Early-life home environment and risk of asthma among inner-city children

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Background: Environmental exposures in early life appear to play an important role in the pathogenesis of childhood asthma, but the potentially modifiable exposures that lead to asthma remain uncertain.

Objective: We sought to identify early-life environmental risk factors for childhood asthma in a birth cohort of high-risk inner-city children.

Methods: We examined the relationship of prenatal and early-life environmental factors to the occurrence of asthma at 7 years of age among 442 children.

Results: Higher house dust concentrations of cockroach, mouse, and cat allergens in the first 3 years of life were associated with lower risk of asthma (for cockroach allergen: odds ratio per interquartile range increase in concentration, 0.55; 95% CI, 0.36-0.86; P < .01). House dust microbiome analysis using 16S ribosomal RNA sequencing identified 202 and 171 bacterial taxa that were significantly (false discovery rate < 0.05) more or less abundant, respectively, in the homes of children with asthma. A majority of these bacteria were significantly correlated with 1 of more allergen concentrations. Other factors associated significantly positively with asthma included umbilical cord plasma cotinine concentration (odds ratio per geometric SD increase in concentration, 1.76; 95% CI, 1.00-3.09; P = .048) and maternal stress and depression scores.

Conclusion: Among high-risk inner-city children, higher indoor levels of pet or pest allergens in infancy were associated with lower risk of asthma. The abundance of a number of bacterial taxa in house dust was associated with increased or decreased asthma risk. Prenatal tobacco smoke exposure and higher maternal stress and depression scores in early life were associated with increased asthma risk. (J Allergy Clin Immunol 2017;139:1553-1563.)

Key words: Asthma, environment, allergy, allergen, microbiome, stress, depression, smoking

Asthma is the most common chronic disease of childhood1 and is responsible for substantial morbidity and health care costs. Environmental exposures in early life appear to play an important role in the pathogenesis of childhood asthma, but more information is needed to identify specific exposures that could potentially be modified to prevent asthma. Childhood asthma is associated

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with sensitization to inhalant allergens, whereas the effect of early-life exposure to these allergens or their sources on asthma risk is unclear and might differ among allergens. Children exposed to farm animals in the early postnatal period have a lower risk of allergies and asthma, and a similar effect of early exposure to pets has been observed in some but not all studies.

Increased early-life exposure to microbial products, such as bacterial endotoxin, appears to be associated with reduced susceptibility to atopic asthma in childhood. A recent study demonstrated that the gastrointestinal microbiome of 3-month-old children with wheezing and atopy at age 1 year differed from that of children with neither wheezing nor atopy. Homes with pet dogs have a distinct microbiome, and mice orally supplemented with house dust from homes with dogs are protected against ovalbumin- or cockroach allergen–mediated airway pathology. Other potentially modifiable factors that might be linked to asthma risk include psychosocial stress, nutritional factors, and exposure to pollutants, such as tobacco smoke.

The Urban Environment and Childhood Asthma (URECA) study was designed to investigate risk factors for asthma in a birth cohort of US high-risk inner-city children, a population with a high burden of asthma morbidity and a distinct environment. In this cohort exposure to higher levels of cockroach, mouse, and cat allergen in the home in the first few months of life was associated with a lower risk of recurrent wheezing at 3 years of age, and the microbial composition of house dust in early life was related to the later development of wheezing and allergic sensitization. In this report we examine exposures in the prenatal period and first 3 years of life, including allergens and microbes in house dust, as potential risk factors for asthma at age 7 years.

**METHODS**

**Study design and participants**

The URECA study is a birth cohort study initiated in 2005 in inner-city Baltimore, Boston, New York City, and St Louis. Pregnant women aged 18 years or older were recruited with selection criteria, including a history of asthma, allergic rhinitis, or eczema, in the mother or father; for full entry criteria, see the Methods section in this article’s Online Repository at www.jacionline.org). Informed consent was obtained from the women enrolled and, after birth, from the parent or legal guardian of the infant.

Data collection

Maternal questionnaires, including those on smoking, stress, and depression, were administered prenatally and annually after the child’s birth. Postnatal child health questionnaires were administered to a parent every 3 months throughout the first 3 years of life, and the number of colds within each of the first 3 years was analyzed as a potential predictor of asthma at age 7 years.

Levels of allergen-specific IgE (ImmunoCAP; Phadia, Uppsala, Sweden) for milk, egg, peanut, and German cockroach were measured yearly until age 3 years and then at the ages of 5 and 7 years. Levels of specific IgE for dust mites, dog, cat, mouse, and Alternaria species were measured at 2, 3, 5, and 7 years of age. Skin prick testing was performed at 3 years of age and again at 5 and 7 years of age for 14 common aeroallergens (listed in the Methods section in this article’s Online Repository). Aeroallergen sensitization was defined as a wheal of 3 mm or more larger than that elicited by the saline control on skin prick testing or a specific IgE level of 0.35 kU/L or greater.

At age 7 years, spirometry was performed in accordance with American Thoracic Society guidelines and repeated after 4 inhalations of albuterol by a modified diffusion filter sampler (Ogawa Sampler; Ogawa & Company USA, Pompano Beach, Fla).

**Primary outcome**

The prespecified primary study outcome was asthma at age 7 years. Children were classified as having asthma at age 7 years if at least 1 of 3 conditions was met (see Table E1 in this article’s Online Repository at www.jacionline.org): (1) a parent-reported physician’s diagnosis of asthma between age 4 and 7 years combined with asthma symptoms or the use of asthma controller medication for 6 of the past 12 months; (2) a methacholine PC20 value of 4 mg/mL or less or albuterol-induced FEV1 reversibility of 10% or more combined with asthma symptoms or use of asthma controller medication for 6 of the past 12 months; or (3) report in the past 12 months of 2 or more wheezing episodes, 2 or more doctor’s office visits for asthma/wheeze, 1 or more hospitalizations for asthma/wheeze, or use of controller medications for 6 of the past 12 months.

**Statistical analysis**

We used multiple imputation by chained equations to impute missing data (approximately 10%; details are provided in the Methods section in this article’s Online Repository). An allergen exposure index was derived for Bla g 1, Mus m 1, Fel d 1, and Can f 1, the 4 allergens that were significantly or nearly significantly associated with the development of asthma, by summing the quartiles (0, 1, 2, or 3) of exposure levels for each allergen (potential range, 0-12; details are provided in the Methods section in this article’s Online Repository).

Relationships of demographic, perinatal, and family factors to asthma at age 7 years were assessed by using logistic regression. The relationships of environmental exposures in early life to asthma at age 7 years were assessed by means of logistic regression, with adjustment for sex, race, maternal asthma, and (except for models of stress and depression as risk factors) maternal Perceived Stress Scale score. Allergen and other environmental measurement data were log-transformed before analysis.

Microbiota data were analyzed in QIIME. The relative abundance of bacterial operational taxonomic units in house dust at 3 months of age was analyzed in QIIME. The relative abundance of bacterial operational taxonomic units in house dust at 3 months of age was analyzed in QIIME.
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