

Scientific Advisory Committee on Nutrition

Scientific Advisory Committee on Nutrition & COMMITTEE ON TOXICITY OF CHEMICALS IN FOOD CONSUMER PRODUCTS AND THE ENVIRONMENT

FISH INTER-COMMITTEE SUB-GROUP
Aviation House, Conference Room 1
21st November 2003

DRAFT MINUTES

Members

Professor Alan Jackson (Chair)
Dr Tim Key
Professor Christine Williams

Secretariat

Dr Alison Tedstone (FSA)
Dr Sheela Reddy (DH)
Dr Peter Sanderson (FSA)

1. The Chair defined the purpose of the meeting: to evaluate the health benefits of oily fish and fish oil consumption. The Committee requested several minor amendments to the draft papers presented: additional columns to be inserted into the table of randomized controlled trials in the paper on effects of fish consumption on risk of cardiovascular disease; and not to use the word effect when describing results from observational studies. The minutes from the previous meeting were approved prior to approval at the joint committee.

Action: Secretariat

The effect of fish consumption on risk of cardiovascular disease

2. The draft paper describing the effects of fish consumption on risk of cardiovascular disease (CVD) was discussed. It was noted that the results of the recently published Diet and Reinfarction Trial (DART) 2, Burr *et al*, 2003, were contrary to the existing body of evidence: an adverse effect of fish consumption, and particularly fish oil supplementation, was observed upon cardiovascular events (especially sudden cardiac death) in men with angina.
3. The Committee requested further information from the authors and other international experts. The original DART trial, Burr *et al*, 1989, was accepted as valid by Committee on Medical Aspects of Food Policy in their 1994 report on the Nutritional Aspects of Cardiovascular Disease, and as the Committee could find no reason for DART2 to be invalid, it was felt to be important that

the DART2 trial should be considered in depth.

Action: Secretariat

4. The Committee requested further changes to the CVD paper – particularly regarding the tabular presentation of the disease outcome randomized controlled trials (RCT). The Bucher *et al* (2002) meta-analysis of disease outcome RCTs was discussed, and details of RCTs not included in the Committee paper on CVD were requested to be included. Members agreed to provide comment on which RCTs should be included in the risk assessment.

Action: Secretariat

Dose-response nature

5. The dose-response nature of the relationship between fish consumption and risk of CVD, and that it might be different in populations of differing risk of CVD, was discussed.
6. It was noted that the UK population is, relative to other countries, at high risk of CVD and this might affect the dose-response relationship. Also, sub-groups of the population within the UK exhibit differing degrees of risk.
7. The nature of the evidence provided by the RCTs was for short term effects of fish consumption or fish oil supplementation (usually 2-3 yr), whereas the evidence provided from prospective studies was for long term effects (e.g. effects not being seen until 10 yr follow-up). As CVD is a cumulative experience the longer the follow-up period the more likely it was to see disease outcomes in prospective studies.
8. The dietary assessment used in prospective studies was discussed. Food frequency questionnaires (FFQ) were regarded as a reasonable tool to determine habitual dietary intakes of fish; however, the diet was assessed at the start of the study and assumed to be representative of the habitual diet, which may not be the case. Fatty acid composition analyses of blood were regarded as a good indicator of fish intake; however different studies measured different blood compartments, making comparisons difficult.
9. The Committee noted that to accept the conclusions of different investigations it needed to be aware of the methodological limitations and determine whether these were acceptable, e.g. when comparing different populations, exposures, outcomes etc.
10. In prospective studies where fatty acid composition analyses of blood or blood compartments were determined a positive relationship with no plateau was observed; whereas, when the dietary assessment was by FFQ a positive relationship with a plateau was often seen.
11. Coronary heart disease (CHD) has a long aetiology where atherosclerosis is a slow process and thrombosis and arrhythmias can result in acute events. An

accumulation of factors leads to CHD. Platelet aggregation can be modulated following two to three weeks following fish oil supplementation.

12. There are, potentially, different dose-response relationships for different effects, e.g. on atherogenicity, platelet aggregation, and arrhythmias. The antithrombotic effects are observed at relatively high doses (in healthy subjects), although a few trials have reported antithrombotic effects at doses of 1g/d n-3 long chain polyunsaturated fatty acids (PUFA).
13. It was noted that platelet aggregation measures are not very sensitive and that they need to be controlled for other influences. In disease populations it may be that an effect would be more pronounced.
14. It is unlikely, however, that one factor is responsible for the observed effect of fish consumption on risk of CVD. Profound effects on measurable risk factors are not observed at low doses of fish oil supplementation.
15. It was agreed that consensus reports on these issues need to be examined, and the extent of consensus statements on dose-response relationship, long term effects etc. needs to be found out.

Action: Committee and Secretariat

Sources of n-3 PUFA other than fish

16. The issue of the interconvertability of n-3 PUFA was discussed and whether it matters if a person does not consume preformed long chain PUFA (eicosapentaenoic and docosahexaenoic acid – EPA & DHA). The conversion of EPA to DHA is a complex step that is tightly regulated. The conversion of α -linolenic acid (ALNA) to EPA and DHA has been examined in at least two stable isotope studies. It was agreed that there is a paucity of evidence, but it appears that ALNA is converted to EPA at a ratio of approximately 8:1; however only limited conversion to DHA was demonstrated. There was no identified conversion of labelled precursors to DHA in membranes.
17. It was suggested that conversion of ALNA to DHA may occur at significant levels in people with a low DHA status, as DHA levels are tightly regulated. Fish oil studies demonstrate that increased dietary DHA is associated with increased cardiovascular benefit. If no dietary DHA is provided does conversion of ALNA to DHA occur? There is insufficient evidence available to comment.
18. It was noted that studies of vegan populations observed plasma levels of DHA and EPA to be 30% of those observed in the Italian population. In humans a pathway for DHA synthesis from ALNA exists, but flux appears to be variable. Is maximum flux sufficient to support the DHA requirement, e.g. in pregnant vegans? The evidence demonstrates that people consuming fish have higher DHA status. The functional consequence of a lower DHA status is not known.

19. There is need to integrate the different aspects of the evidence from the molecular all the way up to the RCTs. The uncertainties should be articulated rather than ignored.

The effects of fish consumption on growth and cognitive function

20. The draft paper on the effects of fish consumption on growth and cognitive function was discussed. It was noted that the trials investigating the effect of n-3 PUFA supplementation of formulas in preterm and term infants on neurodevelopment were difficult to conduct; and that trials in preterm and term infants need to be considered separately because of differences in physiology with maturation.
21. It was agreed that the stoichiometry of the transfer of n-3 PUFA from the mother to the fetus/infant needs to be determined. There is a substantial demand on the maternal status, particularly in the third trimester. There is a need to consider the effect of pregnancy number – are the second or third pregnancies the same as the first? Does endogenous synthesis of DHA from ALNA occur adequately to meet the needs?
22. How appropriate visual acuity measures as proxies for cognitive development was considered. It maybe more informative to examine effects on higher integrative functions. It was agreed that there is a relatively immature literature compared with the issues to be explored. It may not be possible to address the relevant issues with the evidence available. Parity issues are difficult to address.
23. The beneficial effects observed on visual acuity measures were relatively short term – no difference was observed in long-term follow-ups, although subtle differences may not be seen. The higher order tests are also complicated by other factors that can influence the outcomes, e.g. parents' education, making interpretation difficult.
24. It was agreed that the evidence supports supplementing infant formulas with n-3 PUFA in preterm infants, but the evidence for term infants is less clear.
25. The mother's capacity to maintain the supply of n-3 PUFA in the third trimester is important. The importance of the effects of diet and endogenous synthesis were discussed. It was noted that there is no information available on the mobilization from adipose depots of specific fatty acids or the effects of the size of adipose depots. The supply of DHA could be acting around the margins of requirements, especially in the second and third trimesters.
26. Behavioural effects have been observed in animal studies relative to DHA status. Pregnant women could be affected by low DHA status. It is important to determine the quantities of long chain n-3 PUFA required to assess any effects of different diets, e.g. in vegans, fish eaters etc. What are the amounts required to produce the beneficial effects observed in the preterm infant trials was queried.
27. It was agreed that two issues should be considered: the requirements for

preterm and term infant n-3 PUFA intake; and what role maternal status plays.

28. The effects of maternal n-3 PUFA status on breast milk n-3 PUFA levels were discussed. The relevance to the UK population of the WHO recommendation for breastfeeding to be continued for six months was discussed. It was agreed that the surrounding issue of adequate n-3 PUFA status needs to be considered as part of this issue and, also, the impact of extended breast feeding on maternal status and its consequences need to be considered.
29. The Committee requested that the SACN member, Anthony Williams, should be invited join the group.

Action: Secretariat

30. It was noted that as it may not be possible to undertake some of the scientific investigations that are required and there may not be enough evidence to provide a definitive risk assessment. This should be reflected in the Committee's conclusions.
31. The Chair agreed to provide modelling data to evaluate the amounts of n-3 PUFA required to be transferred from mother to fetus/infant, which will aid the determination of the importance of fish consumption and endogenous synthesis.

Action: Chair

32. The Committee will undertake a risk analysis of the evidence investigating visual acuity.

Action: Secretariat

33. The next SACN inter-committee subgroup meeting will be held on 3 March 2004.

References

Bucher HC, Hengstler P, Schindler C & Meier G. N-3 polyunsaturated fatty acids in coronary heart disease: a meta- analysis of randomized controlled trials. *Am J Med.* 2002; **112**:298-304.

Burr ML, Fehily AM, Gilbert JF, Rogers S, Holliday RM, Sweetnam PM, Elwood PC & Deadman NM. Effects of changes in fat, fish, and fibre intakes on death and myocardial reinfarction: diet and reinfarction trial (DART). *Lancet.* 1989; **2**:757-61.

Burr ML, Ashfield-Watt PAL, Dunstan FDJ, Fehily AM, Breay P, Zotos PC, Haboubi NAA & Elwood PC. Lack of effect of dietary advice to men with angina: results of a controlled trial. *Eur J Clin Nutr.* 2003; **57**:193-200