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## Maternal Depressive Symptoms, Maternal Asthma, and Asthma in School-Aged Children

Medsker BH, Brew BK, Forno E, et al. *Ann Allergy Asthma Immunol*. 2017;118(1):55–60

PURPOSE OF THE STUDY. To determine if maternal asthma with depression increases the risk for asthma in children compared with maternal asthma without depression.

STUDY POPULATION. Two cross-sectional studies of 6- to 14-year-old children in Puerto Rico (PR) ($n = 655$) and Sweden (SW) ($n = 6887$).

METHODS. In the PR cohort, children were randomly selected based on 2009–2010 US census data. A screening questionnaire assessed for self-reported maternal asthma, physician-diagnosed asthma, and wheeze in the child within the preceding year. In the SW cohort, 2005–2010 twin registry data were used to identify children and mothers and provided data on self-reported maternal asthma and physician-diagnosed maternal depression. The validated Center for Epidemiologic Studies Depression Scale was used to assess for maternal depressive symptoms.

RESULTS. Maternal depression was not significantly associated with childhood asthma in the absence of maternal asthma in either cohort. Compared with mothers who had neither asthma nor depressive symptoms, children of mothers who had asthma without depressive symptoms had 3.2 (95% confidence interval [CI] 2.1–4.8) and 2.8 (95% CI 2.1–3.7) times increased odds of asthma in the PR and SW cohorts, respectively. Children of mothers who had both asthma and depressive symptoms had 6.5 (95% CI 3.3–13) and 4.0 (95% CI 1.7–9.6) times increased odds of asthma in the PR and SW cohorts, respectively. There were no statistically significant additive interactions of maternal asthma and depression on childhood asthma development, although there was a trend toward an increased estimated effect of depressive symptoms and depression on childhood asthma.

CONCLUSIONS. Maternal depressive symptoms and depression in the presence of maternal asthma increased the risk of childhood asthma development in this cross-cultural study.

REVIEWER COMMENTS. This study highlights the importance of managing childhood asthma with a family approach. It is postulated that maternal depression can influence childhood asthma through impaired attention to asthma management with poor health care and medication use. Depression during pregnancy has also been postulated to alter immune responses and the hypothalamic-pituitary adrenal axis, leading to an increased risk of asthma development. Providers should consider probing for maternal or caregiver depression when treating children for asthma.

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## Siblings Promote a Type 1/Type 17-Oriented Immune Response in the Airways of Asymptomatic Neonates

Wolsk HM, Chawes BL, Folsgaard NV, et al. *Allergy*. 2016;71(6);820–828

PURPOSE OF THE STUDY. To determine whether having siblings affects the airway immune response in healthy neonates, a characteristic that could be attributed to an underlying immune modulatory pathway.

STUDY POPULATION. Five hundred seventy-one 1-month-old, asymptomatic neonates from the Copenhagen Prospective Studies on Asthma in Childhood 2010 ($COPSAC_{2010}$) birth cohort were studied.

METHODS. Unstimulated airway mucosal lining fluid was sampled via the nose at 1 month of age. A variety of cytokines and chemokines were assayed by multiplex array, high-sensitivity enzyme-linked immunosorbent assay. Mediator profiles were grouped into Type I, Type 2, Type 17, and T regulatory responses. The association between airway mediator levels and the presence of siblings was investigated by using conventional statistics and principal component analysis.

RESULTS. Neonates with siblings had higher levels of airway immune mediators, predominately in the Type 1 and Type 17 categories. There was a highly significant difference between neonates with and without siblings ($P > 10^{-10}$), which persisted after adjustment for potential confounding variables, such as pathogenic airway bacteria and viruses ($P < .0001$). With increasing time from the previous childbirth, the immune responses skewed toward the levels found in neonates without siblings.

CONCLUSIONS. The results of this study show that there is an immune modulatory effect of having siblings that leads to more enhanced Type 1 and Type 17 responses versus Type 2 responses. This appears to reflect possible in utero priming because the observed effect decreased with increased time from the previous childbirth. Such responses could have a role in risk for later development of asthma and allergy.

REVIEWER COMMENTS. The researchers in this study lay the foundation for future analysis to determine whether the cytokine and chemokine phenotype for the 20 mediators examined in the neonatal cohort affects the long-term development of asthma and/or allergy. The microbiome and/or exposome mentioned in the discussion may also have a determining role.

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

Papathoma E, Triga M, Fouzas S, Dimitrious 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 ≥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

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