



Letter

Higher fractional exhaled nitric oxide and Der p 1 exposure in children with asthma living in tropical environments

The interaction between environmental exposure and airway inflammation in pediatric asthma is multifactorial, but a specific clinical association exists.^{1,2} We attempted to study allergens common to our patient population who live in 2 distinctly different indoor environments and their effect on markers of airway inflammation. Our primary objective was to evaluate specific allergen sensitivities and exposures that would affect clinical airway inflammatory markers.^{3,4} Skin test results and levels of indoor allergens of dust mites, cat, dog, and cockroach were examined and compared with respiratory markers, fractional exhaled nitric oxide (FeNO) and spirometry, and systemic atopic markers, serum eosinophils, and total IgE.^{5,6}

A retrospective medical record review of children with atopic asthma from an allergy specialist clinic during a 4-year period was performed. The diagnosis of mild to moderate asthma was made from history, physical examinations, and respiratory tests of spirometry, bronchodilator reversibility, and FeNO. Atopy was defined as children with allergy symptoms and signs in their history and physical examination with positive prick skin test results to indoor allergens. Only children with prick skin testing and indoor allergen sampling to environmental allergens were included. From their history, children with preexisting dust mite bed covers or any secondhand cigarette smoke exposures were excluded from the study. Families were taught the method for indoor dust collection using Duststream collectors, and samples were collected from the child's bedrooms⁷ during the rainy season. All indoor allergen dust samples were processed with a MARIA 8plex assay (Indoor Biotechnologies, Charlottesville, Virginia) for Der f 1, Der p 1, Fel d 1, Can f 1, and Bla g 2 at National Jewish Health's Immunology Laboratory. These indoor dust samples results were compared to each child's allergy sensitivity by history and skin prick testing.

By history, all the children lived in a tropical environment with high (>60%) outdoor humidity year-round, but there was a large difference in the presence or absence of central air-conditioning units in the homes. Homes that did not have central air-conditioning ($n = 75$) were compared with those that had indoor central air-conditioning ($n = 57$) running 24 hours a day on a preset thermostat. Unlike those without central air-conditioning, those living with central air-conditioning never opened their windows because of high outdoor humidity. Differences in the presence or absence of central air-conditioning units came from cultural backgrounds and not from socioeconomic factors. This study protocol was exempted from institutional review board approval by the Salus Institutional Review Board.

A total of 132 children (86 males and 46 females; mean age, 8 years; age range, 6–17 years) who met the inclusion criteria for the study had the following clinical indexes analyzed: skin prick testing, indoor dust allergens (MARIA), FeNO, spirometry (forced expiratory volume in 1 second [FEV₁], ratio of forced vital capacity [FVC] to FEV₁), blood eosinophils, and total IgE. The overwhelming indoor allergen sensitivity from positive skin prick testing was dust mites, either *Dermatophagoides farinae* or *Dermatophagoides pteronyssinus*, in 98% of children. Elevated levels of Der f 1 or Der p 1 from indoor dust sampling was found in almost 75% of the children's bedrooms. In comparison, a low percentage of children had positive skin test results for allergen sensitivity or indoor exposures from dust sampling present to the other allergens for accurate comparisons to be made (<11% Fel d 1, <40% Can f 1, 1% Bla g 2).

The mean level of FeNO was 34 ppb (median, 24 ppb) in children from homes without central air-conditioning and 27 ppb (median, 16 ppb) in those from homes with central air-conditioning ($P = .05$). The mean level of Der p 1 from indoor samples was 136 ng/mL (median, 52 ng/mL) from homes without central air-conditioning and 60 ng/mL (median, 2.6 ng/mL) from homes with central air-conditioning ($P < .0001$). Moreover, there was a significant positive correlation ($\rho = 0.324$; $P < .03$) between FeNO and Der p 1 dust from the homes without central air-conditioning (Fig 1). In addition, there were significant positive correlations ($\rho = 0.424$; $P < .005$) between FeNO and both species of *Dermatophagoides* wheal-and-flare skin test sizes in the homes without central air-conditioning. No correlations were found in the homes with central air-conditioning because many had very low to undetectable levels of Der p 1 in their dust samples. There was a trend found with mean blood eosinophils at 7.6% in children from the homes without central air-conditioning to 5.8% in children from the homes with central air-conditioning ($P < .08$). There were no significant differences in the other measurements, including Der f 1 from dust sampling, FEV₁, or FVC/FEV₁ from spirometry, and serum total IgE between both groups.

These results are unique because they are the first to show that higher levels of FeNO are found in children with asthma living in homes without indoor central air-conditioning. As in previous studies,^{8,9} we found elevated dust sample levels of Der p 1 and not Der f 1 in environments with high humidity. In addition, the study results are novel because they show FeNO and Der p 1 dust samples directly correlate in children with asthma from homes without running central air-conditioning. Previous work has found elevated FeNO in children with asthma explained almost entirely from allergen sensitivity by elevated specific IgE to *D pteronyssinus*.⁹ Our results reveal elevated FeNO correlating with Der p 1 allergic sensitivity as measured by skin testing and the level of Der p 1 in the indoor dust.

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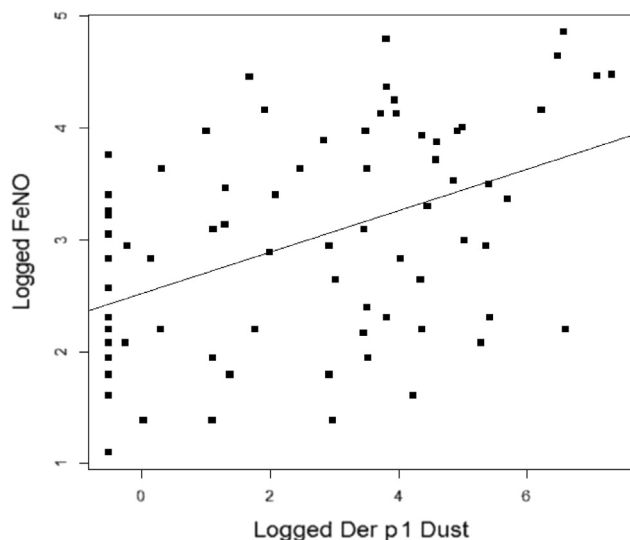


Figure 1. Correlation of fractional exhaled nitric oxide (FeNO) and dust samples of *Dermatophagoides pteronyssinus* (Der p 1) in children from the high indoor humidity group ($\rho = 0.324$; $P < .03$). Measurements plotted as logged values.

Limitations to our study were that data were collected from a retrospective medical record review and from a single site. In addition, most children from our site were of Hispanic/Latino descent. The possibility exists that these results are indicative of this specific ethnicity because there was not a case-control group. Nevertheless, our patient study group consisted of various Hispanic/Latino descents, including Cuban, Colombian, Dominican, Ecuadorian, Salvadorian, and Venezuelan, and studies have found that there is a wide genetic heterogeneity of asthma severity within even different groups of Hispanics/Latinos.^{10,11}

To improve the clinical utility of biomarkers for asthma, such as FeNO, all factors that contribute to higher or lower levels of airway inflammation must be addressed. To develop an accurate understanding of FeNO application for asthma diagnosis and management, long-term environmental exposures to sensitized allergens in those with asthma must be considered. With the advent of new biologics for asthma and the necessity for a biomarker that can accurately predict therapy response, the need to assess all factors that affect these biomarkers is crucial. Otherwise, a biomarker may not be used to its fullest potential when using them because affecting factors are not addressed before its use. We hope to

conduct a prospective, interventional, controlled, multicenter study to confirm these results and to examine the interaction of other allergens with inflammatory biomarkers in asthma.

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