investigated and develop protocols for confirming clinical FA in a large sample.

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The Prevalence and Natural Course of Food Protein-Induced Enterocolitis Syndrome to Cow's Milk: A Large-Scale, Prospective Population-Based Study

Katz Y, Goldberg MR, Rajuan N, Cohen A, Leshno M. *J Allergy Clin Immunol.* 2011;127(3):647–653

PURPOSE OF THE STUDY. To prospectively determine the prevalence, clinical characteristics, and natural history of food protein–induced enterocolitis (FPIES) in association with cow's milk protein (CMP).

STUDY POPULATION. In this birth-cohort study, 13 019 of 13 234 newborns (98.4%) born over a 2-year period from June 2004 to June 2006 were enrolled.

METHODS. Information on reactions to CMP were obtained for all infants, and those with probable reactions were evaluated with skin-prick testing and oral challenge if clinically indicated. Criteria for CMP FPIES included onset at less than 9 months; vomiting, diarrhea, or both within 24 hours after the ingestion of milk in the absence of other immunoglobulin E (IgE)-mediated symptoms; and a positive challenge to milk that resulted in the symptoms listed above or removal of milk resulting in resolution of the symptoms.

RESULTS. The cumulative incidence of CMP FPIES was 0.34% (44 of 13 019). The most common symptoms were vomiting (100%), lethargy (77%), diarrhea (25%), pallor (14%), and bloody diarrhea (4.5%). All patients were diagnosed before the age of 6 months. Fifty percent of the cases resolved around the age of 1, and 90% resolved by age 3. Eight patients with FPIES had IgE-mediated milk allergy, and none had concomitant soy allergy.

CONCLUSIONS. The prevalence of FPIES is low but significant. Most patients with FPIES recover in early childhood. A significant proportion of CMP FPIES might convert to IgE-mediated milk allergy.

REVIEWER COMMENTS. This study is unique because of its large size and prospective design. It provides much needed information on the prevalence and natural history of CMP FPIES and highlights the possible overlap between FPIES, which is considered a non–IgE-mediated allergy, and IgE-mediated milk allergy. Soy might be a reasonable alternative to hypoallergenic formulas in infants with CMP FPIES, although previous US studies revealed a higher rate of soy reactivity among infants with CMP FPIES.

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Can Early Introduction of Egg Prevent Egg Allergy in Infants? A Population-Based Study

Koplin JJ, Osborne NJ, Wake M, et al. *J Allergy Clin Immunol*. 2010;126(4):807–813

PURPOSE OF THE STUDY. Earlier guidelines, in which delaying the introduction of potentially allergenic foods to infancy in an effort to prevent food allergy was recommended, were based on little evidence. These researchers sought to determine if the development of egg allergy by 12 months of age is associated with the age at which egg and solids are introduced and the duration of breastfeeding.

STUDY POPULATION. Subjects aged 11 to 15 months were recruited during immunization visits as part of the Australian HealthNuts study, which was a single-center, population-based, cross-sectional study of food allergy.

METHODS. During the clinic wait period after immunization, skin-prick tests for egg white, saline, and histamine were administered. Before the results were read, a questionnaire was administered to the parents regarding age of egg introduction. A second self-administered questionnaire collected information regarding duration of breastfeeding and age of solids introduction. Infants with positive skin-prick-test results to egg (wheal size $\geq$1 mm greater than negative saline control) were offered oral food challenges within the next 4 to 8 weeks. Infants with a history of reaction to egg in the previous month and/or a positive skin-prick-test result who were currently avoiding egg were considered egg allergic and excluded from oral food challenges.

RESULTS. Of 3552 eligible infants, 2589 (73%) were recruited. Results of egg skin-prick tests were positive for 448 infants, and 340 infants underwent an oral food challenge. Overall, 231 infants (8.9%) were determined to be egg-allergic. Egg introduction at 4 to 6 months was associated with a decreased risk of egg allergy, whereas egg introduction after 10 months was associated with an increased risk of egg allergy in both low- and high-risk infants. High-risk infants with a family history of allergy or a personal history of food allergy or eczema had a much higher risk of egg allergy (odds ratio [OR]: 6.7 [95% confidence interval (CI): 4.7–9.6]). Age of introduction of cooked egg (boiled, scrambled, fried, or poached) was significantly associated with egg allergy, whereas age of introduction of baked egg

(egg-containing products such as cakes or biscuits) was not. The lowest risk for egg allergy was found in infants introduced to cooked egg at 4 to 6 months (OR: 0.2 [95% CI: 0.06–0.71]; $P = .012$). There was no association of egg allergy with duration of breastfeeding (after adjustment for family and personal history of allergy) or age of introduction of other solid foods.

CONCLUSIONS. Introduction of cooked egg (boiled, scrambled, fried, or poached) at 4 to 6 months of age might protect against egg allergy irrespective of family or personal history of allergy. Duration of breastfeeding and age of introduction of other solids does not seem to affect development of egg allergy.

REVIEWER COMMENTS. In light of the changing perception that early instead of delayed exposure of commonly allergenic foods might lead to tolerance, this study is an important step in determining how the timing of introduction and form of food introduced (eg, cooked versus baked) might influence the development of food allergy. A large population was studied, and 75% of positive skin-prick-test results were confirmed with oral food challenges; however, egg-introduction history was retrospective and might have been subject to recall bias. The next step would be a prospective study on egg introduction to confirm these observations and to determine if the protective effect is limited only to egg or affects other food allergies such as those to peanut.

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Early Exposure to Cow's Milk Protein Is Protective Against Immunoglobulin E (IgE)-Mediated Cow's Milk Protein Allergy

Katz Y, Rajuan N, Goldberg MR, et al. *J Allergy Clin Immunol.* 2010;126(1):77–82

PURPOSE OF THE STUDY. The investigators determined the prevalence of cow milk allergy, the cross-reactivity with soy, and risk factors for the development of cow milk allergy in a large-scale, population-based prospective study.

STUDY POPULATION. All infants (13 234) born from June 10, 2004, to June 30, 2006, at the Assaf-Harofeh Hospital in Zerifin, Israel, were eligible for enrollment. The feeding history was obtained for 98.4% (13 019) of these infants, mostly by telephone interview.

METHODS. In the newborn period, after routine anticipatory guidance, in which breastfeeding was encouraged and other alternative cow milk–based feeding programs were reviewed, parents were asked to either fill in a questionnaire or contact the allergy clinic immediately after any suspected adverse reaction to the initiation of cow milk–protein feeding. If no unusual event was noted, the families were asked to contact the allergy clinic 14 to 30 days after initiation of cow milk–based feeding. Any parents who noted a possible adverse reaction were interviewed by an investigator and invited for examination and testing. Final diagnosis of immunoglobulin E (IgE)-mediated cow milk–protein allergy was made independently by 2 investigators, and any disagreement (2 cases) was resolved with conjoint discussion. Skin-prick testing to cow's milk and soy was conducted, as were open cow milk challenges.

RESULTS. The cumulative incidence of IgE-mediated cow milk allergy was 0.5% (66 of 13 019). The mean age of cow milk introduction was significantly different ($P < .001$) between healthy infants (61.6 ± 92.5 days) and those with IgE-mediated cow milk allergy (116.1 ± 64.9 days). Only 0.05% of the infants who were started on regular cow milk–protein formula within the first 14 days versus 1.75% who were started on formula between the ages of 105 and 194 days had IgE-mediated cow milk allergy ($P < .001$). None of the patients with IgE-mediated cow milk allergy proved to have an IgE-mediated soy allergy.

CONCLUSIONS. In this patient population, IgE-mediated cow milk allergy is less prevalent than previously reported. Early exposure to cow milk protein seemed to be protective against cow milk allergy.

REVIEWER COMMENTS. The results of this study, as well as those of other recent investigations, go against the previous mantra that prolonged restriction of specific food allergens might be helpful in the prevention of food sensitivity in the early years. Early introduction of specific dietary proteins seems to lead to tolerance, although the exact timing and dose required have not been determined. It is remarkable that none of the subjects with IgE-mediated milk allergy proved to have soy allergy, contrary to a reported co-reactivity of 10% to 14%. Because the reported rate of IgE-mediated milk allergy is lower in this study population than has been reported previously, additional studies are required to confirm these findings.

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Peanut Oil and Peanut Allergy, Foes or Folks?

Ho MH, Lee S, Wong WH, Lau Y. *Arch Dis Child.* 2011; 95(10):856–857

PURPOSE OF THE STUDY. Peanut allergy seems to be increasing among children in Hong Kong. The authors of this study report suggested that this increase might be a result of changes in edible oils. Crude peanut oil (protein content:

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