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Repeatedly high polycyclic aromatic hydrocarbon exposure and cockroach sensitization among inner-city children

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ABSTRACT

Background: Exposures to traffic-related air pollutants including polycyclic aromatic hydrocarbons (PAH) have been associated with the development and exacerbation of asthma. However, there is limited evidence on whether these pollutants are associated with the development of cockroach sensitization, a strong risk factor for urban asthma. We hypothesized that repeatedly high PAH exposure during childhood would be associated with increased risk of new cockroach sensitization.

Methods: As part of the research being conducted by the Columbia Center for Children's Environmental Health (CCCEH) birth cohort study in New York, a spot urine sample was collected from children at age 5 years (2003–2008) and again at age 9–10 years (2008–2012; $n=248$) and analyzed for 10 PAH metabolites. Repeatedly high PAH (High–High) exposure was defined as measures above median for age 5 PAH metabolites at both time points. Child blood samples at age 5 and 9 years were analyzed for total, anti-cockroach, mouse, dust mite, cat and dog IgE. Relative risks (RR) were estimated with multivariable modified Poisson regression.

Results: Individual PAH metabolite levels, except for 1-naphthol (1-OH-NAP), increased by 10-60% from age 5 to age 9–10. The prevalence of cockroach sensitization increased from 17.6% (33/188) at age 5 to 33.0% (62/188) at 9 years ($p=0.001$). After controlling for potential covariates including cockroach sensitization at age 5 in regression analyses, positive associations were found between repeatedly high exposure (High–High) to 1-OH-NAP, 3-hydroxyphenanthrene (3-OH-PHEN), or 1-hydroxypyrene (1-OH-PYR) and cockroach sensitization at age 9 (p-values < 0.05). Compared to Low–Low exposure, the relative risk (RR) [95% CI] with repeatedly high exposure was 1.83 [1.06–3.17] for 1-OH-NAP, 1.54 [1.06–2.23] for 3-OH-PHEN, and 1.59 [1.04–2.43] for 1-OH-PYR.

Conclusions: Repeatedly high levels of urinary PAH metabolites during childhood may increase likelihood of sensitization to cockroach allergen in urban inner-city children at age 9 years.

Abbreviations: BC, black carbon; CCCEH, Columbia Center for Children's Environmental Health; DEP, diesel exhaust particle; EC, elemental carbon; ETS, environmental tobacco smoke; IgE, immunoglobulin E; NYC, New York city; OR, odds ratio; PAH, polycyclic aromatic hydrocarbons; PM, particulate matter; RR, relative risk; 1-OH-NAP, 1-naphthol; 2-OH-NAP, 2-naphthol; 2-OH-FLUO, 2-hydroxyfluorene, 3-OH-FLUO,3-hydroxyfluorene; 9-OH-FLUO, 9-hydroxyfluorene; 1-OH-PHEN, 1-hydroxyphenanthrene; 2-OH-PHEN, 2-hydroxyphenanthrene; 3-OH-PHEN, 3-hydroxyphenanthrene; 4-OH-PHEN, 4-hydroxyphenanthrene; 1-OH-PYR, 1-hydroxypyrene; SG, specific gravity

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1. Introduction

Allergic sensitization is a key risk factor for the development of allergic diseases such as asthma, rhinitis, and eczema (Pawankar et al., 2011). In particular, sensitization to cockroach allergen combined with high allergen exposure is one of the strongest identified risk factors for more severe asthma in inner-city children (Rosenstreich et al., 1997; Togias et al., 2010). Similarly, our group at the Columbia Center for Children's Environmental Health (CCCEH) showed that early sensitization to cockroach and mouse allergens, pervasive urban environmental allergens, increased the risk of wheeze, rhinitis and atopic dermatitis among inner-city children aged 2–3 years (Chang et al., 2010; Donohue et al., 2008).

While many epidemiological studies have demonstrated that long-term exposure to traffic-related air pollution (e.g., particulate matter less than 2.5 μm ($PM_{2.5}$) and polycyclic aromatic hydrocarbons (PAH)) were associated with the increased risk of developing asthma and asthma-related symptoms in children (Gehring et al., 2010; Jung et al., 2012; McConnell et al., 2010), it is less clear whether traffic-related air pollutants contribute to the development of allergic sensitization given inconsistent results. For example, while few studies reported positive associations between long-term exposure to outdoor traffic-related air pollution (e.g., $PM_{2.5}$, $PM_{2.5}$ absorbance and NO_x) and allergic sensitization to outdoor allergens (i.e., pollen) (Morgenstern et al., 2008; Nordling et al., 2008), a meta-analysis on five European Birth prospective cohort studies (i.e., BAMSE-Sweden, LISAplus and GINIplus-Germany, MASS-Great Britain, and PIAMA-The Netherlands) indicated that the long-term exposure to those air pollutants was not associated with the development of allergic sensitization in children (Gruzieva et al., 2013). To date, most epidemiologic studies of air pollution and allergic sensitization have been extensively focused on outdoor air pollution from traffic sources. However, investigations on the effect of PAH, which are important constituents of traffic-related air pollution as well as indoor air pollution (Jung et al., 2010), on the development of allergic sensitization, are scarce.

PAH are a class of ubiquitous environmental pollutants produced during the incomplete combustion of organic materials. Urban children are exposed to high levels of lower-molecular-weight semivolatile PAH such as phenanthrene and pyrene from indoor sources (e.g., space heating, cooking, smoking, burning incense or candles) as well as higher-molecular weight nonvolatile PAH (e.g., benzo[a]pyrene) from outdoor traffic source (Jung et al., 2010). In addition to exposure during inhalation, children also may be exposed to PAH through ingestion of food containing PAH such as grilled and charred meats, and through dermal contact with PAH contaminated water or soil (ATSDR, 1995). Hence, measures of urinary PAH metabolites indicate children's overall exposure levels that are integrated from inhaled, dietary, and dermal absorption.

The present study focused on the development of cockroach sensitization, in particular, because of substantially higher prevalence of cockroach sensitization in our inner-city cohort (17.6–33.0%) compared to nationally (Salo et al., 2014), and its large contribution to increased asthma morbidity and recurrent wheezing in children living in the US inner cities (De Vera et al., 2003; Wang et al., 2009). We previously reported that increased levels of PAH metabolites in single spot urine were associated with higher anti-mouse IgE among young inner-city children 5 years of age in cross-sectional analyses (Miller et al., 2010). Also, young children with higher prenatal exposure to PAH combined with prenatal cockroach allergen exposure had a greater risk of developing cockroach allergic sensitization at the ages of 5–7 years, compared to those with lower PAH exposure (Perzanowski et al., 2013). These results suggest that single measures of PAH exposure at either prenatal or age 5 may be associated with a greater likelihood of sensitization to mouse or cockroach allergens. Yet, to date, the prediction of repeated measures of exposure to PAH during early childhood and preadolescent period, that may represent long-term exposure in childhood, in the development of cockroach and other indoor allergen sensitization has not been addressed.

The goal of this study was to examine whether repeated measures of PAH exposure, at age 5 (early childhood) and again at age 9–10 years (preadolescent), is associated with the development of sensitization to cockroach allergens among inner-city children. We hypothesized that these surrogates for chronic PAH exposure would be associated with increased risk of new cockroach sensitization in this age group. Our approach was to examine data collected longitudinally from the CCCEH cohort at two ages during childhood (5, 9–10 years) when PAH exposure assessments and phenotypic outcomes were measured comprehensively.

2. Methods

2.1. Study population

A total of 727 nonsmoking, pregnant African American or Dominican women aged 18–35 living in Northern Manhattan and the South Bronx were enrolled between March 1998 and August 2006 and their children were followed prospectively (Miller et al., 2004; Perera et al., 2003). The mother of the child was compensated for study participation at both ages 5 and 9-10 years. Questionnaires were administered to the participants prenatally, every 3 months through age 2 years, subsequently every 6 months through age 5 years, and annually thereafter. Environmental tobacco smoke (ETS) exposure during pregnancy and cockroach or mouse allergen exposure were assessed by questionnaire. The study was approved by the Columbia University Institutional Review Board and written informed consent was obtained from all study participants. The Centers for Disease Control and Prevention (CDC) laboratory was determined not to be engaged in human subjects research since no personally identifiable information was made available to CDC researchers.

2.2. PAH assessment

Measures of PAH metabolites excreted in the urine, especially 1-hydroxypyrene (1-OH-PYR) the main metabolite of pyrene, have been used as a biomarker of PAH exposure from inhaled, dietary and dermal routes (Brant and Watson, 2003; Li et al., 2010). A spot urine sample was collected from each child at clinic visits at age 5 years (2003–2008; $n=434$) and again at home visit at age 9–10 years (2008–2012; $n=258$). Samples were stored at -80 °C until they were shipped frozen on dry ice to the CDC for PAH metabolite analysis. Of the 258 children with age 9–10 urinary sample, 248 children had age 5 urinary samples (Fig. 1). The urinary concentrations of 10 PAH metabolites were measured at CDC using a method described in detail previously (Li et al., 2014). In brief, urine samples (1 mL) were first spiked with ^{13}C-labeled internal standards, subjected to overnight enzymatic deconjugation, and followed by semi-automated liquid–liquid extraction. The sample extracts were thereafter evaporated, re-constituted, and derivatized to yield the trimethylsilyl derivatives of the OH-PAHs. Analytical measurement was performed by isotope dilution gas chromatography tandem mass spectrometry (GC–MS/MS). Each OH-PAH analyte had its own ^{13}C-labeled internal standard used for quantification.

All OH-PAH analyses were subjected to a series of quality control and quality assurance checks as described elsewhere (Li et al., 2014). Two quality control materials (QCs)—QC High and QC