Allergy

PREDICTION, PREVENTION, AND THE “HYGIENE HYPOTHESIS”

Age at First Introduction of Cow Milk Products and Other Food Products in Relation to Infant Atopic Manifestations in the First 2 Years of Life: The KOALA Birth Cohort Study

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PURPOSE OF THE STUDY. To evaluate any associations between the introduction of cow’s milk products/other solid food products and infant atopic manifestations in the second year of life.

STUDY POPULATION. Mother-infant pairs previously enrolled in the ongoing prospective KOALA Birth Cohort Study to study the cause of allergic disease. A total of 2834 pregnant women were recruited at 34 weeks of gestation. Data from 2558 infants in the Netherlands were analyzed.

METHODS. Data on introduction of cow’s milk products and other food products, eczema, recurrent wheeze, allergies, and confounders were collected with repeated questionnaires at 34 weeks of gestation and 3, 7, 12, and 24 months after delivery. Allergen-specific immunoglobulin E was assessed from serum obtained from children at age 2 years. Analyses were performed through multivariate logistic regression. Reverse causation was addressed by performing risk-period–specific analyses that excluded infants with early symptoms of eczema or wheeze.

RESULTS. More delay (eg, >7 months of age) in introduction of cow’s milk products was associated with a higher risk for eczema. In addition, delayed introduction of other food products was associated with an increased risk for atopy development at the age of 2 years. Exclusion of infants with early symptoms of eczema and recurrent wheeze (to avoid reverse causation) did not essentially change the results.

CONCLUSIONS. Delaying the introduction of cow’s milk products or other food products may not be favorable for preventing the development of atopy.

REVIEWERS COMMENTS. In giving advice to “allergic families,” we used to think that it was a good idea to keep children clean, away from pets, and to delay the introduction of “highly allergenic” foods such as cow’s milk. Were we wrong on all counts? There are many confounders when evaluating the relationship between early introduction of food products to infants and later development of atopy. The authors of this article used several statistical approaches to account for the main confounders, including breastfeeding, family history, and, importantly, reverse causation. Although it is difficult to absolutely exclude reverse causation, this authors suggested that delayed introduction of milk was associated with increased eczema. Because of studies such as this one, the focus has shifted away from the delayed introduction of cow’s milk protein and other food products as a means to decrease the risk of developing atopy. These findings provide a rationale for conducting interventional studies to determine whether early introduction of milk and other foods will actually help to prevent food allergies.

Antibiotic Use in the First Year of Life and Risk of Atopic Disease in Early Childhood


PURPOSE OF THE STUDY. To investigate an association with antibiotic use in the first year of life and subsequent development of atopic disease in the first 5 years of life.

STUDY POPULATION. A prospective birth cohort of 198 children considered to be at high atopic risk was recruited prenatally and monitored for 5 years. Risk was based on ≥1 parent with a doctor’s diagnosis of asthma, hay fever, or eczema.

METHODS. Parents kept a daily diary of their child’s symptoms, including history of respiratory illnesses, and antibiotic use. The study physician evaluated children at regular intervals for the presence of eczema, and annual interviews took place, during which parents reported a diagnosis of asthma or wheezing. At 5 years of age, all children underwent skin-prick testing and gave serum samples for measurement of total immunoglobulin E. To determine the effect of antibiotic use on future atopic disease, a logistic regression model was used with propensity score adjustment, with adjustments for a calculated antibiotic predictor score, number of doctor visits, gender, child care, and pets.

RESULTS. Fifty-four percent of the children (107 of 198 children) received ≥1 course of antibiotics in the first year of life. Acute respiratory illness, and in particular lower respiratory illness, was the most common reason for use of antibiotics. Children who received antibiotics for wheezing lower respiratory illness between 7 and 12 months were more likely to be diagnosed with asthma (odds ratio [OR]: 3.1 [95% confidence interval (CI): 1.2–7.3]; P < .05). Asthma in general was associated with antibiotic use (unadjusted OR: 2.3 [95% CI: 1.2–
The Association of Early Life Exposure to Antibiotics and the Development of Asthma, Eczema and Atopy in a Birth Cohort: Confounding or Causality?


PURPOSE OF THE STUDY. The goal was to examine the association between antibiotic exposure in infancy and the development of asthma, eczema, and atopy in early childhood. A secondary goal was to determine whether the association is secondary to confounding chest infections in infancy.

STUDY POPULATION. Expectant mothers were recruited from a random sample of midwives in 2 major New Zealand cities between 1997 and 2001; full details on the non-responding mothers are incomplete.

METHODS. This was a birth cohort study that collected reported antibiotic exposure before 3 months and before 15 months, along with outcomes (wheeze, asthma, eczema, rash, and inhaler use) at 15 months (N = 1011) and 4 years (N = 986). Questionnaires were administered by study nurses at recruitment and 3, 15, 24, 36, and 48 months of age, in home visits at 3 and 15 months and subsequently by telephone. Outcome measures were collected by using identical questions at 15, 24, 36, and 48 months, covering the period since birth or the previous visit. Analyses were limited to outcomes at 15 months (covering the recall period from birth to 15 months) and at 4 years (covering the recall period from 3 to 4 years). Atopy was defined as >1 positive skin-prick test result at 15 months of age with a panel of common inhalant and food antigens.

RESULTS. Antibiotic exposure before 3 months was significantly associated with asthma developing between birth and 15 months (odds ratio [OR]: 2.32 [95% confidence interval [CI]: 1.5–3.7]; P = .0004); however, with adjustment for chest infections (univariate analysis), this association was reduced (OR: 1.6 [95% CI: 0.96–2.60]) and only trended toward statistical significance (P = .07). Multivariate analysis (with adjustment for gender, ethnicity, family history, parity, otitis media, and antibiotic use between 15 months and 4 years) further decreased this association (OR: 1.3 [95% CI: 0.8–2.2]; P = .4). Similarly, although the association of antibiotics with atopy initially trended toward statistical significance (OR: 1.44 [95% CI: 0.96–2.14]; P = .08), the association was reduced after adjustment for chest infections (OR: 1.36 [95% CI: 0.91–2.05]; P = .14). There was no effect of antibiotic exposure before 15 months on asthma developing after 15 months and remaining present between 3 and 4 years (OR: 1.4 [95% CI: 0.9–2.1]; P = .20). Antibiotic exposure before 3 months was not significantly associated with eczema and rash developing between 0 and 15 months, but exposure before 15 months was significantly associated with both eczema (OR: 1.8 [95% CI: 1.1–3.1]; P = .02) and rash (OR: 1.6 [95% CI: 1.02–2.53]; P = .04) developing after 15 months and remaining present at 4 years; however, these associations also lost statistical significance with both univariate and multivariate analyses.

CONCLUSIONS. There is a statistically significant association between antibiotic exposure in infancy and the subsequent presence of asthma and eczema; however, these associations lose statistical significance with adjustment in univariate and multivariate analyses. The effect of antibiotics on respiratory disease may be a result of confounding by chest infections at an early age when asthma may be indistinguishable from infection.

REVIEWERS COMMENTS. Increases in both asthma prevalence and use of antibiotics in recent years have led some to postulate connections between the 2. Retrospective studies in general have shown strong associations between early antibiotic use and the symptoms of asthma, although these associations have been weaker in prospective studies. Reverse causation as an explanation has been suggested by some (ie, people with asthma may tend to have more respiratory infections that require treatment with antibiotics). This study was limited by a
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