Gene Polymorphisms, Breastfeeding, and Development of Food Sensitization in Early Childhood

PURPOSE OF THE STUDY. This study looked at the effect of breastfeeding on the development of food sensitivity (FS) and explored whether this relationship was modified by an array of functional single nucleotide polymorphisms (SNPs).

STUDY POPULATION. The study included children from the Boston Birth Cohort, consisting of multiethnic, predominantly African American mother-infant pairs, participating in a postnatal children’s health study assessing growth, development, and health outcomes.

METHODS. Follow-up visits were scheduled at 6 to 12 months and 2, 4, and 6 years, with blood samples obtained at these times. Breastfeeding history was obtained with a standardized questionnaire. FS was defined as specific IgE of 0.35 kU/L or greater to any of 8 common food allergens (egg white, cow milk, peanut, soy, shrimp, walnut, wheat, and cod). Eighty-eight potentially functional SNPs were genotyped from 18 genes involved in innate immunity or TH1/TH2 imbalance. Logistic regression models were used to test the effects of breastfeeding and gene-breastfeeding interactions on FS.

RESULTS. The children (n = 970) were followed for an average of 2.5 ± 2.2 years. Overall, 37.2% had FS, 76.0% were ever breastfed, and 21.0% were exclusively breastfed for at least 4 months. The prevalence of FS was higher in breastfed children (39.6%) than in those never breastfed (29.4%). With adjustment for pertinent covariates, breastfed children were at 1.5 times higher risk for FS than never breastfed children. The percentages of ever and exclusive breastfeeding were similar in those with and without family histories of allergic disease. Of the 88 SNPs successfully genotyped, 5 revealed statistically significant gene-breastfeeding interaction. Children carrying the GT/TT genotype for an SNP in the IL-12 receptor beta gene had a decreased risk of FS (odds ratio 0.6), but those with the GG genotype for that SNP had an increased risk of FS (odds ratio 2.0). Similar interactions were observed for SNPs in Toll-like receptor 9 (TLR9) and thymic stromal lymphopoietin (TSLP). Most striking, in the group with exclusive breastfeeding, children carrying the TLR9 TT genotype had odds ratios of 3.3 and 13.2 for breastfeeding <4 months and >4 months respectively.

CONCLUSIONS. The effects of breastfeeding on FS are modified by SNPs in the IL-12 beta receptor, TLR9, and TSLP genes, both individually and jointly. These findings underscore the importance of considering individual genetic variations in assessing this relationship.

REVIEWER COMMENTS. How often have pediatricians and allergists confronted a distraught mother who feels she did everything to avoid allergic disease in her young child by adhering to breastfeeding and delaying the introduction of notoriously allergenic foods? We know now from other studies that the latter tactic is generally the wrong course, and this article might help us understand why prior studies regarding the allergy-prevention benefits of breastfeeding have yielded mixed results.

Parental Eczema Increases the Risk of Double-Blind, Placebo-Controlled Reactions to Milk but Not to Egg, Peanut, or Hazelnut

PURPOSE OF THE STUDY. The authors investigated whether history of parental atopic diseases are associated with a higher risk of reaction to common allergenic foods in children.

STUDY POPULATION. In this Dutch study, 396 children (251 male, 145 female) with suspected food allergy were recruited from a pediatric allergy outpatient clinic. Median age was 5.4 years (range, 6 months to 17.8 years).

METHODS. The parents and children were asked if they each had a previous diagnosis of asthma, allergic rhinitis, atopic dermatitis, or (in the parents) food allergy. Children were identified as having food sensitivity through an elevated ImmunoCap-specific IgE (>0.35 kU/L) to cow’s milk, hen’s egg, peanut, or hazelnut. The children also underwent double-blind, placebo-controlled food challenges (DBPCFC) to the allergenic food, with a period of at least 2 weeks between food and placebo challenges. Logistic regression analysis was used to compare risk of a reaction to each food tested between children whose parents were not atopic and children with 1 or 2 parents with atopic diseases.

RESULTS. More than 90% of the children had been previously diagnosed with atopic disease, most commonly eczema. A total of 553 DBPCFCs were performed with 274 children tested for 1 food, 92 for 2 foods, 25 for 3 foods, and 5 for all 4 foods. Foods tested included cow’s milk (n = 185), egg (n = 110), peanut (n = 198), and
hazelnut \((n = 60)\). Parental eczema was significantly associated with reaction to milk oral challenges \(\text{odds ratio 3.1, 95\% confidence interval 1.5–6.3, } P < .01\) even after corrected for age, sex, serum IgE test results, and atopic comorbidity. Among children challenged with egg, peanut, or hazelnut, there was no significant association with parental eczema. Other parental atopic conditions \(\text{allergic rhinitis, asthma, hay fever, and eczema} \) were not associated with clinical reactivity to any of the foods. There was also no statistically significant effect for increasing number of parental atopic conditions on the risk of reaction to any of the foods.

CONCLUSIONS. There may be more shared genetic factors between clinical reactivity to milk and parental eczema than there are with other allergenic foods.

REVIEWER COMMENTS. Pediatricians and allergists are often asked if an infant has an increased risk of developing a food allergy based on family history, and this Dutch study suggests parental eczema may be a risk factor for cow’s milk allergy. However, there are still many questions regarding familial and environmental influences on atopic development in young children. What is the definitive answer regarding food avoidance and pregnancy, when is the “safest” time to introduce the more allergenic foods into a child’s diet, and what are the gene(s) that are more involved in atopic diseases? This promises to be a challenging field of study in which large, multicentered trials will help us begin to answer these questions.

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Tobacco and Air Pollution

Prenatal and Passive Smoke Exposure and Incidence of Asthma and Wheeze: Systematic Review and Meta-analysis


PURPOSE OF THE STUDY. To determine estimates of the prospective impact of smoking by parents or household members on the risk of wheeze and asthma at various childhood stages.

STUDY POPULATION. Children up to age 18 years exposed to environmental tobacco smoke

METHODS. Search of Medline, Embase, and conference abstracts to characterize cohort investigations of the incidence of asthma or wheeze in association with exposure to prenatal or postnatal maternal, paternal, or household smoking in individuals up to 18 years of age.

RESULTS. The authors identified 79 prospective studies. Exposure to pre- or postnatal passive smoke was associated with a 30% to 70% increased risk of incident wheezing (strongest effect from postnata maternal smoking on wheeze in children aged ≤2 years, odds ratio \([\text{OR} = 1.70, 95\% \text{ confidence interval } [\text{CI]} = 1.24–2.35, 4 \text{ studies}]\) and a 21% to 85% increase in incident asthma (strongest effect from prenatal maternal smoking on asthma in children aged ≤2 years, \(\text{OR} = 1.85, 95\% \text{ CI } = 1.35–2.53, 5 \text{ studies}\)).

CONCLUSIONS. Exposure to passive smoking increases the incidence of wheeze and asthma in children and young people by at least 20%. Preventing parental smoking is crucially important to the prevention of asthma.

REVIEWER COMMENTS. The study is limited by inclusion of atopic pediatric populations and the difficulty in establishing asthma in young children, as well as confounding impact of smoking of mother, father, and or other household members. However, the authors demonstrate, using 9 times more articles than previous studies, that passive smoking has a devastating effect of 28% to 70% enhanced risk of incidence of wheeze and/or asthma. Clearly, action to limit exposure to passive smoke in pediatric populations with chronic respiratory conditions is imperative.

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Parental Stress Increases the Detrimental Effect of Traffic Exposure on Children’s Lung Function


PURPOSE OF THE STUDY. Recent evidence indicates that the susceptibility to the adverse effects of air pollution is greater in the lower socioeconomic population. This may be as a result of increased psychosocial stress. This study hypothesized that psychosocial stress modifies the effect of traffic exposure on lung function.

STUDY POPULATION. Studied were 1399 children in the Southern California Children’s Health Study who were undergoing lung function testing. The study population came from 8 communities in southern California; these communities were selected to reflect a broad range of regional air pollutant exposures and large gradients in traffic exposure within communities.

METHODS. All children involved in the study underwent spirometric lung function testing during the 2008–2009 school year. Information regarding respiratory illnesses and environmental exposures was collected via a questionnaire. Sociodemographic characteristics (ie, race, income, insurance, tobacco smoke exposure) were assessed via a questionnaire at time of enrollment into the study in 2002–2003. The perceived stress scale, a 4-item questionnaire, was used to measure parental stress at time of enrollment. Exposure to nitric oxide, nitrogen dioxide, and total oxides of nitrogen...
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