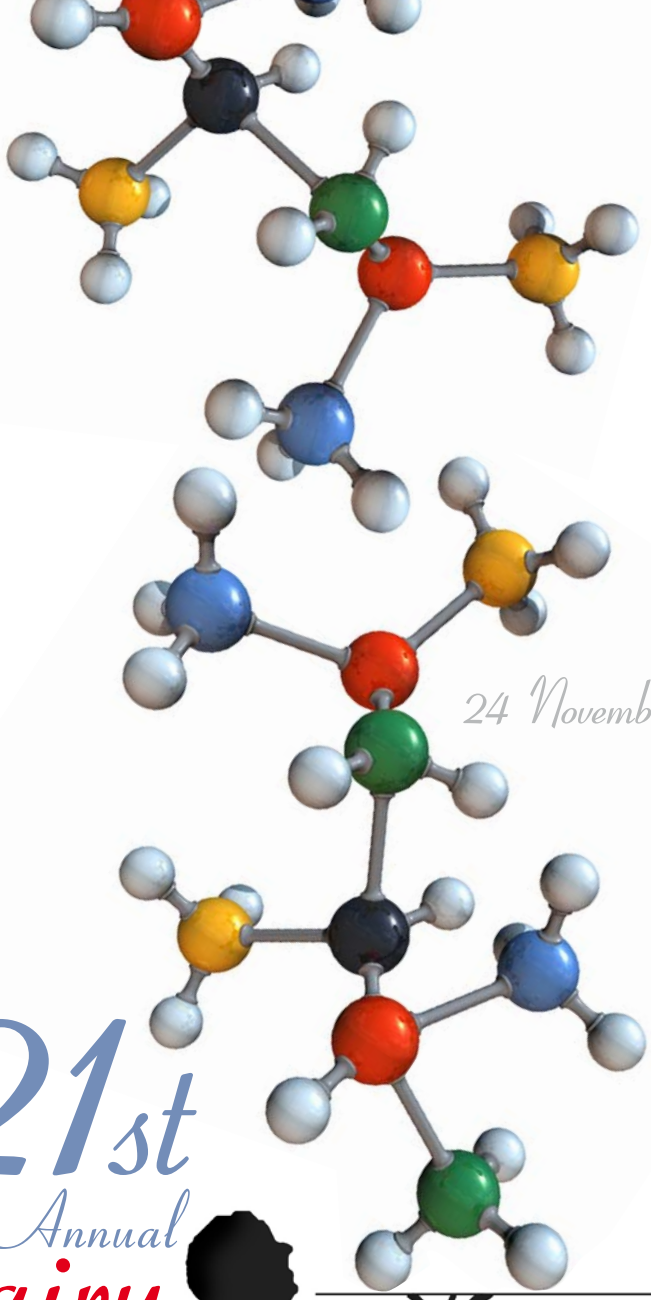


24 November 2010

21st Annual Dairy Council Nutrition Lecture & Anniversary Conference

DAIRY COUNCIL NORTHERN IRELAND

University of ULSTER

Anniversary Conference

09.30 Registration and coffee

10.15 **Welcome & Introduction**
Professor Sean Strain, University of Ulster

10.30 **Obesity** - Chair: Professor Barbara Livingstone, University of Ulster

Personalised nutrition: Opportunities and challenges *page 3*
Professor Mike Gibney, University College Dublin
Resistance and susceptibility in the age of obesity *page 4*
Professor John Blundell, University of Leeds

11.50 Coffee

12.10 **Bone Health** - Chair: Dr Julie Wallace, University of Ulster

Scientific substantiation of health claims on bones and teeth *page 5*
Professor Albert Flynn, University College Cork
Nutrition and bone health in the 21st Century: Current controversies and future perspectives *page 6*
Dr Susan Lanham-New, University of Surrey

13.30 Lunch

14.30 **B-Vitamins** - Chair: Professor Helene McNulty, University of Ulster

The commericalization of basic research *page 7*
Professor John Scott, Trinity College, Dublin
Unmetabolized folic acid in plasma and the exacerbation of vitamin B12 deficiency *page 8*
Dr Jacob Selhub, TUFTS University, Boston

15.50 Coffee

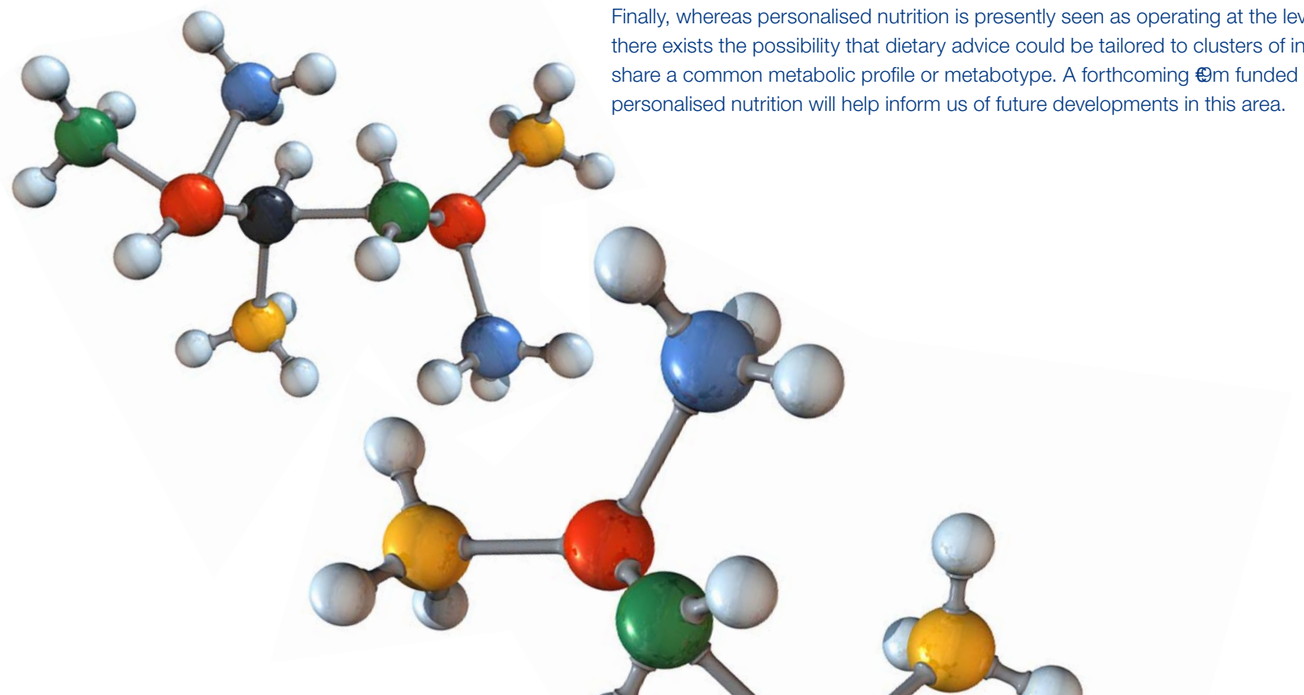
16.10 **Gut Health** - Chair: Professor Rob Welch, University of Ulster

Prebiotics and gut health *page 9*
Professor Glenn Gibson, University of Reading
Bowel cancer and nutrition in the developed world: Understanding the vulnerable mucosa *page 10*
Professor Ian Johnson, Institute of Food Research, Norwich

17.30 Buffet supper

Nutrition Lecture

18.30 **Eating fish for two** *page 11*
Professor Sean Strain, University of Ulster



Personalised nutrition: Opportunities and challenges

Professor Mike Gibney
UCD Institute of Food & Health
University College Dublin

The concept of personalised nutrition has always been related to details of an individual's genetic code and the many enterprises that set out to deliver a service in this area, have failed. Individual SNPs may allow researchers understand diet and gene interactions in metabolism. In recent times, there has been a growth in interest in the pursuit of personalised nutrition, not based on genetic data but based on phenotypic and dietary data. Many services in the public and private sectors offer the opportunity to submit details of one's habitual diet and receive back details of one's pattern of nutrient intake together with advice on where the balance of nutrients needs to be improved. In some instances, advice on improved food choice can be offered and it would not be difficult to envisage in the future that such data could be related to the information technology services of supermarkets.

A second rapidly emerging area is the provision of personalised data on phenotype. This can be in the form of biochemical data, which would also advise the individual on their personal nutrient balance and ultimately their food choice. It can also be in the form of biofeedback information on functional aspects of health. Home based measures of blood pressure are an existing example but this will be extended to many other physiological and indeed psychological measures all of which will again advise individuals on their personalised nutrition choices.

Finally, whereas personalised nutrition is presently seen as operating at the level of the individual, there exists the possibility that dietary advice could be tailored to clusters of individuals who share a common metabolic profile or metabotype. A forthcoming €9m funded EU FP& project on personalised nutrition will help inform us of future developments in this area.

Resistance and Susceptibility in the age of obesity

Professor John Blundell
Institute of Psychological Sciences
University of Leeds

We live in what has been termed an 'obesogenic environment' which encourages overconsumption and discourages physical activity. This generates a positive 'energy gap' which in turn promotes weight gain and obesity. However, even in this unhelpful obesogenic landscape not all people gain weight; some manage to remain lean. This raises the issue of individual resistance and susceptibility. Recent work in genetics has disclosed certain combinations of alleles of particular genes which – although not very potent – could contribute to an underlying susceptibility to weight gain. This effect is quite weak and susceptibility could be characterised in other ways which may be more understandable and more helpful for dealing with the issue of weight gain.

The use of an Energy Balance strategy (within a PsychoBiological Systems approach) has revealed a number of relationships between physiology, metabolism, nutrition and appetite behaviour that can identify features of susceptibility. These include a high level of Disinhibition (trait for opportunistic eating), weak satiety response to dietary fat, high hedonic responsiveness to certain appealing key foods and a low level of leisure time physical activity. These characteristics form a cluster of traits comprising a 'susceptible phenotype'. However, given the large number of allelic variations contributing to body mass, there are likely to be several different pathways (combinations of dispositions) that lead to weight gain.

Since behaviour makes such a huge contribution to the energy balance equation, it is important that the identification of susceptible and resistant phenotypes can contribute to an understanding of behaviour change. The role of physical activity is particularly important; significantly it has been shown to counteract genetically-determined weight gain, and to prevent 'fat' gain. However, the impact of physical activity varies markedly between individuals, and the effects on body weight cannot be predicted in advance. Therefore people are susceptible or resistant to weight loss in response to an exercise programme, just as they are susceptible or resistant to a weight-inducing diet.

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King, N.A., Hopkins, M., Caudwell, P., Stubbs, R.J., Blundell, J.E. (2008) Individual variability following 12 weeks of supervised exercise: identification and characterization of compensation for exercise-induced weight loss. International Journal of Obesity. 32: 177 – 184.
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King, N.A., Hopkins, M., Caudwell, P., Stubbs, R.J., Blundell, J.E. (2009) Beneficial effects of exercise: shifting the focus from body weight to other markers of health. British Journal of Sports Medicine 43: 924 – 927.
Vimareswarlen, K S et al (2009) Physical activity attenuates the body mass increasing influence of genetic variation in the FTO gene. American Journal of Clinical Nutrition. 90: 425 – 428.

Scientific substantiation of health claims on bones and teeth

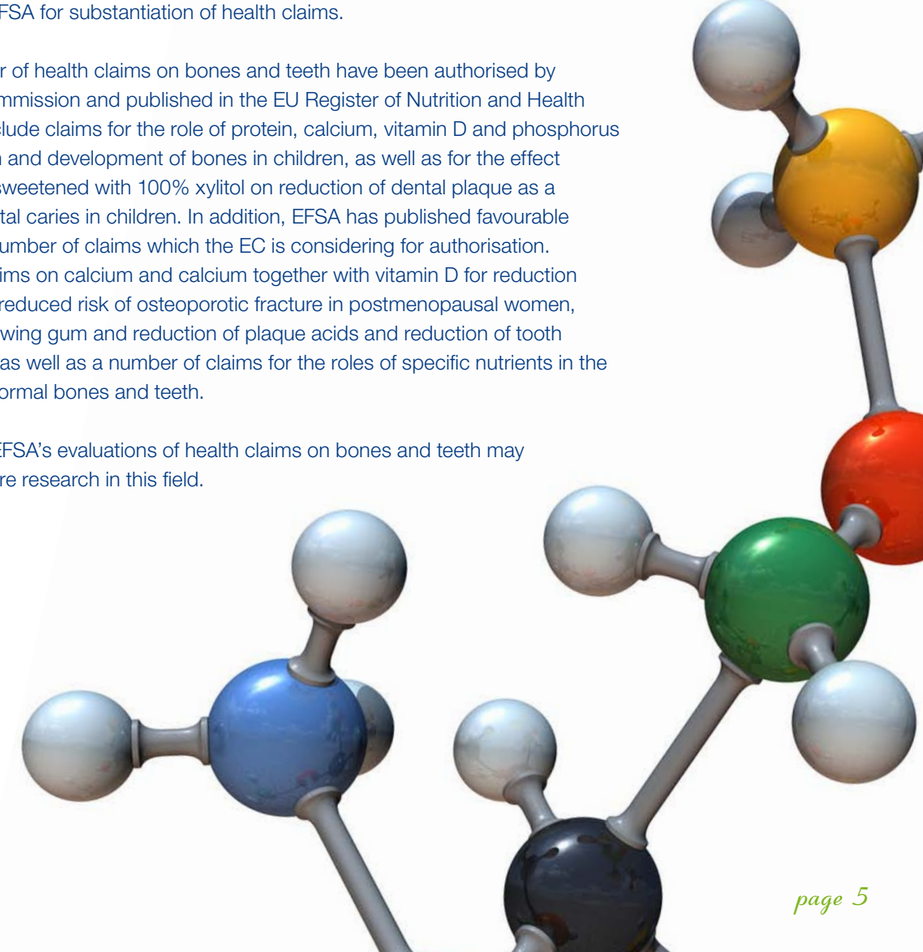
Professor Albert Flynn
School of Food and Nutritional Sciences
University College, Cork

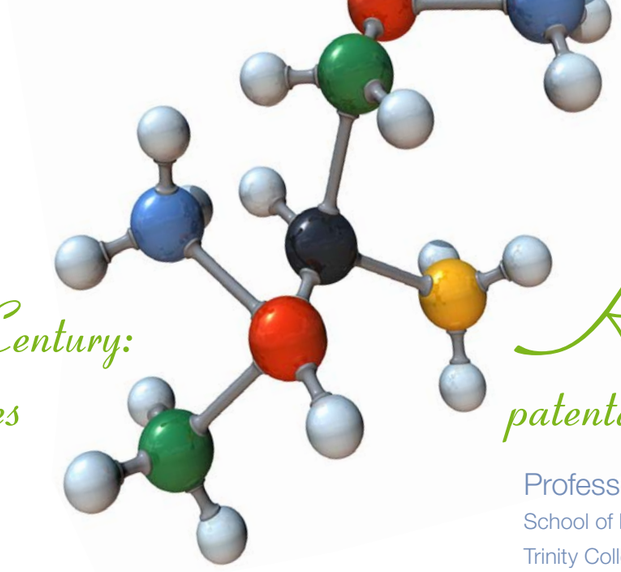
In the EU, legislation on nutrition and health claims made on foods has been harmonised through Regulation (EC) No 1924/2006. According to the Regulation, health claims should be only authorised for use in the Community after a scientific assessment of the highest possible standard to be carried out by the European Food Safety Authority (EFSA). The evaluation of the substantiation of health claims is carried out by EFSA's Scientific Panel on Dietetic Products, Nutrition & Allergies.

EFSA has published extensive guidance to assist applicants in the preparation of applications for authorisations of health claims. This guidance includes the scientific criteria used by EFSA for substantiation of health claims.

To date, a number of health claims on bones and teeth have been authorised by the European Commission and published in the EU Register of Nutrition and Health Claims. These include claims for the role of protein, calcium, vitamin D and phosphorus for normal growth and development of bones in children, as well as for the effect of chewing gum sweetened with 100% xylitol on reduction of dental plaque as a risk factor for dental caries in children. In addition, EFSA has published favourable evaluations of a number of claims which the EC is considering for authorisation. These include claims on calcium and calcium together with vitamin D for reduction of bone loss and reduced risk of osteoporotic fracture in postmenopausal women, on sugar free chewing gum and reduction of plaque acids and reduction of tooth demineralisation, as well as a number of claims for the roles of specific nutrients in the maintenance of normal bones and teeth.

The outcome of EFSA's evaluations of health claims on bones and teeth may help to guide future research in this field.





Nutrition and bone health in the 21st Century: Current controversies and future perspectives

Dr Susan Lanham-New
Nutritional Sciences Division
University of Surrey

Predisposition to poor bone health, resulting in osteoporotic fracture, is a major public health problem with recent estimates suggesting an overall cost to the Exchequer of £1.8 billion per annum. Two mechanisms principally determine adult bone health: (i) maximum attainment of peak bone mass (PBM) (ii) the rate of bone loss with advancing age. Both aspects are determined by endogenous and exogenous factors and although genetics account for 75% of the variation in bone mass there is still much room for the modifiable factors (such as nutrition & physical activity) to play a vital role in bone health.

Calcium (Ca) is important to PBM development. Ca supplementation studies in general have shown an association between higher Ca intake and increased bone mineral status (in the order of 1-5%), with the effect greatest in the early stages of supplementation period. However, the strength of this effect is limited due to the findings of some studies that the bone gain disappears upon withdrawal of the supplement and clearly further research work is required. There is good data to suggest that Ca supplements are effective in reducing bone loss in late menopausal women (>5 years post-menopause), particularly in those with low habitual Ca intake (< 400mg/d). Ca does not appear to be effective during the early stages of the menopause, but this is an area for further investigation. Interestingly, Ca & vitamin D supplementation has been shown to be effective in reducing fracture rates in both institutionalised and free-living elderly populations, but not vitamin D alone.

Vitamin D deficiency/insufficiency is a problem in the UK population. Findings of the NDNS surveys (4-18 years; 19-64 years; 65+ years) and the 1958 British Birth Cohort indicate that hypovitaminosis D is widespread in the UK (e.g. plasma 25 hydroxyvitamin D (25OHD) level <25nmol/l was found in 24% of men/28% of women in the NDNS 19-24 age groups). Currently, in the UK there is no DRV for vitamin D for 19-64 years if sunlight exposure is not inhibited, but some countries have redefined their recommended values: e.g. the US adequate intake is 5µg/d for 0-50 years, rising to 15µg/d for 70+ years and the new US recommendations will be published on the 30th November 2010. Poor vitamin D status is implicated for a number of health outcomes, not just bone health. Hence, understanding what levels of vitamin D are optimal/suboptimal is critically important

Recent population studies suggest a positive association between high intakes of fruit & vegetables and bone health, observations which are considerably strengthened by the reduction in urinary Ca excretion in the fruit & vegetable supplement group participating in the DASH intervention trial (Dietary Approaches to Stopping Hypertension). This link may be explained by the growing recognition of the role of the skeleton in acid-base balance and is an exciting area for further research.

Our knowledge of the influence of other micronutrients (e.g. phosphorus, magnesium, vitamin K, vitamin C etc.) on the skeleton remains limited. Further work is required to establish the essential ingredients for optimum bone health, particularly in those individuals who are genetically susceptible to osteoporosis.

Application of basic science to patentable inventions

Professor John Scott
School of Biochemistry & Immunology
Trinity College, Dublin

There is often public frustration and confusion as to why there should be taxes to fund basic research, when the chances of its commercialisation seem remote. Patents and commercialisation, except those of a very limited technical nature, rarely emerge from groups involved in applied research. What is more usual is that a group, aware of fundamentals in a particular area, see opportunities that have commercial value in a related area. To do this they must either have learned or been taught to see opportunities early on and to avoid disclosure, which would of course invalidate a patent. They must have their institutional or governmental support to continue the basic idea through proof of concept, patent searches and the formulation and execution of a patent application.

The examples below illustrate how my research team at Trinity College Dublin in collaboration with Professor Helene McNulty and colleagues at University of Ulster, Coleraine approached two patent possibilities.

Example 1: Supermilk

It is well established that folate is deficient in most people's diet. This puts them at increased risk of anaemia, stroke and possibly increase of cognitive decline. There is a particular need to improve folate status periconceptionally, before the neural tube closes, to make the spinal column 28 days post conception. This extra folate is currently supplied as the synthetic form of folate, namely folic acid. There are concerns with this practice since folic acid is not controlled in the same way as natural folate in the body. More recently, evidence has emerged that folic acid might accelerate the growth of existing cancers and exacerbate cognitive decline.

A big problem is that while the natural folates are widely distributed in most foods there is really no good source of folate that one could recommend as an alternative to folic acid added to food or to folic acid tablets. Natural folate chemically produced has half of it as an inactive isomer, is expensive and not really a practical proposition.

Milk is an average source of natural folate but like other food, is low in concentration. Our idea was why not feed the cheap synthetic folic acid to cattle. They would then, during metabolism, convert some or most of this into natural folate. This would be reflected in an increase in the cow's circulating level, an increase in mammary folate and an increase in the concentration in milk. We foresaw that one glass of milk per day would exceed the RDA and make the need for use of synthetic folic acid in food unnecessary.

Example 2: Reduction of blood pressure

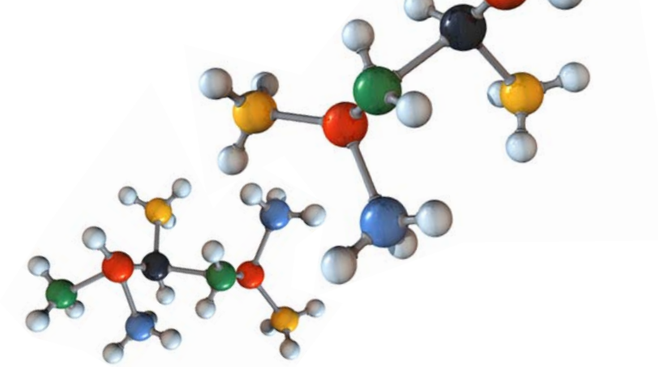
Elevation of Blood Pressure (BP) is one of the principal risks for stroke and heart disease. With increasing age, the vast majority of people require anti-hypertensive drugs. With Helene McNulty and her colleagues in the University of Ulster, my group in Trinity College found that people with a very common genetic variant C677T for the enzyme MTHFR had elevated BP even after treatment with the usual range of antihypertensives. Those TT for the variant frequently had BP of 160/90 compared to CT and CC with more normal values of 130/80. We observed that when those three groups were given vitamin B2 (riboflavin) a cofactor for the damaged enzyme, that a circulating biomarker homocysteine decreased only in TT groups. This would be expected. What was not expected was that there was also significant decrease in systolic blood pressure. We have been granted a patent on this discovery.

Unmetabolized folic acid in plasma and the exacerbation of vitamin B12 deficiency

Dr Jacob Selhub
Human Nutrition Research Center on Aging
Tufts University, Boston

Historic reports on the treatment of pernicious anemia with folic acid suggest that high-level folic acid fortification delays the diagnosis of, or exacerbates the effects of, vitamin B-12 deficiency, which affects many seniors. This idea is controversial, however, because observational data are few and inconclusive. Furthermore, experimental investigation is unethical. We used data from the post folate fortification 1999-2002 National Health and Nutrition Examination Survey (NHANES) to demonstrate an interaction between plasma folate and low B12 status (defined as plasma B12 <148 pmol/L or methylmalonic acid (MMA) >210 nmol/L) with respect to anemia and cognitive impairment. With subjects with both normal plasma folate (<59nmol/L) and normal B12 status as the referent category, odds ratios for the prevalence of anemia versus normal hemoglobin level were 1.9 (95% CI 1.01 3.6) for those with low B12 status in combination with normal plasma folate, and 4.8 (95% CI 2.4, 10.3) for those with low B12 status in combination with plasma folate >59 nmol/L. For cognitive impairment, the corresponding odds ratios were 1.6 (95% CI 0.95, 2.8) and 4.9 (95% CI 2.5, 9.2), respectively. Actual B12 concentrations in those with low B12 status were 228 pmol/L for those with normal folate compared to 354 pmol/L in those with high folate. In a second paper we have shown that in subjects with serum vitamin B12 <148 pmol/L, concentrations of Hcy and MMA increased as serum folate increased. Specifically, at plasma folate concentrations >50nmol/L, Hcy was 30% higher and MMA was 100% higher than values observed at plasma folate concentrations <20 nmol/L. At normal B12 concentrations, the increase in plasma folate was associated with decreases in serum concentrations of both MMA and Hcy. In a third study we have shown that circulating unmetabolized folic acid was detected in about 1/3 of the subjects. In seniors with serum vitamin B-12 <148 pmol/L or plasma methylmalonic acid >210 nmol/L, the presence versus absence of detectable circulating unmetabolized folic acid was related to lower cognitive test scores and lower mean cell volume. In the same subgroup, higher serum 5MeTHF was related to increased odds of anemia and marginally significantly decreased odds of macrocytosis. In seniors with normal vitamin B-12 status, higher serum 5MeTHF was related to higher cognitive test scores.

Results of these epidemiologic studies suggest that in B12 deficiency high folate is associated with exacerbation of B12-deficiency related symptoms. The role of unmetabolized folic acid in this interaction requires further attention.



Prebiotics and Gut Health

Professor Glenn Gibson
Department of Food and Nutritional Sciences
The University of Reading

The human large intestine is an intensively colonised area containing bacteria that are health promoting, as well as pathogenic. This has led to functional food developments that fortify the former at the expense of the latter. Probiotics have a long history of use in humans as live microbial feed additions. In contrast, a prebiotic is a non digestible food ingredient that beneficially affects the host by targeting indigenous components thought to be positive. Dietary carbohydrates, such as fibres are candidate prebiotics but most promise has been realised with oligosaccharides. As prebiotics exploit non-viable food ingredients, their applicability in diets is wide ranging.

Main prebiotic targets at the moment are bifidobacteria and lactobacilli (although this may change as our knowledge of the flora diversity and functionality expands). Any dietary component that reaches the colon intact is a potential prebiotic, however much of the interest in the development of prebiotics is aimed at non-digestible oligosaccharides such as inulin type fructooligosaccharides (FOS) and trans-galactooligosaccharides (TOS). In Europe, FOS and TOS have been shown to be prebiotics, through numerous volunteer trials, as evidence by their ability to positively change the gut flora composition after a short feeding period. Other prebiotics are emerging. Some prebiotics occur naturally in several foods such as leek, asparagus, chicory, Jerusalem artichoke, garlic, artichoke, onion, wheat, banana and oats. However, these foods contain only trace levels, so developments have taken the approach of removing the active ingredients from such sources and adding them to more frequently consumed products in order to attain levels whereby a prebiotic effect may occur, e.g. cereals, confectionery, biscuits, infant feeds, yoghurts, table spreads, bread, sauces, drinks, etc.

As gastrointestinal disorders are prevalent in terms of human health, both probiotics and prebiotics serve an important role in the prophylactic management of various acute and chronic gut derived conditions. Examples include protection from gastroenteritis and some inflammatory conditions.

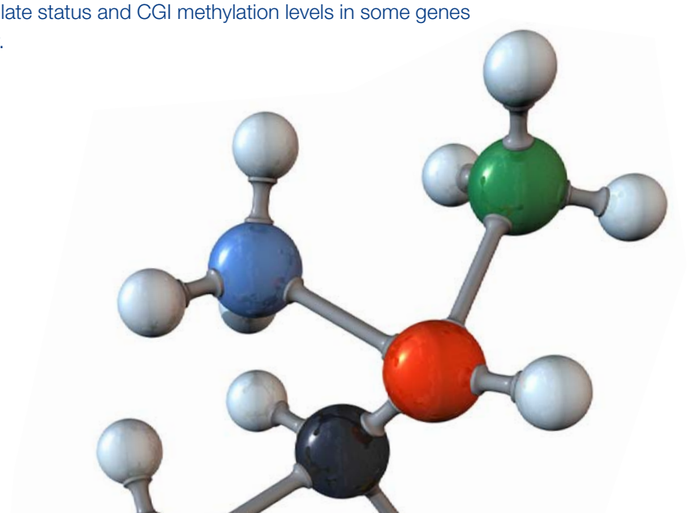
The rationale for using probiotics and prebiotics to reduce risk will be reviewed. On the contrary, the role of the gut flora in various clinical states will be briefly discussed. Building upon this information, research will be presented on the generation and testing of a novel prebiotic (TOS) which has led to the development of products designed to improve immune health in the elderly, reduce the symptoms of Irritable Bowel Syndrome and help prevent traveller's diarrhoea.

Bowel cancer and nutrition in the developed world: Understanding the vulnerable mucosa

Professor Ian T Johnson
Plant Natural Products and Health
Institute of Food Research, Norwich

On a global basis, colorectal cancer is the third most common of all cancers in men, and the second most common in women, but the incidence varies more than ten-fold between countries. One striking feature of this variation is an inverse relationship between the risk of colorectal cancer and prosperity, so that the highest rates occur in Japan, North America and Europe. This consistent epidemiological pattern provides clear evidence for an adverse effect of the environment in western industrialised countries on the vulnerability of the colorectal mucosa to cancer, but the mechanisms are unknown.

Over the past several years, the Institute of Food Research and the Human Nutrition Research Centre at Newcastle University have collaborated to explore the use of proteomic techniques, and the quantitative assessment of DNA methylation applied to morphologically normal mucosa, to identify biomarkers of field effects associated with increasing vulnerability to colorectal neoplasia. Early studies confirmed that the presence of localised lesions (e.g. adenomatous polyps and carcinoma) was associated with field-wide changes in both protein expression, and the level of methylation of CpG islands (CGI) in genes of the Wnt pathway, which is a key regulator of epithelial cell proliferation. The latter effects are potentially important because aberrant methylation of such genes is an epigenetic signal that may disrupt cellular signalling pathways in the early stages of neoplasia. These observations are consistent with, though do not prove, the presence of field-wide changes rendering the mucosa more vulnerable to cancer. More recently we have studied the impact of age, metabolic factors and diet on protein expression and CGI methylation in mucosal biopsies from 200 subjects having no evidence of colorectal disease at endoscopy. Overall there was little evidence for major effects of diet or metabolic status on the expression of epithelial proteins, although we observed unexpected effects of plasma fatty acid levels that deserve further investigation. The most important factor influencing CGI methylation was age. However, multivariate statistical analysis suggested the presence of subtle effects associated with metabolic and nutritional variables, including a tendency for a positive relationship between blood folate status and CGI methylation levels in some genes associated with the Wnt signalling pathway.



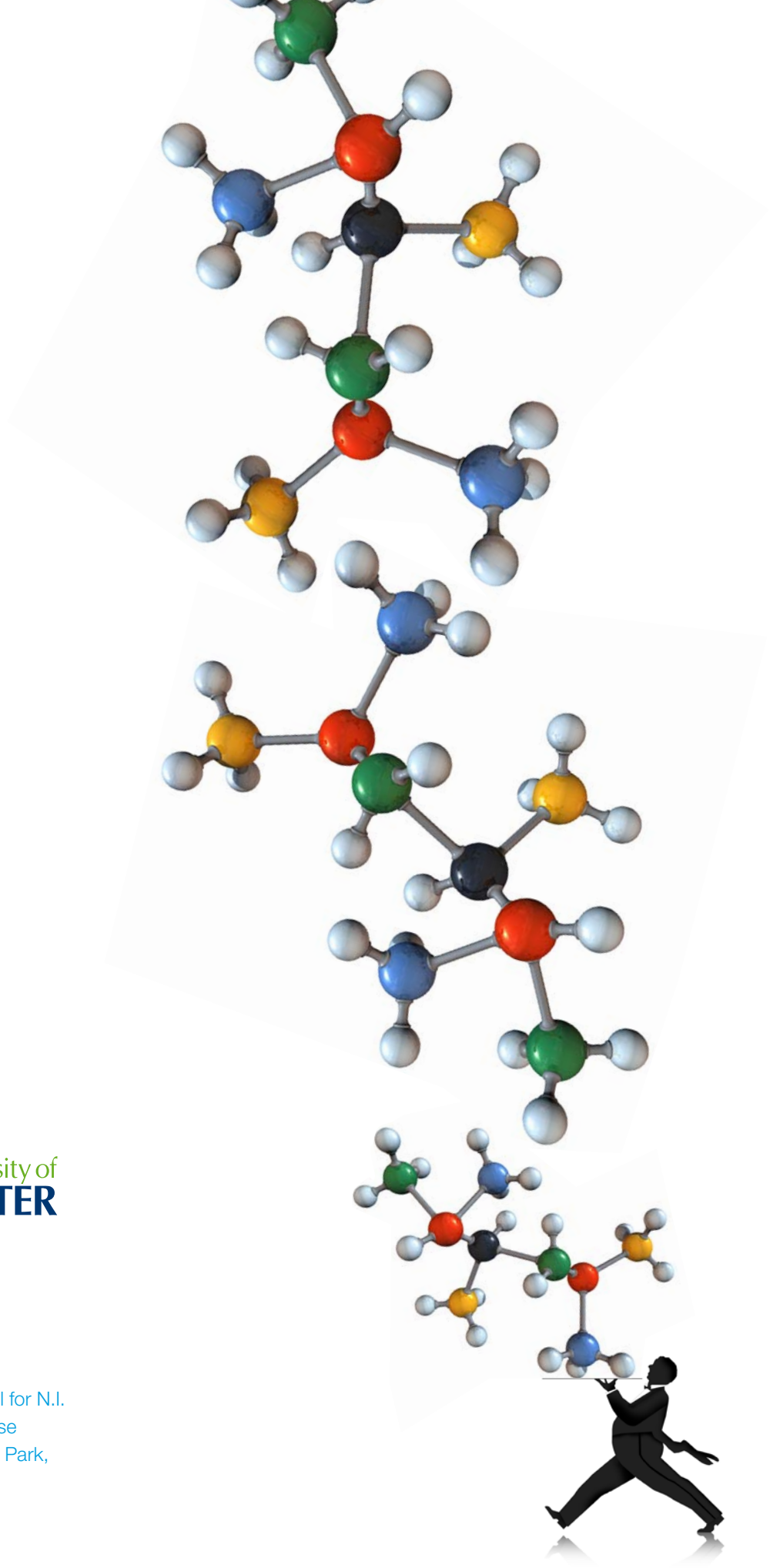
21st Annual Dairy Council Nutrition Lecture

Eating fish for two

Professor Sean Strain
Northern Ireland Centre for Food and Health (NICHE)
University of Ulster

A form of mercury, called methylmercury, found almost exclusively in fish, is a potential neurotoxin to which the foetal brain is especially susceptible. All fish contain some methylmercury; those fish, which are higher in the food chain, tend to have higher concentrations of this neurotoxin. Even though there is no evidence that children born to mothers who were high fish consumers (up to and greater than 12 times per week) do less well in a range of developmental tests than children born to mothers who were low fish consumers, advice to pregnant women tends to recommend no more than two fish meals per week. Dietary advice on such matters, however, varies from country to country. It is important to give pregnant women optimal dietary advice as fish contain various nutrients, including a form of fat or oil (omega-3 polyunsaturates), which can promote neuro-development, and fish consumption also has potential benefits for the mother. Moreover, nutritional and other environmental influences on foetal development can have long-term consequences for health and well being through various mechanisms including what is known as epigenetic modifications to the genome. Epigenetic modifications refer to changes in gene expression, which take place without a change in the DNA sequence, and such modifications include parent of origin influences on neurodevelopment.

The Seychelles Child Development Studies were set up initially to explore risks of methylmercury exposure from fish consumption on child development. More recently, emphasis has been placed on how nutritional factors in fish and the overall maternal diet might mask any detrimental developmental effects of methylmercury by providing benefits to the offspring. Foremost amongst these nutritional factors appear to be the omega-3 fatty acids. On-going work is exploring the interplay between methylmercury exposure and maternal status of omega-3 fatty acids and the antioxidants, selenium and vitamin E, on child development in the Seychelles.



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