

VIEWPOINT ARTICLE

What if it is the other way around? Early introduction of peanut and fish seems to be better than avoidance

Göran Wennergren (goran.wennergren@pediat.gu.se)

Department of Paediatrics, University of Gothenburg, Queen Silvia Children's Hospital, Gothenburg, Sweden



Keywords

Early introduction, Eczema, Fish, Food allergy, Oral tolerance induction, Peanut

Correspondence

Göran Wennergren, MD, PhD, Department of Paediatrics, University of Gothenburg, Queen Silvia Children's Hospital, SE-416 85 Gothenburg, Sweden.

Tel: +46 (0)31-343-46-12 |

Fax: +46 (0)31-40-24-24 |

Email: goran.wennergren@pediat.gu.se

Received

20 February 2009; revised 2 April 2009; accepted 6 April 2009.

DOI:10.1111/j.1651-2227.2009.01342.x

Abstract

For many years, the advice to prevent food allergy was to postpone the introduction of allergens like egg, fish and peanut. However, elimination of food allergens during pregnancy and infancy failed to prevent food allergy. Instead, several studies indicate that early introduction of food like fish and peanuts may be beneficial. The most compelling illustration of this has been presented for peanuts. The prevalence of peanut allergy is lower in children in Israel than in the UK, despite introduction of peanut during infancy in Israel. Other studies have reported that early introduction of fish reduced the risk of allergic sensitization and allergic diseases like eczema.

Conclusion: Early introduction rather than avoidance may be a better strategy for the prevention of food allergy. The mechanism may be that early introduction of food allergens during infancy might induce tolerance, thereby preventing the development of allergy.

For many years, the advice to prevent allergies, particularly food allergy, was to avoid the allergens in question. For example, during 1979–2001 the guidelines of the Swedish Society for Paediatric Allergology recommended that fish and eggs should not be introduced the first year of life in infants with high hereditary risk of allergy. Also, peanuts should be avoided during the first year of life. Paediatric allergists all over the Western world gave similar advice (1). The intention was undoubtedly good, but evidence was scarce. Now such advice has been removed from the Swedish guidelines since evidence supporting them was insufficient (2). Actually, studies eliminating food allergens during pregnancy, lactation and infancy have failed to prevent IgE-mediated food allergy (3,4).

MAYBE IT IS THE OTHER WAY AROUND

Several studies indicate that instead it may be the other way around. Early introduction of food like fish and peanuts may be beneficial. The most compelling illustration of this was recently presented for peanuts. In Israel, peanut-containing food is introduced already during the first year of life. Many Israeli infants are given peanut-flavoured snacks, for example Bamba, when they are as young as 6 months of age (5).

Despite this, or possibly due to this, the rate of peanut allergy is low.

EARLY INTRODUCTION OF PEANUT AND LOWER ALLERGY PREVALENCE

In a recent study by du Toit et al., the prevalence of peanut allergy was compared between Jewish children in the UK and Israel (6). The UK and Israel are both industrialized countries with high levels of atopy. The questionnaire-determined prevalence of peanut allergy in the UK in children 4–18 years was 1.85% (73/3943) while it was 0.17% (8/4657) in Israel ($p < 0.001$). After adjusting for atopy, age and food allergy, the relative risk for peanut allergy in the UK compared to Israel was as high as 5.8 (95% CI 2.9–11.8) for all children and 9.8 (95% CI 3.1–30.5) for primary school children. In contrast, the adjusted relative risks for egg and milk allergy were only 1.8 (95% CI 1.0–3.1) and 1.3 (95% CI 0.9–1.9), respectively.

The most obvious difference in the diet of the infants in the UK and Israel was seen in the introduction of peanuts (6). Israeli infants were introduced to peanut during early weaning. They continued to eat peanut more frequently and in higher amounts than UK infants, who avoided peanuts

in line with recommendations from the health authorities. Differences regarding introduction of cow's milk and duration of breastfeeding were small. Cow's milk was introduced earlier in Israel, while the rate of exclusive breastfeeding was higher and breastmilk was given longer in the UK. Different methods of preparing peanuts were unlikely to account for the different rates in peanut allergy. Commonly consumed peanut-containing foods in both countries are derived from roasted peanut butter.

INDUCTION OF TOLERANCE?

The findings by du Toit et al. raise the question whether early and frequent ingestion of high doses of peanut protein during infancy might induce tolerance and thereby prevent the development of peanut allergy. As the authors point out, their findings suggest that early introduction rather than avoidance of peanut in infancy is the better strategy for the prevention of peanut allergy. The findings are in consonance with experimental findings in mice where oral tolerance was induced by high doses of peanut, while low doses of peanut protein tended to induce sensitization (7).

Is this the only example of beneficial effects of early introduction of food that earlier was thought should be avoided? No. Kull and coworkers in the Stockholm BAMSE study found that regular fish consumption before age 1 year was associated with a reduced risk of allergic disease and sensitization to food and inhalant allergens during the first 4 years of life (8). Recently, another Swedish birth cohort study, Infants of Western Sweden, reported that early introduction of fish (i.e. before 9 months of age) reduced the risk of eczema (9). Furthermore, the age at which cow's milk or eggs were introduced did not affect the risk of eczema. Neither did early introduction of milk or eggs increase the risk of wheezing disorder (10).

It should be pointed out that the normal, physiological immune response to oral administration of food proteins is a state of systemic immunological hyporesponsiveness, that is oral tolerance (11). Interestingly, there is an increasing immunological knowledge of the mechanisms leading to induction of oral tolerance instead of the development of hypersensitivity responses to food antigens (12–14).

Results from large birth cohort studies like the German GINI study have not supported that a delayed introduction of solids beyond the 4th month, or a delayed introduction of the most potentially allergenic solids beyond the 6th month, decreases the prevalence of eczema (15). Delayed introduction of solids beyond 4 or 6 months was not associated with the prevention of asthma, allergic rhinitis or allergic sensitization in the German LISA study (16,17). Along the same lines, the Australian Childhood Asthma Prevention Study did not find that later introduction of solid foods prevented the onset of asthma, eczema or allergic sensitization by age 5 years (18). A recent report from the American Academy of Pediatrics concluded that there is 'little evidence that delaying the timing of the introduction of complementary foods beyond 4 to 6 months of age prevents the occurrence of atopic disease' (19). An Australian report by Prescott et al.

in 2008 concluded that 'there is mounting concern that the current recommended practice of delaying complementary foods until 6 months of age may increase, rather than decrease, the risk of immune disorders' (20). The report found that tolerance to food allergens appeared to be driven by regular, early exposure to those food proteins during a 'critical early window' of development. The authors concluded that current evidence suggests that this time window most likely is between 4 and 6 months. Delayed exposure beyond this period may increase the risk of food allergy (20).

IMPORTANT TO DISCRIMINATE BETWEEN PREVENTION AND TREATMENT

Severe allergic manifestations can occur in children with allergic sensitization to peanuts. Therefore, it should be emphasized that it is important to discriminate between prevention of food allergy and treatment of children with allergic sensitization. At 4 years of age, allergic sensitization towards peanut was the most common food allergy among children with food hypersensitivity in the BAMSE study (21).

The risk of cross-reactivity between peanut and pea and soy is well known (22). Less well known is the cross-reactivity between peanut and lupine (23). Lupine flour is protein rich and is increasingly used in food production in Europe. Peanut allergic subjects may experience a severe allergic reaction when eating for example bread containing lupine flour. Lupine allergy can occur either together with peanut allergy or separately (24,25), although sensitization to lupine is not synonymous with clinical lupine allergy (25).

CONCLUSIONS

In conclusion, the prevalence of peanut allergy is lower in children in Israel than in the UK, despite introduction of peanut during infancy in Israel. Other studies have reported that early introduction of fish reduced the risk of allergic sensitization and allergic diseases like eczema. Early introduction rather than avoidance may be a better strategy for the prevention of food allergy. The mechanism may be that early introduction of food allergens during infancy might induce tolerance, thereby preventing the development of allergy.

References

1. Zeiger RS. Food allergen avoidance in the prevention of food allergy in infants and children. *Pediatrics* 2003; 111: 1662–71.
2. The Swedish Society for Paediatric Allergology. Available at: www.barnallergisektionen.se (accessed May 1, 2009).
3. Fälth-Magnusson K, Kjellman NI. Allergy prevention by maternal elimination diet during late pregnancy—a 5-year follow-up of a randomized study. *J Allergy Clin Immunol* 1992; 89: 709–13.
4. Zeiger RS, Heller S. The development and prediction of atopy in high-risk children: follow-up at age seven years in a prospective randomized study of combined maternal and infant food allergen avoidance. *J Allergy Clin Immunol* 1995; 95: 1179–90.
5. Couzin J. Testing the line between too much and too little. *Science* 2007; 318: 740–1.

6. Du Toit G, Katz Y, Sasieni P, Mesher D, Maleki SJ, Fisher HR, et al. Early consumption of peanuts in infancy is associated with a low prevalence of peanut allergy. *J Allergy Clin Immunol* 2008; 122: 984–91.
7. Strid J, Thomson M, Hourihane J, Kimber I, Strobel S. A novel model of sensitization and oral tolerance to peanut protein. *Immunology* 2004; 113: 293–303.
8. Kull I, Bergström A, Lilja G, Pershagen G, Wickman M. Fish consumption during the first year of life and development of allergic diseases during childhood. *Allergy* 2006; 61: 1009–15.
9. Alm B, Erdes L, Möllborg P, Pettersson R, Norvenius G, Åberg N, et al. Early introduction of fish decreases the risk of eczema in infants. *Arch Dis Child* 2009; 94: 11–15.
10. Alm B, Erdes L, Möllborg P, Pettersson R, Åberg N, Norvenius G, et al. Neonatal antibiotic treatment is a risk factor for early wheezing. *Pediatrics* 2008; 121: 697–702.
11. Weiner HL. Oral tolerance, an active immunologic process mediated by multiple mechanisms. *J Clin Invest* 2000; 106: 935–7.
12. Karlsson MR, Rugtveit J, Brandtzaeg P. Allergen-responsive CD4+CD25+ regulatory T cells in children who have outgrown cow's milk allergy. *J Exp Med* 2004; 199: 1679–88.
13. van Wijk F, Wehrens EJ, Nierkens S, Boon L, Kasran A, Pieters R, et al. CD4+CD25+ T cells regulate the intensity of hypersensitivity responses to peanut, but are not decisive in the induction of oral sensitization. *Clin Exp Allergy* 2007; 37: 572–81.
14. van Wijk F, Nierkens S, de Jong W, Wehrens EJ, Boon L, van Kooten P, et al. The CD28/CTLA-4-B7 signaling pathway is involved in both allergic sensitization and tolerance induction to orally administered peanut proteins. *J Immunol* 2007; 178: 6894–900.
15. Filipiak B, Zutavern A, Koletzko S, von Berg A, Brockow I, Gröbl A, et al. Solid food introduction in relation to eczema: results from a four-year prospective birth cohort study. *J Pediatr* 2007; 151: 352–8.
16. Zutavern A, Brockow I, Schaaf B, Bolte G, von Berg A, Diez U, et al. Timing of solid food introduction in relation to atopic dermatitis and atopic sensitization: results from a prospective birth cohort study. *Pediatrics* 2006; 117: 401–11.
17. Zutavern A, Brockow I, Schaaf B, von Berg A, Diez U, Borte M, et al. Timing of solid food introduction in relation to eczema, asthma, allergic rhinitis, and food and inhalant sensitization at the age of 6 years: results from the prospective birth cohort study LISA. *Pediatrics* 2008; 121: e44–52.
18. Mührshahi S, Ampon R, Webb K, Almqvist C, Kemp AS, Hector D, et al. The association between infant feeding practices and subsequent atopy among children with a family history of asthma. *Clin Exp Allergy* 2007; 37: 671–9.
19. Greer FR, Sicherer SH, Burks AW; American Academy of Pediatrics Committee on Nutrition; American Academy of Pediatrics Section on Allergy and Immunology. Effects of early nutritional interventions on the development of atopic disease in infants and children: the role of maternal dietary restriction, breastfeeding, timing of introduction of complementary foods, and hydrolyzed formulas. *Pediatrics* 2008; 121: 183–91.
20. Prescott SL, Smith P, Tang M, Palmer DJ, Sinn J, Huntley SJ, et al. The importance of early complementary feeding in the development of oral tolerance: concerns and controversies. *Pediatr Allergy Immunol* 2008; 19: 375–80.
21. Östblom E, Wickman M, van Hage M, Lilja G. Reported symptoms of food hypersensitivity and sensitization to common foods in 4-year-old children. *Acta Paediatr* 2008; 97: 85–90.
22. Sicherer SH. Clinical implications of cross-reactive food allergens. *J Allergy Clin Immunol* 2001; 108: 881–90.
23. Moneret-Vautrin DA, Guérin L, Kanny G, Flabbee J, Frémont S, Morisset M. Cross-allergenicity of peanut and lupine: the risk of lupine allergy in patients allergic to peanuts. *J Allergy Clin Immunol* 1999; 104: 883–8.
24. Peeters KA, Nordlee JA, Penninks AH, Chen L, Goodman RE, Bruijnzeel-Koomen CA, et al. Lupine allergy: not simply cross-reactivity with peanut or soy. *J Allergy Clin Immunol* 2007; 120: 647–53.
25. Lindvik H, Holden L, Løvik M, Cvancarova M, Halvorsen R. Lupin sensitization and clinical allergy in food allergic children in Norway. *Acta Paediatr* 2008; 97: 91–5.