Allergy

RISK FACTOR, PREVENTION, AND THE HYGIENE HYPOTHESIS

Antibiotic Exposure in the First Two Years of Life and Development of Asthma and Other Allergic Diseases by 7.5 yr: A Dose-Dependent Relationship


PURPOSE OF THE STUDY. The goal of this study was to investigate the associations of antibiotic use in the first 2 years of life with the development of asthma, eczema, and hay fever by age 7.5 years in a longitudinal birth cohort.

STUDY POPULATION. Subjects were 4952 children from ALSPAC (Avon Longitudinal Study of Parents and Children), a population-based cohort that recruited 14,541 expectant mothers with due dates between April 1, 1991, and December 31, 1992, in Avon, United Kingdom.

METHODS. Child antibiotic use and asthma, eczema, and hay fever symptoms were maternally reported through questionnaires collected annually when subjects were ≥6 months of age. In 3 questionnaires covering the periods 0 to 6, 6 to 15, and 15 to 24 months, mothers reported whether their child had taken any antibiotics, the number of courses, and when the courses were taken. The primary outcome was asthma at 7.5 years, defined as maternal report of a physician’s diagnosis of asthma and symptoms of wheezing during the previous 12 months. Two secondary outcomes (eczema and hay fever) were maternally reported at the same time. Atopy was assessed by skin prick tests at age 7.5 years and defined as a positive response (≥2 mm wheal) to Dermatophagoides pteronyssinus, grass, or cat allergen. Headache reported at 7.5 years, which has no plausible link with antibiotic use, was used as a positive control to test for reporting bias. Data were analyzed by using multivariate logistic regression.

RESULTS. Children reported to have taken antibiotics during infancy (0–2 years) were more likely to have asthma at 7.5 years (odds ratio: 1.75 [95% confidence interval: 1.40–2.17]), and the odds increased with greater numbers of courses. When accounting for reverse causation, the association was weakened but still evident. In addition, the association was evident but weaker for eczema and hay fever compared with asthma. The effect seemed to be associated with cumulative dose rather than a critical period of exposure during the first 2 years of life. There was no association between infant antibiotic use and atopy on skin prick testing at 7.5 years or reported headaches at the same age.

CONCLUSIONS. The authors found a strong, dose-dependent correlation between increased antibiotic exposure during the first 2 years of life and the development of asthma at 7.5 years, which did not seem to be mediated through an association with atopy.

REVIEWER COMMENTS. The worldwide prevalence of atopic diseases, including asthma, has increased considerably over the last 30 years in developed, Westernized countries. Possible explanations for such a rise include recent trends in vitamin D deficiency, the hygiene hypothesis, and an increase in antibiotic prescriptions. Antibiotic exposure in infancy causes disruption to the developing gut microbiota, which could predispose subjects to asthma and allergic diseases because this period is critical in immune development.

Although the authors have found a strong, dose-dependent association between antibiotic use in infancy and later asthma, the lack of association with objectively measured atopy contradicts this proposed mechanism. The authors interestingly suggest that there may be other mechanisms involved in mediating effects of alterations in the gut microbiota, such as nonatopic inflammation.

Enterovirus Infections in Early Childhood and the Risk of Atopic Disease—A Nested Case-Control Study


PURPOSE OF THE STUDY. The goal of this study was to assess the relationship between enterovirus infections in the first 2 years of life and atopic diseases. It also studied the importance of different enterovirus serotypes in atopic diseases.

STUDY POPULATION. The study population was derived from the Finnish DIPP (Diabetes Prediction and Prevention) Study. Newborn infants with HLA-DQB1 risk alleles had clinic visits every 3 to 6 months for the first 2 years of life and at subsequent intervals of 6 to 12 months. At each visit, children had a comprehensive history and physical examination performed and a venous blood sample obtained. For the present study, 71 subjects were identified as case children if they had the following: a diagnosis of asthma, atopic dermatitis, or allergic rhinitis; who had stored serum obtained at 1, 2, and 5 years available; and had serum-specific immunoglobulin E antibodies against a mixture of aeroallergens (birch, timothy, mugwort, cat, dog, horse, mite, and Cladosporium). There were 142 control subjects matched for HLA-DQB1 genotype, age, and gender.

METHODS. This study had a nested case-control design. Serum samples obtained at 1 year were analyzed for the presence of neutralizing antibodies against 5 echovirus serotypes. Serum samples obtained at 2 years were analyzed for the
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*Pediatrics* 2014;134;S135

DOI: 10.1542/peds.2014-1817E

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