CONCLUSIONS. There is an enhanced risk of asthma exacerbations and unscheduled visits to primary care physicians strongly related to return to school after summer vacations.

REVIEWER COMMENTS. This study is the largest epidemiologic trial to date demonstrating a well-recognized peak in asthma exacerbations after the return to school, particularly in September; this peak is likely related to viral illness, environmental allergens, and/or lack of controller medications. Prophylaxis, particularly with inhaled steroid controller medication beginning at the end of August, is recommended by the authors, particularly for children with multifactorial asthma.

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Consequences of Antibiotics and Infections in Infancy: Bugs, Drugs, and Wheezing
Ong MS, Umetsu DT, Mandl KD. Ann Allergy Asthma Immunol. 2014;112(5):441–445.e1

PURPOSE OF THE STUDY. Previous studies have investigated the association between early antibiotic exposure and the development of asthma, with inconsistent results and concern that any observed association was confounded by lower and upper respiratory tract illnesses in early childhood. Given the inconsistencies of existing data, the purpose of this study was to clarify if an association exists between antibiotic exposure in the first year of life and the development of asthma up to age 7 years.

STUDY POPULATION. From a retrospective cohort of children enrolled in a nationwide, employer-provided health insurance plan in the United States, this study examined 62,576 children who were continuously enrolled from birth to at least 5 years of age.

METHODS. The children were evaluated for an association between antibiotic exposure during the first year of life and subsequent development of 3 asthma phenotypes: transient wheezing (began and resolved before 3 years of age), late-onset asthma (began after 3 years of age), and persistent asthma (began before 3 years of age and persisted through 4–7 years of age). Antibiotic exposure was defined as the receipt of at least 1 antibiotic prescription of 7 to 10 days’ length in the first year of life. Children were identified as having persistent asthma if at least 1 of the following criteria was met in the 2 years before the measurement year: (1) at least 1 emergency department visit with asthma as the principal diagnosis; (2) at least 1 acute care inpatient encounter with asthma as the principal diagnosis; (3) at least 4 outpatient asthma visits with asthma as one of the listed diagnoses and at least 2 asthma medication–dispensing events; and (4) at least 4 asthma medication–dispensing events. Exclusion criteria included having >1 physician-diagnosed lower and upper respiratory tract illness in the first year of life.

RESULTS. Antibiotic use in the first year of life was associated with the development of transient wheezing (odds ratio [OR]: 2.0 [95% confidence interval (CI): 1.9–2.2]; P < .001) and persistent asthma (OR: 1.6 [95% CI: 1.5–1.7]; P < .001). A dose–response effect was observed. When ≥5 antibiotic courses were received, the odds of persistent asthma doubled (OR: 1.9 [95% CI: 1.5–2.6]; P < .001). There was no association between antibiotic use and late-onset asthma.

CONCLUSIONS. Antibiotic use in the first year of life is associated with an increased risk of early-onset childhood asthma before 3 years of age. The apparent effect has a clear dose response.

REVIEWER COMMENTS. The exclusion of respiratory tract illnesses in the first year of life removes a significant potential confounding factor that has led to inconsistent conclusions in previous studies examining a link between antibiotic use in infancy and the development of asthma. The finding that more frequent antibiotic use leads to an increased risk of early-onset asthma seems to support the microbiota hypothesis, which postulates that antibiotic use in early life increases the risk of atopic disorders by altering the diversity and composition of the intestinal microbiota, thereby disrupting mucosal mechanisms of immune tolerance and increasing susceptibility to Th2 cytokine-dependent allergic inflammation. Antibiotic use in infancy should be limited to reduce the possibility of driving this process.

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Food Allergy and Increased Asthma Morbidity in a School-Based Inner-City Asthma Study

PURPOSE OF THE STUDY. The goal of this study was to investigate the relation between food allergy and asthma morbidity in inner-city students with asthma.

STUDY POPULATION. A total of 300 elementary school students with physician-diagnosed asthma were enrolled over a period of 6 years in the School Inner-City Asthma Study in the northeastern United States. Subjects were eligible if they had wheezing, used controller medications, or had unscheduled health care visits for asthma in the previous 12 months. This population was primarily a nonwhite (>95%), impoverished cohort with 47% of caregivers reporting an annual income of <$25 000.
METHODS. An extensive baseline survey was administered to the child’s caregiver. Asthma morbidity outcomes included clinical symptoms, the effect on activities of daily living, resource utilization, and lung function measurements. Food allergy history included symptoms experienced within 1 hour of ingestion of reported allergic foods. Pulmonary function testing was performed according to American Thoracic Society guidelines.

RESULTS. Twenty-four percent of the study population had physician-diagnosed food allergy, with peanut and then tree nuts being the most prevalent foods involved. Multiple food allergies were present in 49% of the subjects with food allergy. Subjects with any food allergy had almost double the increased risk of daytime symptoms and more than twice the risk of lifetime hospitalization but no increase in missed school days due to asthma or unscheduled asthma visits to a health care provider. The percent predicted forced expiratory volume in 1 second (FEV₁) scores were significantly lower in the food allergy group. Subjects with multiple food allergies had >3 times the increased risk of daytime asthma symptoms and >5 times the risk of lifetime hospitalization, as well as significantly higher number of unscheduled health care visits. Lung function was also lower, including percent predicted FEV₁ and FEV₁/forced vital capacity scores.

CONCLUSIONS. This study found an increased risk of asthma morbidity in children with any food allergy and even more so in children with multiple food allergies. There was also an increased prevalence of food allergy in children with asthma compared with the national prevalence rates, consistent with previous findings.

REVIEWER COMMENTS. The association between food allergy and several measures of asthma morbidity was clearly demonstrated in the current study population. Whether these same findings would apply to a population with different demographic characteristics remains to be studied. It is also not clear whether asthma exacerbations were triggered by exposure to the food allergen. Nonetheless, increased monitoring of children with concomitant asthma and food allergy seems appropriate.

Remission and Persistence of Asthma Followed From 7 to 19 Years of Age

PURPOSE OF THE STUDY. The goal of this study was to analyze the remission and persistence of childhood asthma in adolescents.

STUDY POPULATION. The study population included 205 subjects with asthma studied from age 7 to 8 years up until the study end-point age of 19 years.

METHODS. Subjects with asthma were identified by distributing an extended International Study of Asthma and Allergies in Childhood questionnaire to the families of all children in the first and second grade in 3 municipalities in northern Sweden. The diagnosis of asthma was confirmed in 248 of the subjects identified according to the questionnaire by using structured interviews and clinical assessments. These subjects were then assessed for their status of asthma, family history of asthma, asthma medication use (including inhaled corticosteroids), asthma severity score, presence of physician-diagnosed rhinitis or eczema, and traffic exposure and home exposure to dampness by using annual questionnaires until 19 years of age. In addition, some patients underwent skin prick testing for 10 common allergens. Positive skin prick test results were validated in relation to serum-specific immunoglobulin E levels. Lung function testing was also performed in all patients in the asthma cohort, and some patients received methacholine bronchial challenge tests.

RESULTS. A total of 205 subjects remained in the study until the end-point age of 19 years. Of these patients, 21% had asthma that was in remission, 38% had periodic asthma, and 41% had persistent asthma. Remission was more common in boys. Sensitization to furred animals at baseline as identified by skin prick testing and serum-specific immunoglobulin E levels was inversely associated with remission (odds ratio: 0.14 [95% confidence interval: 0.04–0.55]), as was severe asthma (odds ratio: 0.19 [95% confidence interval: 0.07–0.54]). Eighty-two percent of children with these characteristics had persistence of asthma in adolescence.

CONCLUSIONS. Remission of asthma during adolescence is common. Female gender, sensitization to furred animals, and more severe asthma all inversely correlate with the chance of asthma going into remission.

REVIEWER COMMENTS. The take-home message from this article is the importance of long-term clinical follow-up of patients with asthma, as large numbers of patients have persistent disease. Furthermore, the identification of the risk factors for disease persistence will allow better identification of at-risk patients and allow patient-specific care with medical interventions that are appropriate in intensity, well timed, and improve the long-term outcomes of patients without overburdening the system.


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## Food Allergy and Increased Asthma Morbidity in a School-Based Inner-City Asthma Study

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