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## Cesarean Section Delivery and Development of Food Allergy and Atopic Dermatitis in Early Childhood

Papathoma E, Triga M, Fouzas S, Dimitriou G. *Pediatr Allergy Immunol.* 2016;27(4):419-424

**PURPOSE OF THE STUDY.** To investigate the association between cesarean delivery and physician-diagnosed food allergy and atopic dermatitis during the first 3 years of life.

**STUDY POPULATION.** A prospective birth cohort study of children born at  $\geq 34$  weeks' gestation at the University Hospital of Patras, Greece, between August 2009 and March 2011.

**METHODS.** Four hundred fifty-nine children born in the same tertiary maternity unit were examined at birth and followed up at 1, 6, 12, 18, 24, 30, and 36 months of age. Those with symptoms suggestive of food allergy or atopic dermatitis were evaluated by a pediatric allergy specialist to confirm the diagnosis.

**RESULTS.** Food allergy was diagnosed in 5.2% and atopic dermatitis in 13.5% of study participants. Cesarean delivery (odds ratio [OR] 3.15; 95% confidence interval [CI] 1.14-8.70), atopic dermatitis (OR 3.01; 95% CI 1.18-7.80), parental atopy (OR 4.33; 95% CI 1.72-12.1), and gestational age (OR 1.57; 95% CI 1.07-2.37) were significant and independent predictors of food allergies. Children with at least 1 allergic parent delivered by cesarean delivery had higher odds of developing food allergy compared with vaginally delivered children of nonallergic parents (OR 10.0; 95% CI 3.06-32.7). The effect of cesarean delivery on atopic dermatitis was not significant (OR 1.35; 95% CI 0.74-2.47). Antibiotic use and prolonged rupture of membranes did not have a significant effect on food allergy or atopic dermatitis.

**CONCLUSIONS.** Children born by cesarean delivery had threefold higher odds of food allergy, independent of a range of confounding factors, including gestational age, birth weight, smoking, family history of atopy, breastfeeding, and others. Those delivered by cesarean delivery with at least 1 allergic parent had 10-fold higher odds of developing food allergy compared with children who were born vaginally to nonallergic parents. Parental atopy, atopic dermatitis, and gestational age were independent predictors of food allergies as well. Cesarean delivery was not related to the development of atopic dermatitis.

**REVIEWER COMMENTS.** In this study, the authors provide data for a homogeneous birth cohort in Greece. The strengths of this study include the 3-year follow-up period, the similarities between those who remained in the study

and those who were lost to follow-up, physician diagnosis of food allergy rather than self-report, and the ability to control for multiple factors, such as atopy, breastfeeding, and family history.

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## Early-Life Antibiotic Use and Subsequent Diagnosis of Food Allergy and Allergic Diseases

Hirsch AG, Pollak J, Glass TA, et al. *Clin Exp Allergy.* 2017;47(2):236-244

**PURPOSE OF THE STUDY.** To evaluate associations of early-life antibiotic use with subsequent occurrences of a food allergy and other allergies in childhood.

**STUDY POPULATION.** Children born in Pennsylvania between 2001 and 2011.

**METHODS.** The Geisinger Clinic electronic health record data on children born between 2001 and 2011, who had at least 2 outpatient encounters in the first 3 months of life, were assessed. Subjects' data were collected up to 7 years of age. Diagnoses were classified as milk allergies, nonmilk food allergies, or other allergic conditions. Disease processes were determined by *International Classification of Diseases, Ninth Revision* codes. Incidence density sampling was used to identify 5 controls for every case individually, matched on sex and age. The Medi-Span Generic Product Identifier Therapeutic Classification System was used to identify the number and type of antibiotic orders before diagnosis of the allergy. Penicillins, cephalosporins, and macrolides were the antibiotic classes analyzed. Other variables studied included sex, race, use of public medical assistance, mode of delivery, outpatient encounters, and inpatient admissions.

**RESULTS.** Of the total population studied, 30 060 patients met eligibility criteria. Children with 3 or more antibiotic orders had greater odds of having a milk allergy (odds ratio: 1.78; 95% confidence interval: 1.28-2.48), a nonmilk food allergy (1.65; 1.27-2.14), and/or other allergies (3.07; 2.72-3.46) than children with no antibiotic orders. Children with any allergy were significantly more likely than controls to have public medical assistance, outpatient encounters, and antibiotic orders before an allergy diagnosis. Children with milk or nonmilk food allergies were also more likely to have inpatient encounters. Penicillin and cephalosporin orders had a stronger association with overall food allergy diagnoses than macrolides, when prescribed in the first 2 years of life.

**CONCLUSIONS.** The authors of this study found strong associations between antibiotic orders and diagnoses of milk allergies, nonmilk food allergies, and other allergic conditions in patients up to 7 years of age. Limitations of the

study include the use of *International Classification of Diseases, Ninth Revision* codes to establish allergy issues. For food allergies, these codes can reflect an intolerance, adverse reaction, or sensitization, in addition to immunoglobulin E-mediated allergic reactions. For other allergy issues, a diagnosis of asthma or allergic rhinitis may not have been confirmed by spirometry or allergy testing. Compliance with antibiotic prescriptions could also not be studied. However, the strengths of this study include the large sample size and the use of physician diagnosis of allergic issues in relation to antibiotic orders. Consultation or protopathic (reverse-causality) bias alone cannot account for the associations between early-life antibiotic use and subsequent diagnoses of food allergies and other allergic issues.

**REVIEWER COMMENTS.** Children with and without allergies have differences in their microbiota. Antibiotic use in early life has been linked to disruptions in the microbiome. The increase in the prevalence of allergies has paralleled the use of broad-spectrum antibiotics among children. This study adds to the literature supporting judicious use of antibiotics in early life.

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### **Association Between Medication Prescription for Atopic Diseases and Attention-Deficit/Hyperactivity Disorder**

van der Schans J, Pleiter JC, de Vries TW, et al. *Ann Allergy Asthma Immunol.* 2016;117(2):186–191

**PURPOSE OF THE STUDY.** To determine if children with attention-deficit/hyperactivity disorder (ADHD) were more likely than matched controls to have been previously managed for atopic diseases. Furthermore, the authors sought to study the effect on children's ADHD medication use when parents were in treatment for ADHD and atopic diseases.

**STUDY POPULATION.** Children 6 to 12 years of age and their parents from a northern region of the Netherlands were included.

**METHODS.** This was a retrospective case-control study of children identified via regional pharmacy dispensing data from 1994 and 2013. The cases of the children reviewed had at least 2 prescriptions of methylphenidate within a 1-year period. Each child with ADHD was matched to 4 controls on the basis of sex, date of birth, and location. Parental prescription data for ADHD and atopic diseases were linked to the children with ADHD and controls. Data were analyzed by using conditional logistic regression and multivariable conditional logistic regression models.

**RESULTS.** A total of 4257 cases of children treated for ADHD and 17 028 corresponding controls were found. The

mean age of the children on ADHD medication was 8.3 years, and the group was predominantly made up of boys (76.7%); similar findings were seen in the matched control group. Children on ADHD medications were more likely than controls to have received medications for asthma (odds ratio [OR]: 1.4; 95% confidence interval [CI]: 1.3–1.6), allergic rhinitis (OR: 1.4; 95% CI: 1.1–1.8), and eczema (OR: 1.3; 95% CI: 1.1–1.5). The children with ADHD were more likely to have a parent on ADHD medication when compared with the control group (OR: 3.8; 95% CI: 3.3–4.3). Parental use of medications for allergic rhinitis (OR: 1.3; 95% CI: 1.1–1.5) and asthma (OR: 1.2; 95% CI: 1.1–1.3), but not eczema (OR: 1.1; 95% CI: 1.0–1.2), was associated with their child receiving ADHD medication.

**CONCLUSIONS.** Children with a history of medically treated atopic disease are at an increased risk of receiving ADHD drug treatment. Additionally, if the parent of the child had taken medication for asthma or allergic rhinitis, the child was also at an increased risk of using ADHD medication. These findings imply a link between atopic disease and ADHD that may be based on inherited and/or environmental factors.

**REVIEWER COMMENTS.** As ADHD and atopic disease have almost synchronously increased in prevalence, questions into possible etiologies and/or links have been raised. Whether atopic disease is implicated as a causative factor in the etiology of ADHD or may be considered a strong risk factor in its development is not clear and requires further investigation. This study aids in increasing provider awareness that atopic disease may be linked to ADHD. Also, the importance of a thorough family history as means to providing proper anticipatory guidance to patients and families is stressed in this study.

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### **Associations of Physical Activity and Sedentary Behavior With Atopic Disease in United States Children**

Strom MA, Silverberg JI. *J Pediatr.* 2016;174:247–253

**PURPOSE OF THE STUDY.** To determine the association of eczema, asthma, and hay fever with sedentary behavior, including television and/or video game usage, sports participation, and days of vigorous physical activity. The authors of the study also sought to determine if sleep disturbances modify these associations.

**STUDY POPULATION.** The study included 133 107 children aged 6 to 17 years enrolled in the 2003–2004 and 2007–2008 National Survey of Children's Health.

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Girish Vitalpur

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