK population in the absence of co-deficiencies, they may not be suitable in other contexts. This is particularly true for iron, which mediates important functions in the host–pathogen interactions. Reduced iron bioavailability was presented by Dr Dora Pereira (University of Cambridge, UK, and Medical Research Unit, The Gambia) as a key defensive mechanism in human subjects to reduce circulating iron in the face of infection, including malaria and other co-infections. In this context, iron supplementation could carry risks by removing this protection[7]. Informed strategies, taking into consideration how unabsorbed 'free' iron in the gut is an important factor affecting the gut microbiome and enteric infection are needed: current strategies trialled in the Gambia include the iron supplement IHAT (iron hydroxide adipate tartrate) which does not dissolve in the gut, limiting the pool of iron bioavailable for pathogens.

Micronutrient deficiencies play an important role in chronic disease prevention and management, and accurate measurement of the nutritional status is critical. Using thyroid dysfunction as an example, Professor Margaret Rayman (University of Surrey, UK) gave an overview of the nutritional risk factors for autoimmune thyroid disease. Nutrient deficiencies often occur together, as do excessive intake of nutrients (often through supplementation). Specifically, the interplay of iodine (essential for formation of thyroid hormones), selenium (required, as selenocystein in iodothyronine deiodinase to convert thyroxine into triiodothyronine, and in glutathione peroxidase and thioredoxin reductase to protect cells from oxidative damage) and iron status (thyroid peroxidase is a haem-dependent protein) with a potential additional input of vitamin D status were explored as factors influencing auto-immune thyroid disease[8,9]. The timing of the correction of the deficiencies was highlighted as crucial to avoid unintended consequences. In the context of combined severe iodine and selenium deficiency, iodine supplementation should be initiated before selenium supplementation to prevent hypothyroidism[10].The nutrient–nutrient interactions denoted above may become particularly important in the context of lifecourse nutrition. For example, thyroid function is essential during pregnancy to drive neurodevelopment, and may be compromised by inadequate status in one or more of the nutrients. Dr William Rees (The Rowett Institute, University of Aberdeen, UK) addressed the topic of nutrient–nutrient interactions in the maternal diet and its effects on the offspring long-term health, highlighting the complex interactions between macronutrient and micronutrient nutrition, focusing on the metabolism. Whilst the macronutrient dense, micronutrient sparse diets consumed by many in the western world may not result directly in deficiencies, there may be situations where slightly reduced levels of multiple micronutrients together with high energy intake overwhelm selected metabolic pathways. An example included was that of methyl-deficient diets and the role of methyl-donors in the maternal diets in the context of the offspring development and lifelong health.

From a lifecourse nutrition perspective, timing of nutritional intake may be critical for bone health. Meanwhile, from a performance perspective, timing of intake may be important. While carbohydrate and fat intake make modest, and independent, contributions to an individual's capacity to oxidise fat during exercise[11], Dr Gareth Wallis (University of Birmingham, UK) outlined the emerging research focusing on carbohydrate–fat interactions during and after exercise, reflecting on experimental designs testing the optimal time to undertake exercise around eating events[12]. Professor Craig Sale (Nottingham Trent University, UK) focused on major modifiable factors of bone, including nutrition and exercise. Protein, in particular, may be crucial for bone health, but there is a lack of consensus on its exact influence. Describing the acid-ash hypothesis in detail (diets high in protein lead to reductions in bone mineral density), Professor Sale highlighted the lack of evidence in support of this assertion. Instead, data suggest that dietary protein intake may actually be beneficial, but dependent upon interactions with other nutrients such as calcium and vitamin D[13]. These factors may indeed bear important relevance to chronic conditions affecting the bones, including osteoporosis, which are related to nutrition through the lifecourse. Therefore, measuring the nutritional status of an individual is critical, but biochemical assessment of micronutrient status may be confounded by other variables, including inflammatory status. Professor Donald McMillan (University of Glasgow, UK), focused on the interaction between systemic inflammation and plasma micronutrient concentrations in the context of chronic disease and post-surgical outcomes[1]. Acute inflammation (based on measures of plasma C-reactive protein) was shown to lead to a reduction in plasma concentrations of several micronutrients such as selenium and vitamins A, B_6, C and D, with decreases >40%[14]. These effects were seen even with small increases (5–10 mg/l) in C-reactive protein; therefore clinical interpretation of plasma micronutrients should only be made with a concurrent measure of inflammation.

Carotenoids and their metabolites are involved in a broad range of molecular mechanisms, with an important anti-inflammatory action. However, inflammation can also impair vitamin A absorption, and not all the parameters in this relationship are well understood. In two lectures providing deep mechanical insight, Professor George Lietz (Newcastle University, UK) provided an in-depth look into the physiological and genetic

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factors affecting pro-vitamin A bioavailability and bioefficacy, while the importance of the biological activity of carotenoids was illustrated by Dr Ralph Ruehl (University of Debrecen, Hungary), focusing on the importance of bioactive derivatives of carotenoid metabolism in cell signalling.

While research on the role of single nutrients is extensive, this is not necessarily true for multiple nutrients and nutrient–nutrient interactions. This may be particularly important in the physiopathology of a range of chronic illnesses underpinned by inflammatory pathways, for example. The scientific programme concluded with a roundtable discussion, which acknowledged this gap and considered the practical challenges associated with accurately measuring micronutrient status, and defining total nutrient intake (including supplements). The need for advanced biomarker techniques was highlighted, to improve our understanding of mechanisms involved when nutrient interacts. The meeting ended with the agreement that there are opportunities to study nutrient co-deficiencies in more depth, with scope to improve public health messaging and cooperation with industry to improve the nutritional composition of processed foods.

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