
Correspondence

INCREASED PREVALENCE OF NONSTEROIDAL ANTI-INFLAMMATORY DRUG HYPERSENSITIVITY IN ATOPIC INDIVIDUALS

To the Editor:

In an article published 2 years ago, Kupczyk et al¹ observed that 9.44% of patients with severe asthma had aspirin intolerance. Since aspirin-intolerant asthma (AIA) is not generally thought to be associated with atopy, these authors were intrigued by the fact that 69.4% of their patients with AIA were atopic. We would like to further elaborate on this observation.

A few years ago we reported an increased prevalence of atopic diseases and positive skin prick test results to aeroallergens in nonsteroidal anti-inflammatory drug (NSAID) hypersensitive patients.² This association has been consistently present in additional studies from our group and has been confirmed by other investigators.^{3,4} The association of atopy and NSAID sensitivity has been reported not only for patients with the cutaneous pattern of reaction (urticaria and angioedema) but also for patients with aspirin-exacerbated respiratory disease (AERD)⁵ and in patients with systemic (anaphylactic) reactions.⁶

The mechanisms that determine the association between atopy and NSAID intolerance are currently unknown. Since atopy is a genetic predisposition for the development of IgE-mediated diseases such as asthma, rhinitis, dermatitis, and some allergic reactions to foods, we hypothesized that genes that determine atopy could be closely linked to genes associated with cross-reactive reactions to NSAIDs. Among candidate associated genes, those controlling arachidonic acid metabolism (leukotriene C₄ synthase, 5-lipoxygenase, cysteinyl-leukotriene 1 receptor, prostaglandin E₂ receptor subtype 2 [EP2] genes) or other loci within the HLA complex have been reported by various groups.⁷⁻¹⁰

The increased prevalence of some clinical patterns of NSAID hypersensitivity in certain populations also supports a genetic basis for these conditions. Most studies on cutaneous reactions are from southern Europe and Latin America. North American allergists mention that these reactions are present more frequently in individuals of Hispanic background. On the other hand, most reports on respiratory reactions to NSAIDs, such as AIA and AERD, come from countries with a different genetic background, especially Eastern Europe and North America. This might be occurring by chance, but it is provocative to mention it in this letter.

In summary, we would like to call the attention of the allergology community to the association of NSAID hypersensitivity and atopic diseases. The reasons for this unexpected association deserve further investigation. Currently, various research groups are using modern techniques of mo-

lecular genetics for the study of the genetic basis of these diseases with the hope of finding new tools useful for better diagnosis, therapy, and prevention of these common hypersensitivity diseases.

MARIO SANCHEZ-BORGES, MD
ARNALDO CAPRILES, MD
FERNAN CABALLERO-FONSECA, MD
Centro Medico-Docente La Trinidad - Allergy-
Immunology
Caracas, Venezuela

REFERENCES

1. Kupczyk M, Kuprys I, Gorski P, Kuna P. Aspirin intolerance and allergy to house dust mites: important factors associated with development of severe asthma. *Ann Allergy Asthma Immunol.* 2004;92:453-458.
2. Sánchez-Borges M, Capriles-Hulett A. Atopy is a risk factor for non-steroidal anti-inflammatory drug sensitivity. *Ann Allergy Asthma Immunol.* 2000;84:101-106.
3. Rosario NA, Ribeiro AC. Achados clínicos da sensibilidades a analgésicos e anti-inflamatorios não-hormonais. *Rev Assoc Med Bras.* 2000;46:201-206.
4. Quirarte J, Blanco C, Castillo R, et al. Intolerance to nonsteroidal anti-inflammatory drugs: results of controlled drug challenges in 98 patients. *J Allergy Clin Immunol.* 1996;98:678-675.
5. Berges-Gimeno MP, Simon RA, Stevenson DD. The natural history and clinical characteristics of aspirin-exacerbated respiratory disease. *Ann Allergy Asthma Immunol.* 2002;89:474-478.
6. Kemp SF, Lockey RF, Wolf BL, Lieberman P. Anaphylaxis: a review of 266 cases. *Arch Intern Med.* 1995;155:1749-1754.
7. Sanak M, Simon HU, Szczeklik A. Leukotriene C₄ synthase promoter polymorphism and risk of aspirin-induced asthma. *Lancet.* 1997;350:1599-1600.
8. Choi JH, Park HS, Oh HB, et al. Leukotriene-related gene polymorphisms in Asa-intolerant asthma: an association with a haplotype of 5-lipoxygenase. *Hum Genet.* 2004;114:337-344.
9. Jinai N, Sakagami T, Sekigawa T, et al. Polymorphism in the prostaglandin E₂ receptor subtype 2 gene confer susceptibility to aspirin-intolerant asthma: a candidate gene approach. *Hum Mol Genet.* 2004;13:3203-3217.
10. Dekker JW, Nizankowska E, Schmitz-Schumann M, et al. Aspirin-induced asthma and HLA-DRB1 and HLA-DPB1 genotypes. *Clin Exp Allergy.* 1997;27:574-577.

EOSINOPHILIC PNEUMONIA IN A PATIENT WITH BREAST CANCER: IDIOPATHIC OR NOT?

To the Editor:

We would like to comment on a possible causative factor of eosinophilic pneumonia that may have been overlooked in the case reported by Miranowski and Ditto¹ as part of the Clinical Allergy and Immunology Rounds.

Briefly, the authors describe the case of a 59-year-old woman with a history of chronic sinusitis and asthma diagnosed 10 years earlier who presented with fever, cough, subacute dyspnea on exertion, and weight loss. Lung examination revealed inspiratory crackles. The differential white blood cell count in peripheral blood showed high eosinophilia (3.1 g/L). Chest imaging showed bilateral airspace consolidation (and small bilateral pleural effusion). The differential cell count of bronchoalveolar lavage fluid showed 92% eosinophils. The syndrome rapidly resolved with corticosteroid treatment. A similar episode (with pericarditis) had occurred 6 years earlier.

Eosinophilic pneumonia was diagnosed, and it was confirmed by means of transbronchial biopsies. Most known causes of eosinophilic pneumonia were excluded, such as exposure to causative drugs, toxins,² helminthic infections, and allergic bronchopulmonary aspergillosis. Diagnostic criteria for Churg-Strauss syndrome or hypereosinophilic syndrome were not met. Disease onset was not consistent with acute eosinophilic pneumonia. The patient was thus diagnosed as having idiopathic chronic eosinophilic pneumonia (Carrington syndrome).

Although the differential diagnosis is appropriately discussed, the authors do not mention the potential role of radiotherapy as a primer for eosinophilic pneumonia. Hence, this patient also had a history of breast cancer treated with surgery, tamoxifen, and irradiation, the latter being completed 1 month before the patient's admission for chronic eosinophilic pneumonia.

It is now well known that radiotherapy for breast cancer can cause acute and chronic radiation pneumonitis and organizing pneumonia.³ In addition, we described the occurrence of typical chronic eosinophilic pneumonia in women who had recently (1–10 months) received radiotherapy for breast cancer.⁴ All the patients had a history of asthma, allergy, or both. It was hypothesized that lung irradiation may have predisposed the patient to the development of chronic eosinophilic pneumonia by inducing diffuse and persistent alveolitis; such lymphocyte priming may possibly be shifted toward a T-helper type 2 cell response in the months after lymphoid irradiation,⁵ especially in patients with asthma or atopy. Eosinophilic pneumonia may then be triggered by a second "hit," such as antigenic stimulation.^{2,4}

Although the pathogenic role of irradiation cannot be definitively established from descriptive studies, we suggest that radiotherapy was a potential cause (or at least a trigger) of relapse of chronic eosinophilic pneumonia in the patient described by Miranowski and Ditto.¹

VINCENT COTTIN, MD, PhD
JEAN-FRANÇOIS CORDIER, MD
Service de pneumologie
Centre de référence des maladies orphelines pulmonaires
Hôpital Louis Pradel
Hospices Civils de Lyon
Université de Lyon
Lyon, France

REFERENCES

1. Miranowski AC, Ditto AM. A 59-year-old woman with fever, cough, and eosinophilia. *Ann Allergy Asthma Immunol*. 2006; 96:483–488.
2. Solomon J, Schwarz M. Drug-, toxin-, and radiation therapy-induced eosinophilic pneumonia. *Semin Respir Crit Care Med*. 2006;27:192–198.
3. Crestani B, Valeyre D, Roden S, Wallaert B, Dalphin JC, Cordier JF. Bronchiolitis obliterans organizing pneumonia syndrome primed by radiation therapy to the breast: the Groupe d'Etudes et de Recherche sur les Maladies Orphelines Pulmonaires (GERM"O"P). *Am J Respir Crit Care Med*. 1998;158: 1929–1935.
4. Cottin V, Frogner R, Monnot H, Levy A, DeVuyst P, Cordier JF. Chronic eosinophilic pneumonia after radiation therapy for breast cancer. *Eur Respir J*. 2004;23:9–13.
5. Bass H, Adkins B, Strober S. Thymic irradiation inhibits the rapid recovery of T_H1 but not T_H2-like functions of CD4⁺ T cells after total lymphoid irradiation. *Cell Immunol*. 1991;137:316–328.

The above correspondence was referred to the original authors who provided the following response:

We acknowledge that radiotherapy may have triggered a relapse of chronic eosinophilic pneumonia in this patient and could have been included in the differential diagnosis. However, we chose to include in our list of differential diagnoses those that could explain both the current admission and the admission 6 years earlier, thus giving a unifying diagnosis. Although radiotherapy may have contributed to her eosinophilic pneumonia on this admission, it could not account for both episodes. Thus, I do not think it was a cause of chronic eosinophilic pneumonia in this patient but may well have contributed to her second episode. We do think that this is an important point and should have been included in our discussion.

ANNE MARIE DITTO, MD
Division of Allergy Immunology
Northwestern University Feinberg School of Medicine
Chicago, Illinois

ANNE MIRANOWSKI, MD
McLean, Virginia

NOT RUNNING ON EMPTY

To the Editor:

I read with interest the article by Sander et al¹ titled "Dose Counting and the Use of Pressurized Metered-Dose Inhalers: Running on Empty" and the accompanying editorial by Openheimer² in the July issue of the *Annals*. I agree that there is a need for a reliable method to ensure that patients can accurately determine the remaining number of doses of asthma medications to ensure that they do not run out. As Sander et al point out, the Diskus (GlaxoSmithKline) was the first device to have an integrated dose counter.

In addition, I would also like to point out that GlaxoSmithKline launched Ventolin HFA (albuterol sulfate hydroflu-



Figure 1. Ventolin HFA (albuterol sulfate hydrofluoroalkane-134a inhalation aerosol) with an integrated dose counter.

oroalkane-134a inhalation aerosol) with an integrated dose counter in the United States in June 2006 (Fig 1). This provides patients with the ability to know how many doses remain in their rescue inhaler and perhaps keeps them from finding it empty during an asthma exacerbation. Furthermore, plans are currently under way to incorporate integrated dose counters into Flovent HFA (fluticasone propionate hydrofluoroalkane-134a inhalation aerosol) and Advair HFA (fluticasone propionate and salmeterol inhalation aerosol).

Of concern was the large percentage of patients (approximately 45%) with uncontrolled asthma as measured by the use of a short-acting bronchodilator 2 or more times each week and monthly refills. This highlights a need to continue to educate patients about asthma, with a focus on using appropriate controller medications because only 31.6% reported the use of an inhaled corticosteroid-containing product.

Finally, I would like to point out that the opening statement concerning the mortality rate of asthma increasing is inaccurate. Asthma mortality peaked in 1996³ but has continued to decline since then. The most recent estimates from the Centers for Disease Control and Prevention, referencing 2004 data, now show that the number of asthma deaths is less than 4,000 and that the death rate is 1.3 per 100,000 persons.⁴

KATHLEEN A. RICKARD, MD
Respiratory Medicines Development Centre, North America
GlaxoSmithKline
Research Triangle Park, North Carolina

REFERENCES

1. Sander N, Fusco-Walker SJ, Harder JM, Chipps BE. Dose counting and the use of pressurized metered-dose inhalers: running on empty. *Ann Allergy Asthma Immunol.* 2006;97:34–38.
2. Oppenheimer J. Running on empty [editorial]. *Ann Allergy Asthma Immunol.* 2006;97:1–2.
3. American Lung Association Epidemiology & Statistics Unit, Research and Scientific Affairs. Trends in asthma morbidity and mortality: May 2005. Available at: <http://www.lungusa.org>. Accessed June 14, 2006.
4. Miniño AM, Heron M, Smith BL. Deaths: preliminary data for 2004. Available at: <http://www.cdc.gov>. Accessed June 29, 2006.

The above correspondence was referred to the original authors who provided the following response:

We share Dr Rickard's concern about patients with uncontrolled asthma. Alarming, of the 500 randomly selected patients we surveyed, nearly one third (31.6%) named Advair as the medication they reach for when wheezing, coughing, or short of breath. These respondents were eliminated from our survey; however, this finding led to extensive discussion among the authors about why educated patients or parents in their mid 40s were obviously confused about prescribing instructions.

We thank GlaxoSmithKline for their addition of dose counters to Ventolin HFA. We know that patients who have been told that their bronchodilator is a "rescue medication" (a term you used in reference to Ventolin HFA) often wait to use the drug until they are in crisis rather than at the first sign that symptoms are progressing, before exercise, or after exposure to an irritant or allergen.

Similarly, the word "controller" is often used when referring to inhaled corticosteroids, antileukotrienes, and combination products. However, most patients consider all medications used for allergies and asthma to be "controllers" because they control symptoms. This could be the reason one third of respondents reported reaching for the wrong inhaler during acute exacerbations—they reached for what they were told was their "controller" medication.

The use of jargon when prescribing medications can lead to patient treatment failures at home, school, work, or play. We encourage prescribers and pharmaceutical manufacturers to eliminate jargon when communicating treatment plans to patients. We also agree that death rates from asthma have decreased as evidenced by the citation quoted by Dr Rickard.

NANCY SANDER
Allergy & Asthma Network Mothers of Asthmatics
Fairfax, Virginia

SANDRA FUSCO-WALKER
Allergy & Asthma Network Mothers of Asthmatics
Kinnelon, New Jersey

JULIA HARDER, BA
Skaggs School of Pharmacy & Pharmaceutical Sciences
University of California
San Diego, California

BRADLEY E. CHIPPS, MD
Capital Allergy & Respiratory Disease Center
Sacramento, California

FOOD ALLERGY AND THE INTRODUCTION OF SOLID FOODS TO INFANTS: A CONSENSUS DOCUMENT

To the Editor:

The article by Fiocchi et al¹ addresses the influence of the timing of the introduction of complementary (solid) foods on

food allergy. In the abstract of the article, specific advice is presented: infants at risk for allergy should have delayed introduction of dairy products to 12 months, hen's egg to 24 months, and peanut, tree nuts, fish, and seafood to 36 months. Although these recommendations are almost identical to those made previously by the Committee on Nutrition of the American Academy of Pediatrics,² we have concerns that these recommendations are not a logical conclusion of the material presented. Our concerns are particularly strong because this document is presented as a "consensus document" not as a review.

The recommendations about specific solids do not represent a proven approach; they mirror a study by Zeiger and Heller³ in which adherence to the study protocol was poor (a practical limitation) and the outcomes did not show long-term (eg, prevention after age 4 years) reduction of asthma, atopic dermatitis, or food allergy. Furthermore, the recommendations by Fiocchi et al¹ are directed toward "evaluated risk of allergy," which is never specifically defined. Also, would the recommendations apply equally to children who do or do not already manifest atopic disease?

As reviewed in the article, many studies have limitations (reverse causation, additional interventions, nonrandomized, nonadherence, etc) that have precluded evidence-based recommendations about the timing of specific solid/complementary foods. Previous recommendations by the European Society for Paediatric Allergology and Clinical Immunology and the European Society for Paediatric Gastroenterology, Hepatology, and Nutrition⁴ and the European Academy of Allergology and Clinical Immunology⁵ have not provided specific recommendations in this regard because of lack of data. Interestingly, comments in the review support a more cautious recommendation than the one finally proposed. The authors acknowledge that exposure timing and dose may have implications for the development of tolerance; that "there is no evidence to demonstrate that" avoidance of peanuts, nuts, and fish to age 3 years is successful in preventing future allergy; and that such recommendations "are not evidence based."

Although not perfect, the studies by Zutavern et al^{6,7} revealed that delayed introduction of solid foods was not protective, and was possibly causal, of atopic disease. Lack and Golding⁸ suggested that prolonged avoidance of peanut may increase risks of peanut allergy, partly because noningestion exposures could increase sensitization, and there is some evidence that noningestion contact, rather than ingestion, is associated with allergy.⁹ Dietary regimens leading to sensitization or tolerance are not well explored in humans and are likely quite complex, as has been observed in numerous animal models. The recommendations made in the "consensus report" may be correct or countereffective. Advocating dietary avoidance for prevention in the absence of disease for prolonged periods may prove to be nutritionally harmful, may promote allergy, and may impose superfluous stress on caregivers.

The timing of the introduction of major allergens is potentially problematic; for infants who already show signs of atopy, an evaluation may be needed to guide food introductions. Regarding prevention, we support the more tempered advice of previous committees^{2,4,5} regarding solid food introduction. We are concerned that promulgation of advice that is not validated may carry health risks.

JENNIFER M. MALONEY, MD
HUGH A. SAMPSON, MD
SCOTT H. SICHERER, MD
Pediatrics
Mount Sinai School of Medicine
New York, New York
WESLEY A. BURKS, MD
Pediatric Allergy/Immunology
Duke University Medical Center
Durham, North Carolina

REFERENCES

1. Fiocchi A, Assa'ad A, Bahna S; Adverse Reaction to Foods Committee of the American College of Allergy, Asthma and Immunology. Food allergy and the introduction of solid foods to infants: a consensus document. *Ann Allergy Asthma Immunol*. 2006;97:10–21.
2. American Academy of Pediatrics, Committee on Nutrition. Hypoallergenic infant formulas. *Pediatrics*. 2000;106(pt 1):346–349.
3. 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;95:1179–1190.
4. Host A, Koletzko B, Dreborg S, 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 (ESPACI) Committee on Hypoallergenic Formulas and the European Society for Paediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN) Committee on Nutrition. *Arch Dis Child*. 1999;81:80–84.
5. Muraro A, Dreborg S, Halken S, 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.
6. Zutavern A, von Mutius E, Harris J, et al. The introduction of solids in relation to asthma and eczema. *Arch Dis Child*. 2004;89:303–308.
7. Zutavern A, Brockow I, Schaaf B, et al; LISA Study Group. Timing of solid food introduction in relation to atopic dermatitis and atopic sensitization: results from a prospective birth cohort study. *Pediatrics*. 2006;117:401–411.
8. Lack G, Golding J. Peanut and nut allergy: reduced exposure might increase allergic sensitisation. *BMJ*. 1996;313:300.
9. Lack G, Fox D, Northstone K, Golding J; Avon Longitudinal Study of Parents and Children Study Team. Factors associated with the development of peanut allergy in childhood. *N Engl J Med*. 2003;348:977–985.

The above correspondence was referred to the original authors who provided the following response:

Dr Maloney and her colleagues have raised thought-provoking issues about our article titled "Food Allergy and the Introduction of Solid Foods to Infants: A Consensus Document."¹ They also shed light on several aspects that we had difficulty with when writing the article.

Maloney et al make a valid point in that the only current recommendation for infant weaning is by the American Academy of Pediatrics (AAP). The recommendation has been published in several prints of the AAP *Nutrition Handbook*² and was prepared by many experts. To our knowledge, the recommendation has neither been retracted by the AAP nor refuted previously by Maloney or her colleagues, or any other allergy organization. On the contrary, it is widely followed by pediatricians. Although the AAP *Nutrition Handbook* recommendation referenced very few studies, in our article we cited 16 original research articles from 6 developed countries in addition to the United States (references 37–53) and 3 meta-analyses (references 1, 54, and 55). In those studies, the weight of evidence tilts toward the effectiveness of avoidance of major food allergens during early infancy, as exemplified by cow's milk and egg.

We basically share the view of Maloney et al that "many studies have limitations . . . that have precluded evidence-based recommendations about the timing of specific solid/complementary foods." In fact, the studies support cautious recommendations. The precautionary principle is the gist of the article under discussion: the considerations for a rationale to introduction schedules that we presented, targeted to allergists and to pediatricians and nutritionists, aimed to reflect the fact that "exposure, timing, and dose may have implications for the development of tolerance." Also, we concur with Maloney et al that exposure to foods by noningestant routes can be a relevant avenue of sensitization.^{3,4}

We disagree with Maloney et al, however, on certain points.

1. That evidence-based recommendation is not possible at present is exactly the gap in knowledge highlighted by the article. The American College of Allergy, Asthma and Immunology (ACAAI) Adverse Reactions to Foods Committee chose caution in primary prevention because in the present cultural context, epidemiologic studies can be misused as clinical evidence. Regrettably, all the recent studies on this topic are observational and not interventional and may not answer the practical question, "What food should I give my child and when?" However, this has not prevented the authors of such studies from extrapolating their findings to "no evidence supports a delayed introduction of solids beyond the 6th month of life for prevention of AD and sensitization."⁵ Therefore, it was timely to admit how little is actually known about the subject. As Maloney et al point out, a recent review of 13 selected studies⁶ revealed evidence suggestive of an association between early solid feeding and increased risk of

eczema but not of other allergic diseases. All the articles reviewed for our article were retrieved using the algorithm presented in the text, which did not include atopic dermatitis, eczema, or atopic diseases. On the other hand, a noninterventional study⁷ published after the article under discussion showed that introduction of fish during early infancy is not associated with an increase in fish allergy in the first 4 years of life. This finding needs careful interpretation, in the context of applicability to practice, of observational vs interventional studies.

2. That primary allergen avoidance by strict elimination diets may actually result in sensitization remains an interesting hypothesis that has not been tested and deserves investigation in a prospective, interventional setting.⁸ Until then, equating early avoidance with specific risk remains speculative, whereas food allergy in infants certainly reflects early exposure.⁹ All primary prevention of food allergy studies have at least addressed "delayed introduction of solid foods" as a further intervention beyond milk avoidance, and there is no reason to think that other complementary allergenic foods would behave differently than milk. The same possibility has been claimed in retrospective settings in the context of secondary prevention,^{10,11} but no study found that primary avoidance is associated with sensitization.

3. As to definition of the infant at risk for atopic disease, a qualification also used in the AAP recommendation without further definition, our article includes a table that outlines the various definitions used in research studies to identify infants at risk. The definition is broad and extends from a history of atopy in 1 or 2 first-degree relatives to the measurement of cord blood IgE level. Our consensus opinion separated infants at risk for atopy from other infants. There were no recommendations for dietary eliminations in the absence of disease risk, except for the cautious introduction of solids, individually and gradually and in cooked forms. Although individual evaluation of infants with atopic disease is a given, even there the allergy community needs to address additional questions of how to proceed when tests denote sensitization to foods in the absence of symptoms. This would belong to secondary prevention, which was beyond the scope of our article. On the other hand, we should not forget that there is a rise in the prevalence of food allergy in children. Hence, the recommendation on infant feeding should keep in mind that the infant who lacks an overt family history of allergy is the potential new atopic member of the population. Therefore, attention should be given to the highly allergenic foods during weaning of infants "not at risk for atopy" as well.

4. That an avoidance strategy can "carry health risks" is counterintuitive. Because the lack of clinical benefit does not equate with harm, there is no risk from a nutritional point of view. The main problem in developed countries is an excess of protein intake,¹² and our approach delays the introduction of allergenic food proteins. Our review highlighted the differences between the recommendations of the AAP and the European

Society of Pediatric Allergy and Clinical Immunology and the European Society of Pediatric Gastroenterology and Nutrition in a table that clearly shows that the latter organizations have indeed made no specific recommendations relevant to this issue. The lack of specific recommendations leaves the practicing pediatrician and allergist, and most importantly the parents, without any clear guidelines. In fact, this review was prompted by a question from a mother indicating that neither the American Academy of Allergy, Asthma and Immunology nor the ACAAI has provided clear recommendation on the timing of infant weaning and the sequence of introduction of solid foods. Most organizations that have adverse reactions to food committees such as ours at the ACAAI are trying to provide guidelines until firm evidence becomes available for more specific recommendations. The recommendations in the article were based on the weight of the available scientific evidence and the expertise of the members of the Adverse Reactions to Foods Committee of the ACAAI, hence the title "consensus." A consensus document is not a clinical guideline, a meta-analysis, or a systematic review. It merely incorporates experts' best judgement and reflects current understanding.

The time has come to settle these crucial questions by means of joint research efforts applying appropriate study designs. Until then, the onus is on us, pediatric allergists, to advise and orient families, patient organizations, and scientific societies of pediatric nutrition to factor food allergy prevention into the planning of infant diets.

ALESSANDRO FIOCCHI, MD
University of Milan Medical School
Milan, Italy

AMAL ASSA'AD, MD
Cincinnati Children's Hospital Medical Center
Cincinnati, Ohio

SAMI BAHNA, MD
Louisiana State University Health Sciences Center
Shreveport, Louisiana

REFERENCES

1. Fiocchi A, Assa'ad A, Bahna S; Adverse Reactions to Foods Committee of the American College of Allergy, Asthma and Immunology. Food allergy and the introduction of solid foods to infants: a consensus document. *Ann Allergy Asthma Immunol*. 2006;97:10–21.
2. American Academy of Pediatrics. *Nutrition Handbook*. Fifth ed. Elk Grove Village, IL: American Academy of Pediatrics; 2004: 604–605.
3. Lack G, Fox D, Northstone K, Golding J; for the Avon Longitudinal Study of Parents and Children Study Team. Factors associated with the development of peanut allergy in childhood. *N Engl J Med*. 2003;348:977–985.
4. Bahna SL. Adverse food reactions by skin contact. *Allergy*. 2004;59(suppl 78):66–70.
5. Zutavern A, von Mutius E, Harris J, Mills P, Moffatt C, Cullinan P. The introduction of solids in relation to asthma and eczema. *Arch Dis Child*. 2004;89:303–308.
6. Tarini BA, Carroll AE, Sox CM, Christakis DA. Systemic review of the relationship between early introduction of solid foods to infants and the development of allergic disease. *Arch Pediatr Adolesc Med*. 2006;160:502–507.
7. 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: 1009–1015.
8. Lack G, Golding J. Peanut and nut allergy: reduced exposure might increase allergic sensitisation. *BMJ*. 1996;313:300.
9. Dalal I, Binson I, Reifen R, et al. Food allergy is a matter of geography after all: sesame as a major cause of severe IgE-mediated food allergic reactions among infants and young children in Israel. *Allergy*. 2002;57:362–365.
10. Barbi E, Gerarduzzi T, Longo G, Ventura A. Fatal allergy as a possible consequence of long-term elimination diet. *Allergy*. 2004;59:668–672.
11. Flinterman AE, Knulst AC, Meijer Y, Bruijnzeel-Koomen CA, Pasmans SG. Acute allergic reactions in children with AIDS after prolonged cow's milk elimination diets. *Allergy*. 2006;61: 370–374.
12. Agostoni C, Scaglioni S, Ghisleni D, Verduci E, Giovannini M, Riva E. How much protein is safe? *Int J Obes (Lond)*. 2005; 29(suppl 2):S8–S13.

Erratum

In the review "The use of inhaled formoterol in the treatment of asthma" (*Ann Allergy Asthma Immun*. 2006;97:24–33) it is important to note that doses of formoterol were indicated in 2 ways, depending on how they were presented in the relevant reference: metered dose (eg, 6 μg , 12 μg , 24 μg) and delivered dose (eg, 4.5 μg , 9 μg , 18 μg). There is a typographical error on page 30. The correct sentence should read: "Numerous clinical studies with formoterol have demonstrated that it is safe and well tolerated at doses ranging from 9 to 36 $\mu\text{g}/\text{d}$ (delivered dose) in both adults^{14,49,79} and children^{47,58} with asthma and at maintenance plus reliever doses up to 54 μg ^{62,78} in adults with asthma."