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COMMITTEE ON TOXICITY OF CHEMICALS IN FOOD, CONSUMER PRODUCTS AND THE ENVIRONMENT

Review of risks arising from the infant diet and the development of atopic and autoimmune disease: Systematic review A – exclusive/predominant breastfeeding, solid food introduction and risk of developing atopic and autoimmune disease (reserved business)

Introduction

1. The COT has been asked by the Department of Health (DH) to provide advice on the risks arising from the infant diet that are related to the development of atopic and autoimmune disease. This is in support of a review being undertaken by the Scientific Advisory Committee on Nutrition (SACN) Sub-group on Maternal and Child Nutrition (SMCN) of UK Government recommendations on breastfeeding and the introduction of solid foods into the infant diet.

2. To facilitate the COT evaluation, in March 2013 the Food Standards Agency (FSA) commissioned Imperial Consultants to conduct three separate systematic reviews to assess comprehensively and systematically the existing literature on the relationship between early dietary exposures and risk of developing atopic and autoimmune disease. The first of these reviews, systematic review A, is the subject of this paper.

3. Systematic review A examines the relationship between exclusive/predominant breastfeeding, solid food introduction and risk of developing atopic and autoimmune disease. Systematic review B examines the evidence concerning the timing of introduction of allergenic foods into the infant diet during the first year of life and risk of developing atopic and autoimmune disease. Systematic review C explores the evidence concerning the avoidance or exposure to specific dietary patterns, food groups or nutrients during infancy, pregnancy and lactation and risk of developing atopic and autoimmune disease.

4. Prior to the commissioning of the reviews, the COT were presented with proposals from the FSA on the approaches to be taken at their meetings in February 2012 and August 2012. The proposal documents from the secretariat and minutes of the COT discussions can be found on the COT website[1,2,3,4]. Specifically, Members requested that the review should extend to the risks of atopic disease in general rather than just looking at food allergy and that the recent COT reviews on peanut

[1] http://cot.food.gov.uk/sites/default/files/cot/tox201203.pdf
[2] http://cot.food.gov.uk/cotmtgs/cotmeets/cotmeet2012/cotmeet7feb2012/cotmins7feb2012
[3] http://cot.food.gov.uk/sites/default/files/cot/tox201227.pdf
[4] http://cot.food.gov.uk/sites/default/files/cotfinalmins11sept2012.pdf

avoidance and timings for introduction of gluten would not form part of the new systematic reviews.

5. Systematic review A is now complete and the results are presented to the Committee for discussion. This item is to be discussed as reserved business because the results of systematic review A have yet to be accepted for publication in a peer-reviewed journal. Annexes 1-8 contain the final reports for systematic review A which are yet to be published and will therefore be withheld from publication on the Food Standards Agency's website at this time.

Background

6. Diseases such as atopic asthma, atopic eczema, allergic rhinitis and food allergy have increased in prevalence in Westernised societies and are now the leading cause of chronic illness in children and young adults living in the UK (Nwaru et al, 2014; Gupta et al, 2007). Autoimmune diseases such as type I diabetes mellitus and Crohn's disease also appear to have increased in prevalence in some countries (Bach et al, 2002).

7. The relationship between maternal and infant dietary exposures and a child's risk of developing any of the common atopic and/or autoimmune diseases has been an area of considerable scientific uncertainty and debate in recent years. The last review of the evidence relating to dietary exposure to allergenic foods in early life and risk of developing atopic disease was completed by COT in 2008[5]. More recently, COT together with SACN reviewed the evidence relating to the introduction of gluten into the infant diet and risk of developing coeliac disease and type I diabetes mellitus[6]. Since then, there have been several studies published on the subject of sensitisation and allergy to foods in relation to early life dietary exposures, some of these funded by the Food Standards Agency.

8. There is now a need to re-assess the current state of scientific knowledge in this area and, based on the available evidence, to re-consider whether current UK Government advice remains appropriate.

Current UK advice

9. The UK Departments of Health currently advise that breastmilk provides all the nutrients an infant needs up to six months of age and recommend exclusive breastfeeding up to six months of an infant's life. It is recommended that solid foods are introduced at about six months of age, and that breastfeeding continues beyond this time, together with appropriate types and amounts of solid foods. Infant formulae may be used as an alternative when mothers do not breastfeed, or choose to supplement breastfeeding.

[5] http://cot.food.gov.uk/cotstatements/cotstatementsyrs/cotstatements2008/cot200807peanut
[6] http://cot.food.gov.uk/sites/default/files/cot/cotsacnstatementgluten201101.pdf

10. Currently in the UK, there is also advice to avoid the introduction before six months of age of commonly allergenic foods such as peanuts, nuts, seeds, hens' egg, cows' milk, soya, wheat (and other cereals that contain gluten such as rye and barley), fish and shellfish (Department of Health, 1994).

Previous COT recommendations

11. A review carried out by the COT in 2008 explored the published evidence concerning avoidance versus exposure to allergenic foods in early life and the possible influences on the development of sensitisation and clinical allergy to foods, with particular reference to peanut. The COT Statement resulting from that review concluded that the human data then available on whether dietary consumption or avoidance of allergenic foods in childhood has an impact on the development of allergy or sensitisation to allergenic foods were inconsistent. In relation to wider atopic disease, the Statement concluded that the available evidence on dietary exposure to allergenic foods in early life and the risk of developing atopic disease was inconsistent and did not provide a robust indication of either harmful or beneficial effects associated with dietary exposure.

12. Therefore the Committee recommended that the previous precautionary advice to avoid peanut consumption during pregnancy and for the mother whilst breast feeding, where there is atopy or atopic disease in family members, was no longer appropriate. In addition, the Committee recommended that:

- *in common with the advice given for all children, infants with a parent or sibling with an atopic disease should be breast-fed exclusively for around six months; and,*
- *infants and children who are allergic to peanuts or peanut products should not consume them or foods that contain them; and also recommends that:*
- *those who are allergic to peanut should seek advice from medical professionals about avoidance strategies*.

13. A review carried out by the COT together with SACN in 2011 explored the published evidence concerning the timing of introduction of gluten into the infant diet in relation to the risks of developing coeliac disease and type I diabetes mellitus, and published a joint Statement of their views. The Statement arising from that review concluded that the evidence available then provided an indication that dietary introduction of gluten-containing foods in the period up to and including the first three completed months of age is associated with an increased risk of coeliac disease. Furthermore, it was considered there was insufficient evidence to support a conclusion that the introduction of gluten into the infant diet after six completed months of age is associated with an increased risk of coeliac disease.

14. Overall, the evidence available then on the timing of introduction of gluten into the infant diet and subsequent risk of coeliac disease and type I diabetes mellitus was insufficient to support recommendations about the appropriate timing of introduction of gluten into the infant diet beyond three completed months of age, for either the general population or high-risk sub-populations. Therefore, current UK

Government advice to avoid introducing gluten into the infant diet before six months of age remained in place.

Systematic review A

15. Systematic review A has been structured around the need to address evidence relating to exclusive/predominant breastfeeding and the introduction into the diet of solid foods. This included the timing of transition from exclusive/predominant breastfeeding to partial breastfeeding in the first year of life, the total duration of breastfeeding up to two years and the timing of transition from liquid infant milk feed (i.e. breastmilk and/or infant formula) to solid food introduction in the first year of life. Systematic review A aimed to address the following research questions:

- Does the duration of exclusive/predominant breastfeeding during the first year of life influence children's future risk of atopic disease, allergic sensitisation or autoimmune disease?
- Does the total duration of breastfeeding up to two years, influence children's future risk of atopic disease, allergic disease or autoimmune disease?
- Does the timing of introduction of non-milk feeds (i.e. not breastmilk or formula milk) during the first year of life, influence children's future risk of atopic disease, allergic sensitisation or autoimmune disease?

Results of systematic review A

16. An overview of the results of systematic review A are presented in Annex 1 (overview document). The results of systematic review A have been analysed according to disease outcome (i.e. wheeze, eczema, rhino-conjunctivitis, food allergy, allergic sensitisation, type I diabetes mellitus, other autoimmune diseases). Seven separate systematic review analyses have been conducted by Imperial Consultants, the results of each of these analyses are presented in the following annexes:

- Annex 2: Breastfeeding, solid food introduction and risk of wheeze
- Annex 3: Breastfeeding, solid food introduction and risk of eczema
- Annex 4: Breastfeeding, solid food introduction and risk of rhino-conjunctivitis
- Annex 5: Breastfeeding duration, solid food introduction and risk of food allergy
- Annex 6: Breastfeeding, solid food introduction and risk of allergic sensitisation
- Annex 7: Breastfeeding, solid food introduction and risk of type I diabetes mellitus
- Annex 8: Breastfeeding, solid food introduction and risk of other autoimmune diseases

17. The final conclusions of systematic review A are detailed on page 33 of the overview document (Annex 1) and are summarised in the executive summary to that document (Annex 1, p 4-11).

18. Dr Boyle and Dr Garcia will attend the Committee meeting on the 30th June. They will present the results of systematic review A and address any questions the Committee may have. Dr Boyle hopes to submit a version of this work for publication in the peer reviewed literature and therefore the annexes will not be made publically available.

Questions on which the views of the Committee are sought

19. Members are invited to comment on systematic review A and to consider the following questions:

i. Do Members consider that the review provides evidence of a link between the duration of exclusive/predominant breastfeeding during the first year of life and subsequent development of atopic disease or autoimmune disease?

ii. Do Members consider that the review provides evidence of a link between the total duration of breastfeeding up to two years of age and subsequent development of atopic disease or autoimmune disease?

iii. Do Members consider that the review provides evidence of a link between the timing of introduction of non-milk feeds (i.e. not breastmilk or formula milk) during the first year of life and subsequent development of atopic disease or autoimmune disease?

iv. If Members consider there is evidence to support a link in any of the above cases, they are asked to comment on whether this link applies to the general population, those at increased risk of developing atopic or autoimmune disease, or both.

v. Do Members have any other comments on systematic review A or wish to raise any other matters arising from it?

Secretariat
June 2015

References

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The following annexes are attached to this report:

Annex 1 – Overview paper on exclusive/predominant breastfeeding, solid food introduction and risk of developing atopic or autoimmune disease (including Appendices 1 and 2 containing details of search strategies and Figure 1 from section 4.1 and figure 2 from section 4.2).

Annex 2 - Individual study report – Wheeze

Annex 3 - Individual study report – Eczema

Annex 4 - Individual study report – Rhino-conjuctivitis

Annex 5 - Individual study report – Food allergy

Annex 6 - Individual study report – Allergic sensitisation

Annex 7 - Individual study report – Type 1 Diabetes mellitus

Annex 8 - Individual study report – Other autoimmune diseases

Note: The Committee were provided with a pre-publication copy of the work of Imperial Consultants. This was received in confidence and will not be released when this paper becomes publicly available. As indicated, above the work will be submitted for publication following peer review.