presence of neutralizing antibodies against 12 enterovirus serotypes. Conditional logistic regression analysis was used to determine the association between enterovirus infections and atopic diseases. Categorized variables were used for confounding factors of pets at home, maternal education, paternal education, maternal tobacco use during pregnancy, older siblings, and day care attendance.

RESULTS. Cumulative exposure to different enterovirus serotypes by measured neutralizing antibodies was inversely associated with atopy (odds ratio: 0.73 [95% confidence interval: 0.56–0.96]; P = .025). The most pronounced protection was seen when echoviruses were analyzed as a separate group from coxsackieviruses (odds ratio: 0.63 [95% confidence interval: 0.46–0.88]; P = .006). The number of neutralizing antibodies against different coxsackievirus serotypes did not differ between case and control children.

CONCLUSIONS. An inverse association was found between cumulative exposure to echoviruses and atopic diseases with immunoglobulin E sensitization. Exposure to a high number of different echoviruses during the first years of life may protect from atopic diseases.

REVIEWER COMMENTS. The prospective nature and use of serologic assays to detect viral infections in this study are unique. Measurement of virus neutralizing antibodies at 2 time points yields reliable information about accumulation of antibodies over time. Viruses induce a strong T helper 1 response, which may suppress the excessive T helper 2 response typically seen in atopic disease. The present study supports the previously reported theory that atopic diseases develop less frequently in children with early microbial contacts. The gut is an important organ in the development of immunologic tolerance. The study of enteroviruses is particularly interesting because they are transmitted orofecally and replicate primarily in the gut. As acknowledged by the authors, further studies are needed to determine whether enteroviruses are surrogate markers for environmental factors or total infection burden.

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Pacifier Cleaning Practices and Risk of Allergy Development

PURPOSE OF THE STUDY. The study examined the effect of how parents clean their infant’s pacifier on the risk of developing eczema, asthma, or allergic sensitization.

STUDY POPULATION. Subjects were from a cohort of 187 term infants recruited into the AllergyFlora study in Gothenburg, Sweden. Mainly, families with at least 1 parent with allergic disease were approached. A total of 184 children were followed up until 18 months of age, and 174 were followed up to 36 months of age. Fourteen percent were delivered by cesarean delivery, 80% had at least 1 parent with a history of allergic disease, and 74% used a pacifier in the first year of life.

METHODS. When the children were 6 months old, parents were asked: “Does the child use a pacifier?” and “Is it cleaned by boiling, rinsing in tap water, or by the parents sucking on it?” with >1 option possible. A pediatric allergist examined the children and reviewed the medical record at 18 months, 36 months, and when symptoms suggested a diagnosis of eczema or asthma.

RESULTS. Of those who used pacifiers, nearly one-half of the parents (48%) reported they had sucked on the pacifier. By the age of 18 months, 25% of the children had developed eczema and 5% had developed asthma. Sucking the pacifier strongly lowered the risk of eczema (odds ratio: 0.37 [95% confidence interval: 0.15–0.91]; P = .02) and asthma (odds ratio: 0.12 [95% confidence interval: 0.01–0.99]; P = .03). Parents of vaginally delivered infants were more likely to suck the child’s pacifier. The group exposed to both maternal vaginal microbiota and parental oral microbiota via the pacifier had the lowest prevalence of eczema (20%), whereas infants exposed to neither maternal vaginal microbiota nor parental oral microbiota had the highest prevalence (54%). Children who were either vaginally delivered or whose parents sucked on their pacifiers had an intermediate prevalence of eczema (31%). Evaluation of the microbiota present in saliva at 4 months of age according to molecular genetics (terminal-restriction fragment length polymorphism) distinguished patterns of microbes in the saliva depending on pacifier cleaning practices.

CONCLUSIONS. Sucking on the infant’s pacifier before it is given to the infant may protect against early development of eczema and asthma. This practice may influence the infant’s oral microbiota composition. At 18 months of age, the prevalence of eczema was ~2.5 times lower among vaginally delivered children whose parents sucked on their pacifiers than among children born via cesarean delivery whose parents did not suck on their pacifiers (20% vs 54%). Evidence for the transfer of respiratory pathogens according to this practice was not apparent. Dental caries seemed unrelated to close salivary contact.

REVIEWER COMMENTS. Although this association does not prove causation, this surprising finding supports the “hygiene hypothesis” and the role of initial (birth) and subsequent (oral) exposures to microbes in modulating immune responses in a favorable manner. In this situation, the sharing of maternal saliva may replicate saliva and oral microbes likely shared by premastication of food by the mother for feeding to the infant, a practice that is now only rarely
observed in Westernized societies where processed and sterile infant food is available.

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Association of Maternal Anti-HLA Class II Antibodies With Protection From Allergy in Offspring

PURPOSE OF THE STUDY. The goal of this study was to determine if maternal production of anti-HLA antibodies arising from mismatch between mother and fetus is associated with allergic outcomes at 8 years of age. Previous studies have suggested that the prevalence of atopy is lower in children of higher birth order. Higher numbers of pregnancies are associated with increased antibodies against paternal HLA antigens and maternal interferon-γ production (Th1) in response to fetal cells. The authors postulated that the raised levels of interferon-γ secondary to HLA mismatch may be another factor associated with lower risk of allergic disease.

STUDY POPULATION. A total of 269 maternal blood samples from the Asthma in Ashford Study (Ashford, Kent, UK) were analyzed for anti-HLA antibodies. Retrospective anti-HLA antibody analysis was restricted to mothers who had no additional births in the 4-year interval between birth of the child and collection of the blood sample. Parity at the time of birth of the index child ranged from 0 to >4.

METHODS. Maternal sera were tested for antibodies to HLA class I and II molecules. Associations between the presence or absence of maternal anti-HLA antibodies and allergic outcomes at age 8 years were made by using χ² tests. Logistic regression was used to investigate the association between maternal HLA antibodies and birth order with the child’s allergic status. Skin prick testing to pollen mixture, Dermatophagoides pteronyssinus, and cat fur were conducted on the mothers during pregnancy and on children at age 8 years. Allergic outcomes in children were measured by using questionnaires and results of skin prick testing.

RESULTS. The detection of maternal anti-HLA class II antibodies was associated with less positivity to allergens on skin prick testing and less seasonal rhinitis in children at age 8 years. Nonatopic children had a higher birth order and increased presence of maternal anti-HLA class II antibodies. Atopic children did not have a statistically significant difference in maternal HLA antibodies when analyzed for birth order.

CONCLUSIONS. Maternal anti-HLA class II antibodies are associated with birth order and increased protection from allergy in offspring in nonatopic children. Increasing parity-related Th1 cytokine maternal immune responses may contribute to the birth order effect regardless of maternal atopic status.

REVIEWER COMMENTS. This study suggests another mechanism for decreased allergy prevalence in children who have older siblings. This difference has been attributed to the predominance of Th1 cytokines over Th2 cytokines secondary to higher exposure to infections in younger children in many previous studies. The authors of this study offer an alternative explanation based on the presence of anti-HLA antibodies in women with multiple pregnancies. This interesting alternative explanation for decreased allergy in younger siblings has no practical implications at this point.


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Prevalence of Allergic Disease in Foreign-Born American Children

PURPOSE OF THE STUDY. The goal of this study was to determine whether the prevalence of allergic diseases is lower in foreign-born Americans and if prevalence increases with prolonged residence in the United States.

STUDY POPULATION. Data were collected for 91,642 children ages 0 to 17 years in the 2007–2008 National Survey of Children’s Health. A total of 79,667 participants were analyzed.

METHODS. Random telephone numbers were selected for administration of the questionnaire, which was conducted in English, Spanish, and 4 Asian languages (Korean, Mandarin, Cantonese, and Vietnamese).

RESULTS. Children born outside the United States compared with those born within the United States had significantly lower prevalence of allergic disorders (20.3% vs 34.5%; logistic regression odds ratio [OR]: 0.48 [95% confidence interval (CI): 0.38–0.61]; P < .001). Among children born outside the United States, children with foreign-born parents had significantly lower odds of atopic disease than those with US-born parents (18.2% vs 33.4%; logistic regression OR: 0.45 [95% CI: 0.25–0.78]; P = .005). Furthermore, there was an additive effect in which children of 2 foreign-born parents had a lower prevalence of allergic disease than those with 1 foreign-born parent. Among foreign-born children, children who lived in the United States for >10 years, compared with those who resided in the United States for only 0 to 2 years, had significantly higher odds of...
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