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Traffic-Related Pollutants and Wheezing in Children

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Background and aims. Traffic related air pollutants from diesel engine exhaust are found in fine and ultrafine particulates. The Cincinnati Childrens Allergy and Air Pollution Birth Cohort Study was initiated to determine if early exposure to these pollutants increased risk for development of early atopic sensitization and allergic respiratory disease phenotypes in children. **Materials and methods.** Over 700 infants born to at least one atopic parent were recruited to participate in a birth cohort study. Participants received annual medical evaluations and skin testing to two foods and 15 aeroallergens from ages 1–4 and again at age seven. Indoor home assessments were conducted at age one. Outdoor traffic related air pollutant exposure was estimated using proximity and land use regression (LUR) modeling. Clinical outcomes were based upon case definitions for wheezing at ages one and three and allergic rhinitis at age three. **Results.** At age 1 exposure to stop and go traffic was associated with wheezing during infancy and recurrent wheezing was twice more likely among African-American infants. Exposure to high levels of elemental carbon attributable to traffic (ECAT) estimated with a LUR model predicted recurrent wheezing at age 1 as well as multiple wheezing phenotypes at age 3. Exposure to high levels of endotoxin combined with multiple dogs during the first year reduced risk for recurrent wheezing during the first year of life. Early sensitization to tree pollen aeroallergens in foods (egg white, milk) in infancy increased likelihood of allergic rhinitis during age 3. **Conclusion.** High exposure to traffic related air pollutants represent independent risk factors for wheezing during infancy and early childhood. Further studies are needed to explore long-term effects of traffic exposure on development of asthma in childhood. **Scientific significance.** Reduction and mitigation of exposure to traffic related air pollutants could reduce risk of respiratory illnesses during childhood.

Keywords traffic related air pollutants, wheezing, traffic, diesel

INTRODUCTION

Traffic-related air pollutants from diesel engine exhaust are a major contributor to fine particulate matter, otherwise referred to as PM 2.5. In addition to PM 2.5, other important traffic pollutants include coarse particles (PM 10), NO₂, ozone, and ultrafine particles (PM 0.1). Fine and ultrafine particles derived from traffic pollution sources impact human respiratory health because their constituents induce oxidative stress and airway inflammation. Hundreds of compounds from diesel exhaust particles generate reactive oxygen species that can induce direct respiratory effects, elicit airway neutrophilic inflammatory responses, generate cytokines (e.g., IL-6 and IL-8), and enhance nonspecific airway hyperresponsiveness. A diesel particle is composed of sulfates, nitrates, metals, organic carbon, and elemental carbon in its core. For this reason, we have used elemental carbon as a signature in our exposure model (see below), to estimate ambient exposure to diesel traffic pollutants. Intriguing studies published in 1999 reported that diesel exhaust particles act as adjuvants to enhance nasal allergen-specific IgE and Th2 cytokine production among patients with seasonal allergic rhinitis

(1, 2). These investigators demonstrated that concomitant exposure of allergen combined with diesel exhaust particles greatly enhanced the potential for sensitization to a neoantigen, keyhole limpet hemocyanin (KLH), as well as nasal production of Th2 cytokines, further suggesting that chemical constituents of diesel particles may possess pro-allergic adjuvant properties.

Based on these studies, early life exposure to diesel particles was entertained as one hypothesis to explain the rising incidence of atopy and allergic disorders among children in westernized developing countries. However, there was scant epidemiologic evidence to support this concept other than small cross-sectional studies reporting increased prevalence of wheezing and reduced lung function among children exposed to PM 2.5 or living adjacent to busy highways. Recent prospective studies of children who are disease free at enrollment indicate that high PM 2.5 exposure increases the risk for development of incident cases of asthma (3, 4). To address these questions, the collaborative multidisciplinary group at the University of Cincinnati initiated a birth cohort study funded by the National Institute of Environmental Health. The major hypothesis of the study stated that infants with high exposure to traffic pollutants have a different pattern of early aeroallergen sensitization and greater risk of developing atopic disorders in childhood. Beginning in 2001, 762 infants were recruited for our birth cohort study. To qualify, parents of subjects must have exhibited a positive skin prick test to at least one aeroallergen and experienced symptoms of an allergic disease. A control cohort design was utilized, in which subjects living within 400 m of a major highway were recruited

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along with a comparator group living more than 1500 m from a major road. Children were evaluated annually at ages 1–4 and again at age 7 with detailed environmental and health questionnaires, physical examinations, and skin prick testing with 15 common aeroallergens and two foods (egg white and milk).

Indoor and outdoor environmental exposures were assessed. At age 1, a home evaluation was conducted to assess indoor conditions for visible mold and humidity and numbers and types of pets, and house dust samples were collected from the floor of the child's primary living area. House dust samples were processed and evaluated for endotoxin concentration, indoor allergen content, and β -glucan. Traffic pollutant exposure was estimated using a qualitative proximity model and a quantitative land use regression (LUR) model, determined from elemental carbon content of PM 2.5 collected at 27 air sampling stations in the Greater Cincinnati area. The proximity model defined traffic pollutant exposure by distance from major highways including the following categories: (1) stop-and-go traffic or <100 m from a bus route and slow-moving highways; (2) moving traffic or <400 m from a major road with more than 1000 trucks per day; and (3) unexposed defined as >400 m from a bus route or major road (5). The LUR is a multivariate model calculated using the fraction of elemental carbon measured in PM 2.5 samples and the fraction of elemental carbon attributable to traffic (ECAT) emanating from diesel sources. This and other variables including home or school location relative to major roads, bus routes, truck traffic, and elevation are incorporated into the LUR model, allowing estimation of personal exposure of each infant or child at home (6). Subsequent measures obtained after Year 1 indicated that ECAT measures were very consistent from year to year (7, 8). The multivariate LUR model is considered superior to proximity estimates of traffic pollutant exposure because it has been shown to prevent the potential for exposure misclassification.

EVALUATION OF WHEEZING OUTCOMES AT YEARS 1 AND 3

Environmental predictors of wheezing symptoms reported during Year 1 in the absence of a cold were extensively evaluated. A reduced risk of wheezing was identified among infants with high-level exposure to endotoxin and at least two dogs in the home (9). In another study, the relationship between wheezing and traffic pollutant exposure as defined by the aforementioned proximity model was investigated. After adjusting for multiple significant predictors, exposure to stop-and-go traffic was significantly associated with wheezing without a cold in Year 1. Interestingly, the prevalence of reported wheezing was greater in African-American versus Caucasian infants, regardless of the category of traffic exposure (Figure 1). In addition to traffic exposure, maternal asthma, male gender, and non-Caucasian race were also associated with increased risk of wheezing. Being an only child

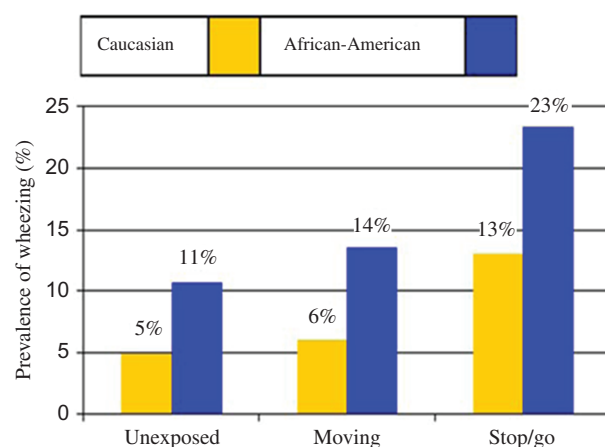


FIGURE 1.—Prevalence of wheezing without a cold was greatest among infants living near stop-and-go traffic and was greater for all categories of exposure among African-American infants (5).

significantly reduced the risk of wheezing during Year 1 (5). The latter findings, with the exception of an inverse association of wheezing with endotoxin and multiple dogs, are consistent with results in other birth cohort studies.

Next, Ryan et al. evaluated the relationship of wheezing during Year 1 and traffic pollutants based upon estimated ECAT exposure (6). Increasing mean levels of ECAT exposure in this study positively correlated with the risk of wheezing during infancy. Subsequently, Dr. Ryan investigated a variety of wheezing outcomes based on clinical evaluations performed in children at age 3. Year 3 case definitions included persistent wheezing defined as wheezing at ages 2 and 3; persistent allergic wheezing defined as persistent wheezing with aeroallergen sensitization; recurrent wheeze (≥ 2 episodes in the past 12 months); and asthma predictive index previously defined as parental asthma, recurrent wheezing, and aeroallergen sensitization possessing a 59% positive predictive value for asthma at ages 6–13. The highest quartile of ECAT during infancy predicted persistent wheeze, recurrent wheezing and the asthma predictive index at age 3. After adjusting for multiple variates, an interaction variable of high levels of indoor endotoxin combined with high ECAT exposure was identified to be significantly associated with an increased risk of persistent wheezing at age 3 (10).

In order to address the question of whether early exposure to diesel exhaust enhances overall risk of development of childhood allergic phenotypes, we next evaluated the relationship between traffic pollutants and allergic rhinitis at age 3 (11). For this epidemiologic evaluation, a case definition of allergic rhinitis was a positive skin prick test to at least one aeroallergen combined with a positive response to the validated International Study of Asthma and Allergies in Childhood questionnaire item, "In the past 12 months, has your child ever had a problem with sneezing, or a runny or a blocked nose when he or she did not

have a cold or flu?" Dr. Codispoti was unable to identify a relationship between ECAT and allergic rhinitis at age 3, or aeroallergen sensitization at age 3. Nevertheless, interesting findings included the following: (1) a reduced risk of allergic rhinitis among African-American infants who were breast-fed; (2) a significant association between being born in the spring or autumn and allergic rhinitis; and (3) skin prick test positivity to tree pollen or foods at age 1 increased the likelihood of allergic rhinitis at age 3. On the other hand, living with two or more siblings reduced the risk of allergic rhinitis at age 3. Exposure during infancy to moderate levels of house dust endotoxin increased the risk for allergic rhinitis, whereas high levels reduced the risk of this outcome.

SUMMARY AND CONCLUSIONS

In summary, the following findings of wheezing outcomes in the Cincinnati Childhood Allergy and Air Pollution Study birth cohort study demonstrated that proximity to stop-and-go traffic was associated with wheezing in Year 1, greater in African-American infants. ECAT measured at Year 1 was associated with recurrent wheeze in Year 1 and with multiple wheezing phenotypes at age 3. Coexposure during infancy to high levels of indoor endotoxin combined with high ECAT levels increased the likelihood of persistent wheezing at age 3. Based on the study of allergic rhinitis, it was concluded that breastfeeding should be encouraged in infants born to high-risk atopic African-American parents. It was also evident that risk assessment of high-risk children born to atopic parents may be facilitated by early skin prick testing, even during the first year of life. Whereas indoor endotoxin exposure may influence development of allergic rhinitis at age 3, early exposure to traffic air pollutants appears to have no such effect.

The limitations of these studies of wheezing and rhinitis outcomes are apparent. Parental reporting bias can lead to misclassification of clinical outcomes. Second, subjective parental reports of wheezing in the first 3 years of life are only modest predictors of asthma diagnosed in childhood. The key question and hypothesis in the study will be tested at age 7 when asthma outcomes will be determined at age 7. In addition to physician diagnosis, objective measures will be used in the case definition of asthma including spirometry, FEV1 reversibility, and methacholine PC₂₀.

DECLARATION OF INTEREST

The author has no conflicts of interest. The author alone is responsible for the content and writing of the paper.

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