between 18 and 35 years, and had lived in northern Manhattan or the South Bronx for at least 1 year.

METHODS. Urine BPA concentrations were measured in spot urine samples collected from mothers during the third trimester and from children at ages 3, 5, and 7 years. During visits at ages 5, 6, and 7 years, questionnaires were used to assess for wheeze in the preceding 12 months. Asthma diagnosis was determined once between ages 5 and 12 years by a physician by using history and physical as well as pre- and postbronchodilator testing. At 7- and 11-year visits, fraction of exhaled nitric oxide values were measured. At the 7-year visit, sero-atopy was determined by measuring specific IgE levels to aeroallergens, with sero-atopy defined as a specific IgE level >0.35. Odds ratios (ORs) for development of wheeze, asthma, and allergic sensitization were determined by using logistic and linear regression models.

RESULTS. BPA concentrations at ages 3, 5, and 7 years were associated with a diagnosis of asthma at ages 5 to 12 years (ORs were 1.5, 1.4, and 1.5 and P values were .005, .03, and .04, respectively). Urinary BPA concentration at age 3 years was associated with wheeze at age 5 years (OR: 1.4; P = .02) and 6 years (OR: 1.4; P = .02). BPA concentration at age 7 years was positively associated with wheeze at age 7 years (OR: 1.4; P = .04) and fraction of exhaled nitric oxide values (β =0.1, P = .02). Contrary to the authors’ hypothesis, prenatal urinary BPA concentrations were inversely associated with wheeze at age 5 years (OR: 0.7; P = .02). BPA concentrations measured at ages 3, 5, and 7 years were not associated with sero-atopy at age 7 years (P = .8).

CONCLUSIONS. Results of this study suggest that BPA exposure increases risk of airway hyperresponsiveness in children.

REVIEWER COMMENTS. This is the first study to report an association between urinary BPA concentrations and asthma in children. This study is limited by use of spot urine samples to assess exposure to BPA, which has a half-life of 6 hours. Further studies may use more rigorous methods of assessing BPA exposure and additionally explore the role of BPA exposure in development of other atopic diseases such as food allergy and atopic dermatitis.

Vitamin D Insufficiency Is Associated With Challenge-Proven Food Allergy in Infants

PURPOSE OF THE STUDY. In light of epidemiologic studies that show increased prevalence of food allergy in populations who reside farther from the equator, investigators sought to determine the association between vitamin D and food allergy.

STUDY POPULATION. From 2007 to August 2011, a total of 7134 infants between 11 and 15 months of age (inclusive) were approached during immunization visits at 120 locations throughout Australia.

METHODS. A total of 5120 infants underwent skin-prick testing (SPT) to peanut, egg, sesame, and cow’s milk or shrimp. Infants with a detectable wheal ≥1 mm as well as a random sample of infants with negative SPT were referred to a food allergy center for oral food challenge and repeat SPT using an extended panel of foods. Infants were deemed food allergic if they had both positive food challenge by objective criteria and an SPT wheal size ≥2 mm or a specific IgE ≥0.35 kUA/L. For foods on the extended spectrum SPT, a wheal size ≥8 mm was considered indicative of food allergy. Infants were labeled food-sensitized tolerant if they had negative oral food challenge despite a wheal size ≥2 mm or a specific IgE ≥0.35 kUA/L. Blood samples were obtained for measurement of 25-hydroxyvitamin D₃ levels and were seasonally adjusted. Vitamin D deficiency was defined as a serum level ≤25 nmol/L (<10 ng/mL), insufficiency as 25 to 50 nmol/L (10–20 ng/mL), and sufficiency as >50 nmol/L (equivalent to 20 ng/mL). Associations between vitamin D and food allergy were analyzed by using multiple logistic regression, adjusting for potential risk factors and confounding variables.

RESULTS. A total of 928 (85%) of the infants with positive SPT test and 197 (20%) controls visited the food allergy referral center. Complete data were available for a total of 481 infants. Among those classified as food sensitized (361), infants with vitamin D insufficiency were 3 times more likely to have food allergy than to be food-sensitized tolerant. For infants of Australian-born parents (271), vitamin D–insufficient infants were 3 times more likely to have any food allergy (P = .032), 10 times more likely to have multiple food allergies (≥2) (P = .014), 11 times more likely to have peanut allergy (P = .006), and 3 times more likely to have egg allergy (P = .025). The relationship between vitamin D status and food allergy was not significant for infants of foreign-born parents. Vitamin D insufficiency did not increase odds of the infant having eczema.

CONCLUSIONS. This is the first study to demonstrate an association between challenge-proven food allergy and vitamin D levels at 12 months, particularly among infants with allergic sensitization.

REVIEWER COMMENTS. This study provides supporting evidence for the hypothesis that vitamin D insufficiency is a risk factor for development of food allergy. It adds to the growing body of literature suggesting that vitamin D...
modifies risk of allergic diseases such as asthma, allergic rhinitis, and food allergy, although, notably, the investigators did not find an association between vitamin D levels and eczema. Further study is needed to determine whether correction of vitamin D insufficiency would result in decreased food allergy and increased tolerance among those sensitized.


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Maternal and Newborn Vitamin D Status and Its Impact on Food Allergy Development in the German LINA Cohort Study


PURPOSE OF THE STUDY. To investigate the relationship of maternal and cord blood vitamin D levels on atopic outcomes in early childhood.

STUDY POPULATION. A total of 378 mother-infant pairs from Leipzig, Germany, a subgroup of the LINA (Lifestyle and environmental factors and their Influence on Newborns Allergy risk) cohort study, were included. Mothers with immune or infectious disease concerns during the pregnancy were excluded.

METHODS. Blood samples were collected from expectant mothers at the 34th week of gestation and from infant cord blood at delivery for measurement of vitamin D (25(OH)D3). Regulatory T cells were also quantified from cord blood samples. Total IgE and allergen-specific IgE measurements were determined at birth (cord blood) and at 1 and 2 years of age in participating children. During pregnancy and at the children’s first and second birthdays, parents completed questionnaires regarding family history of atopy, housing and environmental conditions, and atopic outcomes of their children (doctor-diagnosed atopic dermatitis and/or food allergy or parental report of symptoms consistent with atopic dermatitis).

RESULTS. A high correlation was observed between maternal and cord blood 25(OH)D3 levels ($R = 0.812, P \leq 0.001$). Most pregnant women included in the study were either 25(OH)D3 deficient (<20 ng/mL; 44%) or insufficient (20–29.9 ng/mL; 25.7%), and few received vitamin D supplementation during pregnancy. Maternal 25(OH)D3 levels were positively associated with children’s risk of diagnosis of food allergy (adjusted odds ratio [aOR]: 3.66; 95% confidence interval [CI]: 1.36–9.87) in the second year of life or within the 2-year lifetime period (aOR: 1.91; 95% CI: 1.09–3.37), and with sensitization to food allergens (aOR: 1.59; 95% CI: 1.04–2.45) in the second year of life. Cord blood 25(OH)D3 levels were associated with diagnosis of food allergy in the second year of life (aOR: 4.65; 95% CI: 1.50–14.48) and negatively correlated with regulatory T-cell numbers ($R = -0.168, P = .031$).

CONCLUSIONS. Higher vitamin D levels in pregnancy and at birth were associated with a higher risk of food allergy and lower numbers of regulatory T cells.

REVIEWER COMMENTS. The role of vitamin D in the development of atopic disease remains unclear. Whereas some previous studies have suggested that maternal vitamin D deficiency may increase the risk of developing allergy, and may even be a key reason behind the rapidly rising prevalence of food allergy, this study suggests the complete opposite. Although vitamin D supplementation may be advised for many reasons, the prevention of allergy is not yet one of them.


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Environmental and Demographic Risk Factors for Egg Allergy in a Population-Based Study of Infants


PURPOSE OF THE STUDY. To determine the influence of a variety of environmental and demographic factors on the development of challenge-confirmed egg allergy in infants.

STUDY POPULATION. The study included 5276 infants presenting for their 12-month immunizations in Melbourne, Australia, with a focus on 453 infants with egg allergy confirmed by oral food challenge.

METHODS. At the time of initial testing, parents completed a questionnaire regarding a variety of environmental exposures and demographic factors. Infants underwent skin-prick testing (SPT) to egg regardless of history of reaction. Infants with a positive SPT then underwent additional testing, including allergen-specific immunoglobulin E testing by ImmunoCAP and an oral food challenge to egg. Infants with SPT >2 mm and positive challenge were deemed egg allergic. Multivariable logistic regression was used to determine factors associated with challenge-confirmed egg allergy. Adjustment was made for multiple confounding variables.

RESULTS. Factors that demonstrated a low risk for the development of egg allergy included having older siblings and having a dog in the house. Having siblings <6 years of age and having multiple siblings showed an even
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