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SACN Secretariat
Room 808c
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WC2B 6NH

6 April 2005

Dear Sir

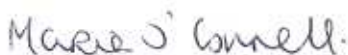
The MRC Collaborative Centre for Human Nutrition Research (HNR) thanks SACN for its invitation to comment on their review of dietary advice on Vitamin A.

This consultation was prepared by Ms Claire Mac Evilly and myself on behalf of senior staff at HNR and does not necessarily reflect the view of the Medical Research Council. HNR scientists have a particular interest in micronutrients and health, so our comments reflect this perspective.

We hope that these comments will make a useful contribution to this consultation and we would be pleased to offer additional input on specific issues should this be required.

If you have any queries regarding this response then, in the first instance, please address them to me at the address below.

Yours sincerely

A handwritten signature in black ink that reads 'Maria O'Connell'.

Dr Maria O'Connell
Senior Research Scientist
Deputy Head of Micronutrient Status Research Section

A response from MRC Human Nutrition Research to the SACN Review of Dietary Advice on Vitamin A

April 2005

MRC Collaborative Centre for Human Nutrition Research (hereafter HNR) was established in 1998 to advance knowledge of the relationships between human nutrition and health by providing a national centre of excellence for the measurement and interpretation of biochemical, functional and dietary indicators of nutritional status and health. HNR conducts basic research in relevant areas, focusing on optimal nutritional status and nutritional vulnerability in relation to health, including the development of innovative methodologies. HNR responds to the strategic priorities of the wider scientific community by conducting research projects, within the scope of HNR's activities, in collaboration with, and on behalf of: other MRC establishments and groups, Government departments, industry, national and international agencies, universities, research foundations and charitable organisations. HNR also acts as an independent, authoritative source of scientific advice and information on nutrition and health in order to foster evidence-based nutrition policy and practice. In light of the work carried out at HNR and the expertise of our staff, our comments are confined primarily to the role of nutrition in securing good health for the whole population.

HNR welcomes the opportunity to comment on this review of current dietary advice on vitamin A and the consideration of strategies to reduce retinol intake. We recognise that the knowledge base for establishing requirements and safe levels of intake is somewhat limited, however we note the need to provide appropriate dietary advice in the context of a healthy, balanced diet and support SACN's efforts to improve this important area of public health nutrition.

We agree with the recommendations that have been made by the Committee, based on the evidence to date. However there are a number of areas that we feel require further clarification.

Terminology and Definitions

We found the varying uses of the terms vitamin A, preformed retinol, preformed vitamin A, total vitamin A and retinol equivalents confusing, especially in Section 1 (current government recommendations on vitamin A intake), Section 2 (Introduction) and in the description of the bone studies (Section 4).

Since retinyl esters are present in food and supplements, it would be helpful to define preformed vitamin A as retinol and retinyl esters throughout, as defined in the Safe Upper Levels for Vitamin and Minerals report. It would also be helpful to clarify the term total vitamin A in the bone studies by mentioning, where possible, which form of vitamin A was measured in the study, ie retinol or β carotene or both. In addition, it would also be useful to define the term retinol equivalent on page 1.

In defining carotenes (p19 Footnote¹³), the correct definition is the sum of the β carotene and half of the α carotene and β cryptoxanthin.

Teratogenicity

We recognize that the report refers mainly to the effects of vitamin A on bone health. However, it may be viewed that it does not give appropriate acknowledgement to the teratogenic effects of vitamin A and therefore it may be useful to state in para 8 that the evidence for teratogenicity has been previously reported in the Safe Upper Limits document.

Study limitations

For consistency, a paragraph on limitations of the study should be included in all bone studies in Section 4. These have been omitted from the first three bone mineral density studies (Sowers and Wallace 1990, Melhus et al 1998, Ballew et al 2001). Some limitations of these studies include: measurement of only one bone site, the radius, in the Sowers and Wallace study, as bone mineral status at this site may not reflect status at other sites; in the Melhus study, retinol intake was not significantly associated with bone mineral density (BMD) in the univariate analysis but was significantly associated in the multivariate analysis and diet records were used rather than food frequency questionnaire to measure retinol intake; and the measurement of serum retinyl esters rather than serum retinol in the Ballew study. Additional limitations of the Houtkooper study may include the sample size (n=66) and all subjects taking calcium supplements, as a result of the study being part of a randomized trial.

Bone Measurement

Although most studies reviewed measured BMD, Freudenheim et al (1986) analysed bone mineral content (BMC) and Sowers and Wallace (1990) measured bone mass. It would therefore be helpful to emphasise these differences in Section 4 and Annex 5.

In addition, the evidence suggests that BMD and BMC measurements are limitations of cross-sectional studies and that BMD measurements may be more useful for prospective studies. It may be helpful to state which bone measurements are more useful for cross-sectional studies, ie size-adjusted BMC.

Additional information

For consistency, it would be helpful to include β carotene intakes where possible in the tabulated studies in Annex 5 and the heading changed to include this. β carotene intakes are included in the Houtkooper and Promislow studies on bone mineral density but are omitted from the earlier studies.

The high intakes of retinol may be a concern for the elderly as liver consumption and bone fracture are higher in this group. However, it is also important to include

reference to the importance of vitamin A in the elderly, for example in vision (para 131).

Additional nutrients that have been positively associated with bone health and should be added include vitamin C, potassium and silicon (para 31).

The Evidence Base

The Committee has set out clearly the framework within which the evidence has been examined. However, there is a need for more scientific research in specialised aspects such as the effects of vitamin A on bone and interactions with other nutrients. In particular, we would stress the importance of ongoing national surveys for surveillance and monitoring purposes. We welcome moves towards a rolling programme of surveys, more responsive to public health imperatives and with the capacity to evaluate the impact of changes in public health policy. Support and input from SACN to a programme of national surveys is essential. Finally, we trust that the recommendations will be reviewed as further evidence becomes available.