The increase of the effect from the *EPHX1* 139Arg allele with higher NO_2 exposure was most marked in the GSTP1 Val allele and GSTM1-present genotype.

CONCLUSIONS. Children with high *EPHX1* activity have an increased risk of asthma and wheezing outcomes. The risk is higher with high NO_2 exposure and a GSTP1 105Val allele or GSTM1-present genotype, which suggests that these common genetic polymorphisms and diplotypes play important roles in asthma pathogenesis among children, depending on airway oxidative stress.

REVIEWER COMMENTS. This article, although technical, sheds light on the scientific background of a basic premise in asthma: the association of air pollution on asthma risk. The results of previous studies have suggested that exposure to air pollution carries an increased risk of asthma. This study examined the genetic basis of this principle with a focus on the epoxide hydroxylase enzyme activity. An increased risk of asthma was seen in children with certain genotypes, and the risk was of higher magnitude depending on environmental NO_2 levels. These results add to the complex pathogenesis of asthma in regards to both genetic and environmental influences.

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FOOD ALLERGY

National Prevalence and Risk Factors for Food Allergy and Relationship to Asthma: Results From the National Health and Nutrition Examination Survey 2005–2006

Liu AH, Jaramillo R, Sicherer SH, et al. *J Allergy Clin Immunol*. 2010;126(4):798–806

PURPOSE OF THE STUDY. To investigate the prevalence and demographic risk factors of food allergy (FA) and its association with other atopic diseases in a population sample.

STUDY POPULATION. Data were collected from 10 348 adult and children older than 1 year, who represented the national population from 30 sites across the continental United States. Blood was collected and specific immunoglobulin E (IgE) panels were run for 79.3% of the subjects.

METHODS. Specific IgE levels to peanut, cow's milk, egg white, and shrimp were collected from subjects aged 6 years and older. Shrimp-specific IgE was not tested for subjects younger than 6 years. Food sensitization was defined as having at least 1 food-specific serum IgE level at ≥0.35 kU/L. FA risk categories included unlikely FA (between ≥0.35 and 2 kU/L), likely FA (egg white: ≥7 kU/L, or ≥2 kU/L if ≤2 years old; milk: ≥15 kU/L, or ≥5 kU/L if ≤2 years old; peanut: ≥14 kU/L; and shrimp: ≥5 kU/L), and possible FA (between 2 kU/L and the likely FA threshold level for each food). Clinical FA rates were based on the sum of 50% of possible FA and 95% of likely FA.

RESULTS. Overall food sensitization was 16.8%. Milk and egg sensitization were highest (22% and 13.9%, respectively) in children aged 1 to 5 years. Peanut sensitization was highest in older children aged 6 to 19 years (10.7%) and young adults aged 20 to 39 years (8.7%). Shrimp sensitization did not vary with age. Overall prevalence of multiple sensitizations was 4.7%. The overall estimated clinical FA rate was 2.5% ([3.1% possible FA × 0.5] + 1.0% likely FA). The highest prevalence of clinical FA was in children aged 1 to 5 years (4.2%) and lowest in adults aged 60 years or older (1.3%). Clinical FA was 1.8% in children aged 1 to 5 years for milk, egg, and peanut. Peanut (2.7%) was the most common clinical FA in older children aged 6 to 19 years. Peanut and shrimp (range: 0.9%–1.2%) were the most common clinical FA in adults aged 20 to 59, and shrimp (0.7%) was the most common clinical FA in adults aged 60 years or older. Overall prevalence of multiple clinical FA was 1.3%. Clinical FA was more prevalent in younger subjects ($P < .001$), male subjects ($P < .001$), and non-Hispanic black subjects ($P < .001$). Household income and education level were not significantly associated with clinical FA. Subjects with doctor-diagnosed asthma were at a higher risk for likely FA; this risk increased with increased asthma persistence and severity and with an emergency department visit for asthma in the previous year. The odds of doctor-diagnosed hay fever were increased for those with possible FA. Eczema was not significantly increased for any FA risk group.

CONCLUSIONS. The estimated population prevalence of clinical FA was 2.5% and was associated with childhood, male gender, and non-Hispanic black race/ethnicity. Asthma and emergency department visits for asthma were associated with likely FA.

REVIEWER COMMENTS. This is an important study that investigated the prevalence of clinical FA in children and adults in the same large population sample; it confirmed early observations of association of FA with childhood, non-Hispanic black race, and asthma. Use of objective data eliminated some limitations of previous survey studies. However, these data most likely underestimate clinical FA, because the study only accounted for 4 common allergenic foods, no clinical history is included (a small but significant percentage of patients with undetectable specific IgE might have clinical FA), and confirmation with oral food challenges was not performed. The next step will be to expand the number of foods

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 ≥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

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