

CONGRESS REPORT

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NUTRITION SYMPOSIUM, 'BIOCHEMICAL AND MOLECULAR BASIS OF DISEASE'

19 - 23 November 2001, Cape Town

The International Union of Biochemistry and Molecular Biology (IUBMB), in conjunction with the South African Society of Biochemistry and Molecular Biology (SASBMB), hosted a special meeting entitled the 'Biochemical and Molecular Basis of Disease' in Cape Town on 19 - 23 November 2001.

At the half-day symposium on nutrition it was evident that nutrition has entered the molecular phase and is now a promising area for young scientists.

Dr Paul Walter, University of Basel, Switzerland, in his presentation entitled 'New concepts for the determination of vitamin requirements', highlighted the increasing scientific evidence indicating, on the basis of molecular mechanisms, that several vitamins exhibit additional functions at higher concentrations than the recommended dietary allowances (RDAs). Such functions include the radical scavenging effect of various antioxidant vitamins, the role of vitamin C on leucocyte function, and the role of folate in the prevention of neural tube defects (NTDs) and of heart diseases. As a result, there are new recommendations for higher intake of vitamins C, D and E and folate.

These recommendations not only support good health but also reduce the risk of chronic disease such as coronary heart disease (CHD), certain eye diseases, and some cancers, and may also be linked to degeneration on mental function in such diseases as Parkinson's disease and Alzheimer's disease.

The concept of 'one vitamin prevents one disease' is no longer acceptable, as evidence shows that optimal prevention is obtained by the intake of the so-called 'balanced diet'. It has also become clear that not only the known micronutrients but also many more compounds such as flavonoids, polyphenols, carotenoids and phytosterols commonly found in plants, grains, and fruits are contributing to the preventive action of the diet. A better knowledge of the functions and possible applications of new bioactive compounds will go a long way in the contribution to maintain good health.

Recent epidemiological research has demonstrated the difficulty of setting specific requirements for single substances, because of their dependence on the presence or absence of other components. Particularly for the lowering of the risk of chronic diseases, a whole array of compounds are needed and therefore health claims for individual compounds are often problematic.

And the solution ... a balanced diet? Owing to lack of enriched and functional food, economic considerations, traditional eating patterns and lifestyle changes, not more than an estimated 10 - 50% of the population comply with these recommendations.

Dr Anne Molloy, Trinity College, Dublin, spoke on 'Molecular aspects of folate in health'. Folate is necessary to maintain low levels of homocysteine and is needed for the synthesis of DNA. A deficiency of folate results in the interruption of DNA synthesis, which affects rapidly dividing cells and results in macrocytic anaemia.

Moderately elevated plasma homocysteine has been associated with an increased risk of CHD, complications of pregnancy, renal diseases, and neuropsychiatric disorders. *In vitro* studies show that raised homocysteine levels contribute to vascular endothelial dysfunction, oxidation of low-density lipoprotein (LDL) cholesterol, proliferation of smooth vascular muscle cells and coagulation abnormalities.

One wonders whether these conditions result from a too high homocysteine level or a too low folate status?

The evidence for the usefulness of folate in the prevention of NTDs is certainly the most convincing. When taken periconceptually, folate supplementation reduces the risk of NTDs substantially. Women carrying fetuses affected by NTDs have been shown to have reduced plasma levels of folate and vitamin B₁₂. Additionally, inadequate folate status may be an important risk factor for a number of chronic diseases as well as some congenital malformations such as cancer, heart disease and depression. Genetic factors contribute to the folate status and metabolism that leaves part of the population at an increased risk of a variety of clinical conditions.

It appears necessary to change from the idea of dietary sufficiency to that of folate supplementation if these benefits are to be realised.

The addition of folate to flour in the USA has resulted in a 20% reduction in the incidence of NTDs.

'Vitamin E's 80th birthday: A many-sided life with some ambiguous facets', presented by *Professor Angelo Azzi, University of Bern, Switzerland*, quoted epidemiological studies that have indicated a role for vitamin E in preventing the progression of atherosclerosis and cancer, versus intervention trials that have produced some contradictory results indicating strong protection in some cases and no significant effect in others.

Apart from its protective role against free radical damage, vitamin E can exert additional biological functions independent of its antioxidant/radical scavenging ability. The Roman god Janus, shown on ancient coins as having two faces in one body, has inspired the new designation of 'Janus molecules' for these substances. This new biochemical face of vitamin E was first described in 1991, with the inhibitory effect on cell proliferation

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and protein kinase C activity. Now, after a decade, this non-antioxidant role of vitamin E is a well-established concept, reported in several authoritative studies on signal transduction and gene regulation. Alpha-tocopherol exerts with one Janus face a protection against radical damage. To obtain this protection some alpha-tocopherol is damaged. The diminished concentration of cell alpha-tocopherol uses its second Janus face by a non-antioxidant mechanism to regulate cell signalling and gene expression. A better knowledge of the molecular events will help in selecting the parameters for clinical intervention studies, such as population type, dose response effects and possible synergism with other compounds.

Dr Ueli Moser, Roche Vitamins, Europe, current President of the Swiss Society for Nutrition Research, entitled his presentation 'Polyunsaturated fatty acids: Mechanistic aspects and importance for health'. Both linoleic acid and alpha-linolenic acid are essential for normal growth and are precursors of the functional long-chain polyunsaturated fatty acids (PUFAs) which the organism can synthesise in various tissues. It has become evident that the transformation of alpha-linolenic acid to eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) is not sufficient to reach the levels required for health benefits, and therefore it is necessary to increase the intake of these particular essential fatty acids.

Long-term daily supplementation of 1 g of DHA plus EPA, which is equivalent to that found in 100 g of fatty fish, lowers the risk of CHD by reducing the blood clotting tendency, lowers the plasma triglyceride levels, decreases the risk of cardiac arrhythmias, and reduces the risk of sudden death by as much as 45%.

The American Heart Association recommends that 30% of total dietary energy should come from fat, 10% of which should be supplied by PUFAs with an omega-6/omega-3 ratio of 5 : 1. During a workshop on the essentiality of omega-6 and omega-3 fatty acids in Bethesda in April 1999, a daily intake of 0.3% of the total energy from EPA plus DHA was recommended. Assuming a daily requirement of 2 000 kcal, this amounts to 0.65 g EPA plus DHA per day. This is in agreement with dietary guidelines revised in 2000 by the American Heart Association together with the qualified health claim issued by the Food and Drugs Administration (FDA) on 31 October 2000.

Since the majority of the population cannot achieve this intake of EPA plus DHA via diet alone, alternative food sources have to be considered.

Additional benefits of adequate intake of DHA plus EPA have been shown to positively influence brain and certain aspects of immune function.

'Vitamin A: From deficiency to adequacy' was presented by *Dr Clive West of Wageningen University in the Netherlands*.

Vitamin A deficiency affects young children and pregnant and lactating women, influencing 500 million people

worldwide by impacting on mortality and morbidity in these vulnerable groups. Vitamin A supplementation has been shown to have a positive effect on measles complications, reversal of anaemia in pregnant women, and general immunity and growth, as well as among individuals with AIDS.

Dr West highlighted the importance of determining bioavailability (proportion of ingested nutrient available for metabolic processes and storage) and bioconversion (proportion of bioavailable nutrient converted to active form of nutrient) of beta-carotene to retinol from commonly consumed foods. The US Institute of Medicine declared on 12 January 2001 that 12 µg dietary beta-carotene is equivalent to 1 µg retinol, referred to as the 'retinol activity equivalence' or RAE. This recommendation impacts on the amount of beta-carotene-containing foods individuals will need to eat in order to reach the recommendations for retinol consumption.

Controlling vitamin A deficiency implies reducing the requirements for vitamin A through public health measures, improving the dietary intake, advocacy of pharmaceutical supplementation, and food-based approaches such as breast-feeding, increased intake of foods of animal origin, increasing the beta-carotene content of certain foods, developing foods with a high vitamin A content via processing and genetic modification, and finally food fortification with vitamin A.

Dr Nelia Steyn from the MRC in Cape Town summarised and presented the most important aspects of the 1999 National Food Consumption Survey (NFCS) — 'Dietary intake of 1 - 9-year-old children in South Africa'.

One of the primary objectives of the NFCS was to assess the usual nutrient and food consumption of children in order to make recommendations regarding vehicles for food fortification. The results of this survey indicated that 45% of South African children have energy intakes of less than two-thirds of the RDA. A high percentage of children, particularly those aged 1 - 3 years, also had inadequate intakes (less than two-thirds of the RDA) of calcium, iron, zinc, folate, vitamin A, thiamin, niacin, riboflavin, and vitamin B₆. The food items most commonly consumed were maize meal, white sugar, tea, whole milk and bread. It is recommended that a variety of these foods be used as the vehicles for fortification with the following micronutrients — calcium, iron, zinc, folate, vitamin A, thiamin, niacin, riboflavin, and vitamin B₆.

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