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### **Asthma During Pregnancy and Clinical Outcomes in Offspring: A National Cohort Study**

Tegethoff M, Olsen J, Schaffner E, Meinlschmidt G.  
*Pediatrics*. 2013;132(3):483-491

**PURPOSE OF THE STUDY.** The goal of this study was to determine the associations between asthma during pregnancy and the offspring's risk of a wide variety of childhood diseases.

**STUDY POPULATION.** Birth data between 1996 and 2002 were prospectively collected from the Danish National Birth Cohort; 66 712 mother-child pairs were eligible and completed the study. Mothers had given birth to live singletons, most were aged >27 years, they had a medium to high socioeconomic status, were in average to very good health, were multiparous, and ~25% of the women reported smoking. A total of 4145 (6.2%) had a diagnosis of self-reported asthma during their pregnancy.

**METHODS.** Computer-assisted interviews at ~12 and 30 weeks' gestation and at 6 months' postpartum were used to gather information about maternal asthma. Information on the children's diseases was obtained from the Danish National Hospital Register. Cox and logistic regression models were used to analyze the associations between asthma during pregnancy and the risk of offspring disease, as well as controlling for potential confounders.

**RESULTS.** Offspring were followed up for mean of 6.2 years (range: 3.6-8.9 years). Positive associations included an increased risk of infectious and parasitic diseases (hazard ratio [HR]: 1.34 [95% confidence interval (CI): 1.23-1.46]) and diseases of the nervous system (HR: 1.43 [95% CI: 1.18-1.73]), ear (HR: 1.33 [95% CI: 1.19-1.48]), respiratory system (HR 1.43 [95% CI: 1.34-1.52]), and skin (HR: 1.39 [95% CI: 1.20-1.60]). Potential associations not confirmed by analysis included endocrine and metabolic disorders (HR: 1.26 [95% CI: 1.02-1.55]), digestive system diseases (HR: 1.17 [95% CI: 1.04-1.32]), and congenital malformations (odds ratio: 1.13 [95% CI: 1.01-1.26]). There was no noted increased risk between maternal asthma and neoplasm, mental disorders, or diseases of the blood and immune system, circulatory system, musculoskeletal system, and genitourinary system.

**CONCLUSIONS.** The observed associations may be secondary to maternal hypoxia restricting fetal oxygenation, increase in cytokine exposure, or dysregulation of the hypothalamic-pituitary-adrenal axis. Results suggest the importance of monitoring and evaluating for maternal asthma during pregnancy and continuing to carefully follow up the offspring postnatally.

**REVIEWER COMMENTS.** This study assessed maternal asthma and its long-term consequences on the offspring. A large patient cohort with prospectively collected data and the inclusion of medically verified diagnoses significantly strengthened the results. Asthma severity information was not assessed by spirometry or the use of asthma controller medications, nor did the study examine the number of maternal asthma exacerbations during the prenatal and perinatal periods. The association between maternal asthma and childhood diseases emphasizes the importance of monitoring the infant postnatally, as well as through childhood, for these diseases.

URL: [www.pediatrics.org/cgi/doi/10.1542/peds.2014-1817CCC](http://www.pediatrics.org/cgi/doi/10.1542/peds.2014-1817CCC)

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### **Seasonality of Asthma: A Retrospective Population Study**

Cohen HA, Blau H, Hoshen M, Batat E, Balicer RD.  
*Pediatrics*. 2014;133(4). Available at: [www.pediatrics.org/cgi/content/full/133/4/e923](http://www.pediatrics.org/cgi/content/full/133/4/e923)

**PURPOSE OF THE STUDY.** The goal of this study was to evaluate whether seasonal variations in asthma (with the highest incidence in September) can be documented in a large cohort of children in primary care and to determine the impact of age, gender, and urban/rural living.

**STUDY POPULATION.** A historical population of children aged 2 to 15 years in Israel's Clalit Health Services registry, seen from 2005 to 2009, were included in this study. A total of 919 873 children were identified.

**METHODS.** Electronic record reviews were conducted. The key study outcomes were the diagnosis of asthma exacerbations and asthma medication prescriptions, analyzed according to week of diagnosis. Statistical models were built to assess relative strength of secular trends, seasonality, and age group.

**RESULTS.** The authors documented that 8.9% of children were asthmatic, and 62% were boys. The age groups were as follows: 49% aged 2 to 5 years, 24% aged 6 to 9 years, and 27% aged 10 to 16 years. There was a 2.01-fold increase in pediatric asthma exacerbations and a 2.28-fold increase in prescriptions of asthma bronchodilator medications during September compared with August. The association between the opening of school and the incidence of asthma-related visits to the primary care physician was greatest in children aged 2 to 5 years (odds ratio: 2.15) and 6 to 11 years (1.90-fold). Adolescents had a lesser peak (1.81-fold). There was a second rise in late fall, with fluctuations throughout winter, and a trough in summer.

**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  $\geq 5$  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 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.

URL: [www.pediatrics.org/cgi/doi/10.1542/peds.2014-1817DDD2](http://www.pediatrics.org/cgi/doi/10.1542/peds.2014-1817DDD2)

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

Friedlander JL, Sheehan WJ, Baxi SN, et al. *J Allergy Clin Immunol Pract.* 2013;1(5):479-484

**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.

## Seasonality of Asthma: A Retrospective Population Study

Christopher Randolph

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