

Maternal and infant diets for prevention of allergic diseases: Understanding menu changes in 2008

Scott H. Sicherer, MD,^a and A. Wesley Burks, MD^b *New York, NY, and Durham, NC*

In 2000, the American Academy of Pediatrics (AAP) Committee on Nutrition published recommendations aimed at minimizing the risk of atopic diseases in infants considered high-risk.¹ The committee noted that conclusive studies were not available for making definite recommendations, but they advised avoidance of certain foods by pregnant and breast-feeding women as well as by infants and young children. This year, the AAP's Committee on Nutrition and Section on Allergy and Immunology published an updated Clinical Report reviewing recent and historical data regarding the impact of nutritional interventions on the development of atopic disease in infants and children.² Included in the report are revised statements that replace the former recommendations. In this Editorial, we review the updated report, compare it to recommendations from other professional societies, and entertain some of the vexing issues that allergists must consider as we advise patients and primary care physician colleagues. We do not attempt an extensive review of these topics, because there are multiple excellent reviews and committee reports³⁻¹¹; however, we incorporate pertinent studies from the past year.

WHAT'S SIMILAR

The 2008 report presents evidence affirming several previous recommendations that are relatively easy for parents to follow. For example, exclusive breast-feeding for at least 4 months (with a goal of 6 months) versus feeding with a standard cow's milk or soy formula is considered beneficial to delay or prevent atopic dermatitis and milk allergy. If supplementation during that period

is needed, then hypoallergenic formulas such as extensive casein hydrolysates, or possibly a less allergenic formula such as a partial whey hydrolysate, is considered beneficial. Roughly similar to the 2000 report, solids are to be avoided until 4 to 6 months of age.

WHAT'S NEW

A subtle difference in the updated report is that "high risk" infants are defined as those with at least 1 parent or sibling with a documented atopic disease, which is less stringent than the 2000 report and is more similar to definitions in European professional societies' recommendations (Table I). A major difference of the new report is that it avoids making recommendations. Instead, statements about possible dietary changes are made along with evidence (or lack thereof) about efficacy. The new report specifically advises the reader that inadequate study design or a paucity of data limits the ability to draw firm conclusions regarding pregnancy and lactation avoidance diets and the timing of introducing specific "allergenic" complementary foods. It also warns that lack of proven efficacy does not equate to an approach being disproven. Within this context, several of the previous "recommendations" are relegated to "lack of evidence" as summarized in Table I. As noted, the new AAP report is very similar to past and current "recommendations" from European professional groups.^{8,9,11,12}

The following is a summary of data highlighted in the AAP report, with consideration of practical issues and more recent studies.

DIET OF PREGNANT WOMEN

A Cochrane database meta-analysis of 4 clinical studies concluded that antigen avoidance during pregnancy is unlikely to reduce the child's risk of developing atopic disease, and dietary restrictions could adversely affect maternal or fetal nutrition.¹³ Although the AAP previously suggested pregnant women with atopy risks avoid peanuts, a subsequent study found no evidence of prenatal sensitization from maternal consumption of peanuts.¹⁴ The AAP report synthesizes these available data, concluding a lack of evidence for maternal pregnancy restriction diets.² It should be appreciated that studies have not been undertaken specifically to evaluate exclusion of peanut in atopy "high risk" pregnancies. Recent publications revealed that very few women in the United Kingdom followed dietary peanut exclusion advice, and an effect, positive or negative, was not detectable (although too few evaluable subjects and the observational nature of the reports reduce the ability to make firm conclusions).^{15,16} Additional recent studies about pregnancy diets reveal that components other than specific allergens, such as fats, may influence atopy outcomes.^{17,18}

From ^athe Department of Pediatrics, Division of Allergy and Immunology, Mt Sinai School of Medicine, New York; and ^bthe Department of Pediatrics, Division of Allergy and Immunology, Duke University Medical Center, Durham.

Disclosure of potential conflict of interest: S. H. Sicherer has consulting arrangements with the Food Allergy Initiative; has received honoraria from the American Academy of Allergy, Asthma & Immunology; has received research support from the National Institutes of Health, National Institute of Allergy and Infectious Diseases, and the Food Allergy Initiative; and has served as a member of the American Academy of Pediatrics and Food Allergy and Anaphylaxis Network. A. W. Burks has consulting arrangements with ActoGeniX NV, Novartis, McNeil Nutritionals, and Mead Johnson; owns stock in Allertein and MastCell, Inc; is on the advisory board for Dannon Co Probiotics; is on the speakers' bureau for EpiPen/Dey; is on a data monitoring committee for Genentech; is on an expert panel for Nutricia; has received research support from the National Institutes of Health, Food Allergy and Anaphylaxis Network, Gerber, and Mead Johnson; has served as an expert witness in food allergy litigation; and has served as a member of the Food Allergy and Anaphylaxis Network, American College of Allergy, Asthma & Immunology, the National Institutes of Health, and the Journal of Allergy and Clinical Immunology.

Received for publication May 5, 2008; accepted for publication May 8, 2008.

Reprint requests: A. Wesley Burks, MD, Professor and Chief, Pediatric Allergy and Immunology, Duke University Medical Center, Durham, NC 27710. E-mail: wesley.burks@duke.edu.

J Allergy Clin Immunol 2008;■■■:■■■-■■■.
0091-6749/\$34.00

© 2008 American Academy of Allergy, Asthma & Immunology
doi:10.1016/j.jaci.2008.05.019

TABLE I. Dietary prevention recommendations/comments from several professional organizations

Definitions/interventions	Group/publication			
	AAP 2008 Clinical Report	AAP 2000 recommendations	ESPACI/ESPGHAN 1999, ESPGHAN 2008 recommendations	SP-EAACI, 2004, 2008 recommendations
Risk category: "high risk"	Parent or sibling with documented allergic disease	Biparental or parent plus sibling history of allergy	Parent or sibling affected (1999)	Parent or sibling with documented allergic disease
Pregnancy avoidance	Lack of evidence	Possibly peanut		No special diet*
Breast-feed "exclusively" until	Evidence for 3-4 mo (waiting 4-6 mo tied to introducing solids*)	6 mo	4-6 mo*	At least 4 mo, prefer 6 mo*
Maternal lactation avoidance of allergens	Some evidence for reduced atopic dermatitis	Peanuts, tree nuts and "consider" egg, milk, fish, and "perhaps other foods"		No special diet*
Prevention formulas	Compared with whole cow's milk protein, evidence for certain extensive hydrolysates, partial hydrolysates, but not soy (see text)	"Hypoallergenic formula" (extensive hydrolysate, possibly partial hydrolysate); not soy.	Confirmed reduced allergenicity (1999)	Extensively hydrolyzed until 4 mo of age (2004); documented reduced allergenicity (2008)
Types of "solids" and complementary foods	Evidence to wait 4 (to 6) mo; lack of convincing evidence for avoiding specific allergenic foods	Solids held to 6 mo Dairy products, age 1 y Egg, age 2 y Peanuts, nuts, fish, age 3 y	Not before 17 wk and no later than 26 wk; no convincing evidence for delaying potentially allergenic foods such as fish, egg (2008)*	No evidence of diet effect after 4-6 mo

ESPACI, European Society for Pediatric Allergy and Clinical Immunology; ESPGHAN, European Society for Pediatric Gastroenterology, Hepatology and Nutrition; SP-EAACI, Section on Pediatrics, European Academy of Allergy and Clinical Immunology.

*Advice that is the same for those not "high risk."

DIET OF LACTATING WOMEN

Regarding maternal lactation diets, a Cochrane database meta-analysis¹³ found some evidence for reduced atopic dermatitis, but suggested more studies are needed. The AAP report presents this view. A previous expert review that was not a structured meta-analysis and did not exclude as many studies as the Cochrane review concluded that special maternal lactation avoidance diets were unnecessary.¹¹

HUMAN MILK VERSUS WHOLE COW'S MILK FORMULA

For atopic dermatitis, there appears to be little controversy that human breast milk feeding prevents or delays disease compared with whole cow's milk protein for infants at risk.^{2,11,19,20}

However, the evidence on whether human milk is protective against development of asthma is contradictory. There appears to be a protective effect in children younger than 5 years old,²¹ but breast-feeding by mothers with asthma has been correlated with an increased risk for asthma in older children and adults.²² The AAP report² presents the benefit (atopic dermatitis) as well as the caveat for asthma associated with breast-feeding. Subsequently, Matheson et al²³ reported long-term follow-up from the Tasmanian Asthma study indicating that at age 7 years, participants who had been exclusively breast-fed and had a history of maternal atopy were less likely to have asthma (odds ratio, 0.8; 95% CI, 0.6-1.0), but by age 14 years, the risk reversed (odds ratio, 1.5; 95% CI, 1-2), and by age 44 years, participants were even more likely to have asthma (odds ratio, 1.57; 95% CI, 1.2-2.1).

The explanation for this effect could be the reduction of early infection leading to less asthma triggered by infection early in life and later increased atopy because of immune dysregulation for lack of infection (ie, the hygiene hypothesis). Currently, data only support the role of breast-feeding in reducing the likelihood of wheezing in young children.

FOOD ALLERGY

The development of food allergy is closely associated with having atopic dermatitis, and it can be difficult to analyze the effect of nutrition on the development of food allergy alone. In an analysis of peer-reviewed observational and interventional studies, Muraro et al¹¹ concluded that exclusive breast-feeding for at least 4 months decreases the risk for cow's milk allergy until 18 months in infants at risk of developing atopic diseases. In contrast, a Cochrane review analyzing optimal length of exclusive breast-feeding concluded that at least 4 months of exclusive breast-feeding does not protect against food allergy at 1 year, although the review included only 1 study with a blind food challenge.²⁴ The AAP report² synthesizes the available data, concluding a reduced cumulative incidence of cow's milk allergy for breast-feeding compared with cow's milk in the first 2 years of life.

HYDROLYZED FORMULA VERSUS COW MILK FORMULA

Partially hydrolyzed and extensively hydrolyzed formulas have been studied for their ability to prevent atopic disease for more

than 15 years. Most studies of these formulas have focused on infants at high risk of developing allergy. Although more than 100 published studies have addressed whether hydrolyzed formulas reduce the risk of atopic disease, fewer than 20 were randomized or quasi-randomized.² The AAP report² relies heavily on data evaluated in a Cochrane database report²⁵ but excluded several studies in which scientific validity was a concern. In addition, data from the German Infant Nutrition Intervention program was considered.²⁶ Subsequently, a 3-year follow-up study from the German Infant Nutrition Intervention trial showed a continued protective effect in the per protocol analysis of atopic dermatitis in high-risk infants not exclusively breast-fed of an extensive casein hydrolysate (odds ratio, 0.53; 95% CI, 0.32-0.88) or partial whey hydrolysate (odds ratio, 0.60; 95% CI, 0.37-0.97), but still no effect on asthma.²⁷ A particular extensively hydrolyzed whey formula did not show protection. Committee reviewers^{2,9} generally synthesize the available data to conclude that compared with a whole cow's milk protein formula, certain studied reduced allergenic formulas have a protective effect on atopic dermatitis, with a slight advantage of the extensively hydrolyzed casein formula (perhaps more effective for those with a stronger atopic family history). The AAP report² suggests cost be a consideration in selecting a formula and cautions that amino acid formulas have not been studied for prevention.

INTRODUCTION OF COMPLEMENTARY FOODS

Various committees have concluded from the available evidence that "solids" should be delayed to 4 to 6 months primarily because the timing of such introduction is tied to the time of exclusive breast-feeding.^{2,9} On the basis of the nature of the available studies, the updated AAP report² has reduced the age of evidence for an effect to 4 months. Subsequent studies continue to fail to show a convincing protective effect of delaying solids.^{28,29} Perhaps more controversial is the previous AAP recommendation for infants at risk of developing atopic disease to avoid milk protein to age 1 year, eggs until 2 years, and peanuts, tree nuts, and fish until 3 years of age.¹ This prevention approach was only studied by Zeiger and Heller,³⁰ but there was uncertain compliance and high dropout, and there were no clear differences in point prevalence of atopic outcomes or sensitization after age 4 years. Regarding the 2000 AAP report,¹ there are no data about whether these recommendations have been followed, nor any attempts at validation. If the previous AAP advice were followed, presumably an "at risk" but healthy 1-year-old would not have ingested common foods such as butter or biscuits and would not have birthday cake (egg) until age 2 years. On the basis of available data, including the apparent role of exposure to whole proteins in the first months of life being associated with atopic outcomes, and the known allergenicity of foods such as milk, egg, peanut, and fish, a consensus document from the Adverse Reactions to Foods Committee of the American College of Allergy, Asthma and Immunology in 2006 suggested following the 2000 AAP recommendations to avoid these allergens for the prescribed period.³ In contrast, in a position paper published in January 2008, the European Society for Paediatric Gastroenterology, Hepatology and Nutrition Committee on Nutrition concluded that there is no convincing evidence that avoidance or delayed introduction of potentially allergenic foods, such as fish and eggs, reduces allergies in infants either at risk or not.⁸ This European Society for Paediatric Gastroenterology, Hepatology and Nutrition committee

recommended that complementary foods be introduced after 17 weeks but no later than 26 weeks. These conclusions were apparently influenced by several negative studies on solid food timing and diversity and by studies showing protective effects of fatty acids in fish³¹ and possible detrimental effects of waiting longer to introduce wheat³² or other solids.²⁹ The updated AAP report² uses the term "no current convincing evidence" regarding protective effects of a delay of solids or specific allergens beyond 4 to 6 months.

DECIDING WHAT SHOULD BE ON OR OFF THE MENU IN 2008

We know that the revised AAP report has caused concern because it is not simply a to-do list of recommendations. The new approach is more sensitive to the notion that when evidence is unclear, physicians and patients should be aware of those caveats. The conclusions of the report (aimed at high-risk infants without current evidence of atopic disease) are summarized as follows: approaches that are generally effective are (1) breast-feeding for the first 4 to 6 months of life; (2) if not breast-feeding, or if supplementing, for the first 4 to 6 months, using an extensively hydrolyzed casein formula (or a partially hydrolyzed whey formula, though it may be less effective), instead of a cow's milk or soy formula; and (3) delaying introduction of solid foods until 4 to 6 months of age.

Approaches that have been tried but remain unproven are (1) dietary allergen restriction during pregnancy, (2) dietary allergen restriction during lactation (there is some evidence that this approach may reduce eczema), and (3) avoidance of allergenic foods for months and years beyond 6 months of age.

An educated consumer should be aware of the limitations of the available data. For example, different studies target different risk groups, and it may be that stricter or more comprehensive prevention programs may have different effects depending on the level of risk. A family in which both parents have multiple severe atopic diseases may be more motivated and may benefit more (although this is an assumption) from interventions compared to one in which the risk of atopy is lower. More studies must carefully consider whether primary allergen avoidance delays, permanently prevents, or simply masks atopic manifestations that would have been transiently evoked. We must remain aware that most of our conclusions are drawn from observational studies and that reverse causation may play a role in affecting results. That is, a family may alter the diet on the basis of observing signs of disease or on the basis of their level of risk, which could lead to dilution of prevention effects (breast-feeding longer if disease is appearing) and erroneous conclusions (waiting longer to give egg appears to be associated with more allergies).

We are also becoming aware of additional subtle influences of diet that raise concerns about suggestions to make changes on a limited evidence base. For example, lipids, antioxidants, and vitamins may influence atopy outcomes.^{5,33} The influence of allergens in the diet during pregnancy or lactation remains controversial.^{33,34} Nongestion (skin contact, inhalation) exposure may be a means of sensitization.^{14,33} Regarding the question of maternal exclusion diets during pregnancy, Rowe et al³⁵ followed T-cell and humoral responses in high-risk infants and could not document evidence for prenatal priming. Liem et al³⁶ evaluated a 1995 Manitoba birth cohort (n = 13,980) by using an administrative database and could not find an increase in food allergy

diagnosis among low-birth-weight or premature infants who might have been considered at risk for early dietary allergen exposures. Oral tolerance presumably requires oral exposure and is affected by dose, timing of exposure, and other factors. Elimination diets could theoretically result in bypassing oral tolerance induction, whereas exposures through sensitizing routes (skin, respiratory) could be sensitizing.¹⁴ Of additional concern, the literature includes cases in which dietary elimination of previously tolerated foods results in new onset of allergy on re-exposure.^{37,38} We are becoming more interested in oral and sublingual immunotherapy to treat food allergy,³⁹ which runs counter to advice to avoid allergens for long periods. These observations create a tenuous situation if one is to advise general prolonged elimination of allergens as a "do no harm" approach.

The situation is especially sticky regarding peanut. Green et al⁴⁰ recently documented an earlier age of presentation of children with peanut allergy to a referral center, compared with previous years. However, the timing between introduction and symptoms has not changed, and the authors could not conclude there was a relationship of early introduction as a risk for inducing peanut allergy. Sicherer and Sampson⁴¹ recently reviewed the complex situation of there being multiple potential risks for peanut allergy, including how peanut is processed (roasting/emulsification), genetic disposition, timing of introduction, and dose. Lack et al¹⁴ have reported a concern that lack of early oral exposure/increased skin exposure may increase the risk of peanut allergy and are studying whether early ingestion influences outcomes in the Learning Early About Peanut allergy study. Although the AAP report describes a lack of evidence on the topic of delaying introducing peanut beyond age 6 months, we caution that this is *not* tantamount to advising introducing peanut at that age as a weaning food!

Regarding the approaches that have been tried but remain unproven, we typically discuss the available data with our patients and try to help them make informed decisions. Families may already be avoiding certain allergens because of an allergic sibling and find it easy to continue to avoid, for example, peanut. We do not discourage this. For infants at risk, we may provide general advice to begin solids with single-ingredient infant foods such as fruits, vegetables, and cereal grains, gradually and in progression, which typically results in the more allergenic foods not being introduced until nearer the first birthday, and only if there have not been signs of atopic disease. Regarding peanut, the sibling history may influence our advice because there is a 7% risk of peanut allergy among siblings⁴²; we may delay peanut until testing is performed. We view the AAP report as aimed to primary prevention; if an infant has signs of atopic dermatitis or food allergy, we may consider testing and longer periods of avoidance.

The updated AAP report underscores the need for additional research on prevention and treatment. It does not preclude following any of a variety of reasonable approaches but does behoove us to present information to our patients in the context of the limitations of our current evidence base.

REFERENCES

1. American Academy of Pediatrics, Committee on Nutrition. Hypoallergenic infant formulas. *Pediatrics* 2000;106:346-9.
2. Greer FR, Sicherer SH, Burks AW. 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.
3. Fiocchi A, Assa'ad A, Bahna S. Food allergy and the introduction of solid foods to infants: a consensus document. Adverse Reactions to Foods Committee, American College of Allergy, Asthma and Immunology. *Ann Allergy Asthma Immunol* 2006; 97:10-20.
4. van Odijk J, Kull I, Borres MP, Brandtzaeg P, Edberg U, Hanson LA, et al. Breast-feeding and allergic disease: a multidisciplinary review of the literature (1966-2001) on the mode of early feeding in infancy and its impact on later atopic manifestations. *Allergy* 2003;58:833-43.
5. Devereux G, Seaton A. Diet as a risk factor for atopy and asthma. *J Allergy Clin Immunol* 2005;115:1109-17.
6. Friedman NJ, Zeiger RS. The role of breast-feeding in the development of allergies and asthma. *J Allergy Clin Immunol* 2005;115:1238-48.
7. Tarini BA, Carroll AE, Sox CM, Christakis DA. Systematic review of the relationship between early introduction of solid foods to infants and the development of allergic disease. *Arch Pediatr Adolesc Med* 2006;160:502-7.
8. Agostoni C, Decsi T, Fewtrell M, Goulet O, Kolacek S, Koletzko B, et al. Complementary feeding: a commentary by the ESPGHAN Committee on Nutrition. *J Pediatr Gastroenterol Nutr* 2008;46:99-110.
9. Host A, Halken S, Muraro A, Dreborg S, Niggemann B, Aalberse R, et al. Dietary prevention of allergic diseases in infants and small children. *Pediatr Allergy Immunol* 2008;19:1-4.
10. Brand PL, Vlieg-Boerstra BJ, Dubois AE. Dietary prevention of allergic disease in children: are current recommendations really based on good evidence? *Pediatr Allergy Immunol* 2007;18:475-9.
11. Muraro A, Dreborg S, Halken S, Host A, Niggemann B, Aalberse R, et al. Dietary prevention of allergic diseases in infants and small children, part III: critical review of published peer-reviewed observational and interventional studies and final recommendations. *Pediatr Allergy Immunol* 2004;15:291-307.
12. Host A, Koletzko B, Dreborg S, Muraro A, Wahn U, Aggett P, et al. Dietary products used in infants for treatment and prevention of food allergy. Joint Statement of the European Society for Paediatric Allergology and Clinical Immunology (ES-PACI) Committee on Hypoallergenic Formulas and the European Society for Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) Committee on Nutrition. *Arch Dis Child* 1999;81:80-4.
13. Kramer MS, Kakuma R. Maternal dietary antigen avoidance during pregnancy or lactation, or both, for preventing or treating atopic disease in the child. *Cochrane Database Syst Rev* 2006;3:CD000133.
14. Lack G, Fox D, Northstone K, Golding J. Factors associated with the development of peanut allergy in childhood. *N Engl J Med* 2003;348:977-85.
15. Dean T, Venter C, Pereira B, Grundy J, Clayton CB, Higgins B. Government advice on peanut avoidance during pregnancy: is it followed correctly and what is the impact on sensitization? *J Hum Nutr Diet* 2007;20:95-9.
16. Hourihane JO, Aiken R, Briggs R, Gudgeon LA, Grimshaw KE, Dunngalvin A, et al. The impact of government advice to pregnant mothers regarding peanut avoidance on the prevalence of peanut allergy in United Kingdom children at school entry. *J Allergy Clin Immunol* 2007;119:1197-202.
17. Chatzi L, Torrent M, Romieu I, Garcia-Esteban R, Ferrer C, Vioque J, et al. Mediterranean Diet in pregnancy protective for wheeze and atopy in childhood. *Thorax* 2008;63:507-13.
18. Calvani M, Alessandri C, Sopo SM, Panetta V, Pingitore G, Tripodi S, et al. Consumption of fish, butter and margarine during pregnancy and development of allergic sensitizations in the offspring: role of maternal atopy. *Pediatr Allergy Immunol* 2006;17:94-102.
19. Gdalevich M, Mimouni D, David M, Mimouni M. Breast-feeding and the onset of atopic dermatitis in childhood: a systematic review and meta-analysis of prospective studies. *J Am Acad Dermatol* 2001;45:520-7.
20. Laubereau B, Brockow I, Zirnigbl A, Koletzko S, Gruebl A, von Berg A, et al. Effect of breast-feeding on the development of atopic dermatitis during the first 3 years of life: results from the GINI-birth cohort study. *J Pediatr* 2004;144:602-7.
21. Gdalevich M, Mimouni D, Mimouni M. Breast-feeding and the risk of bronchial asthma in childhood: a systematic review with meta-analysis of prospective studies. *J Pediatr* 2001;139:261-6.
22. Wright AL, Holberg CJ, Taussig LM, Martinez FD. Factors influencing the relation of infant feeding to asthma and recurrent wheeze in childhood. *Thorax* 2001;56: 192-7.
23. Matheson MC, Erbas B, Balasuriya A, Jenkins MA, Wharton CL, Tang ML, et al. Breast-feeding and atopic disease: a cohort study from childhood to middle age. *J Allergy Clin Immunol* 2007;120:1051-7.
24. Kramer MS, Kakuma R. Optimal duration of exclusive breastfeeding. *Cochrane Database Syst Rev* 2002;1:CD003517.
25. Osborn DA, Sinn J. Formulas containing hydrolyzed protein for prevention of allergy and food intolerance in infants. *Cochrane Database Syst Rev* 2006;4:CD003664.
26. von Berg A, Koletzko S, Grubl A, Filipiak-Pittroff B, Wichmann HE, Bauer CP, et al. The effect of hydrolyzed cow's milk formula for allergy prevention in the first

- year of life: the German Infant Nutritional Intervention Study, a randomized double-blind trial. *J Allergy Clin Immunol* 2003;111:533-40.
27. von Berg A, Koletzko S, Filipiak-Pittroff B, Laubereau B, Grubl A, Wichmann HE, et al. Certain hydrolyzed formulas reduce the incidence of atopic dermatitis but not that of asthma: three-year results of the German Infant Nutritional Intervention Study. *J Allergy Clin Immunol* 2007;119:718-25.
 28. Filipiak B, Zutavern A, Koletzko S, von Berg A, Brockow I, Grubl 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.
 29. 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.
 30. 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.
 31. Kull I, Bergstrom 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.
 32. Poole JA, Barriga K, Leung DY, Hoffman M, Eisenbarth GS, Rewers M, et al. Timing of initial exposure to cereal grains and the risk of wheat allergy. *Pediatrics* 2006;117:2175-82.
 33. Lack G. Epidemiologic risks for food allergy. *J Allergy Clin Immunol* 2008;121:1331-6.
 34. Boyle RJ, Tang ML. Can allergic diseases be prevented prenatally? *Allergy* 2006;61:1423-31.
 35. Rowe J, Kusel M, Holt BJ, Suriyaarachchi D, Serralha M, Hollams E, et al. Prenatal versus postnatal sensitization to environmental allergens in a high-risk birth cohort. *J Allergy Clin Immunol* 2007;119:1164-73.
 36. Liem JJ, Kozyskyj AL, Huq SI, Becker AB. The risk of developing food allergy in premature or low-birth-weight children. *J Allergy Clin Immunol* 2007;119:1203-9.
 37. Flinterman AE, Knulst AC, Meijer Y, Bruijnzeel-Koomen CA, Pasmans SG. Acute allergic reactions in children with AEDS after prolonged cow's milk elimination diets. *Allergy* 2006;61:370-4.
 38. Savage JH, Limb SL, Brereton NH, Wood RA. The natural history of peanut allergy: extending our knowledge beyond childhood. *J Allergy Clin Immunol* 2007;120:717-9.
 39. Buchanan AD, Green TD, Jones SM, Scurlock AM, Christie L, Althage KA, et al. Egg oral immunotherapy in nonanaphylactic children with egg allergy. *J Allergy Clin Immunol* 2007;119:199-205.
 40. Green TD, LaBelle VS, Steele PH, Kim EH, Lee LA, Mankad VS, et al. Clinical characteristics of peanut-allergic children: recent changes. *Pediatrics* 2007;120:1304-10.
 41. Sicherer SH, Sampson HA. Peanut allergy: emerging concepts and approaches for an apparent epidemic. *J Allergy Clin Immunol* 2007;120:491-503.
 42. Sicherer SH, Furlong TJ, Maes HH, Desnick RJ, Sampson HA, Gelb BD. Genetics of peanut allergy: a twin study. *J Allergy Clin Immunol* 2000;106:53-6.