

Letters to the Editor

Comparison of indoor allergen levels in urban and suburban Detroit

To the Editor:

Children living in the inner city have a higher prevalence of asthma¹ with greater asthma morbidity than does the general population.² Higher levels of cockroach antigen have been reported to be associated with an increased incidence of poorly controlled asthma among urban populations.³ In addition, exposure to indoor allergens such as dog, cat, and dust mite has been linked to the onset of allergy and asthma in various reports.⁴⁻⁶ These findings have raised the question of whether the differential rates of asthma and asthma morbidity that exist between urban and suburban children could be due to differences in allergen levels between urban and suburban homes. However, there are few publications that have directly compared allergen levels between urban and suburban homes in the same region.

Using data collected as part of the Wayne County Health, Environment, Allergy, and Asthma Longitudinal Study birth cohort project, we compared common housing characteristics in an urban environment (residents of the city of Detroit) with those in suburban homes (Table I). Urban and suburban populations were defined by ZIP code. During a 1-month postpartum home visit, dust samples were collected from the floor of the room in which the cohort's infant participant usually slept. Using mAb-based assays, we measured allergen levels for dust mite (Der f 1), German cockroach (Bla g 2), dog (Can f 1), and cat (Fel d 1). χ^2 tests were used to compare the proportions of homes that had detectable and nondetectable allergen levels. Within homes with detectable allergen levels, Wilcoxon rank sum tests were used to compare urban and suburban homes. Logistic regression models (data not shown) were used to assess differences in allergen levels after adjustment for season of sample collection and type of flooring (carpet vs not carpet).

Detroit homes had detectable levels of allergen from dust mite in 36% of urban homes versus 39% of suburban homes ($P = .30$) (Table II). In contrast, the proportion of urban homes with detectable levels of cockroach allergen was greater than the proportion of suburban homes with detectable levels of cockroach allergen (12.2% vs 4.2%; $P < .001$) (Table II). Suburban homes were more likely to have a dog or cat in residence (dog: 26.4% vs 18.8%; cat: 21.0% vs 7.2%; both $P < .01$) and, as expected, more likely to have detectable levels of both dog and cat allergen (dog: 65% vs 55.1%; cat: 81.3% vs 73.6%; both P values $< .01$) (Table II). Furthermore, even in homes without indoor dogs, more suburban homes had detectable levels of dog allergen (54.3% vs 45.5%; $P = .015$). However, among homes without cats, differences in the prevalence of homes with detectable cat allergen levels between suburban and urban homes abated (76.9% vs 71.4%; $P = .069$).

We evaluated season of sample collection, floor type, and whether the pet was allowed in the child's room as possible confounders. We found that carpet was more common in suburban homes (81.9% vs 71.9%; $P < .00178$) and that suburban homes were more likely to allow the pet in the child's room (for dog, 28.7% urban vs 65.4% suburban, $P < .001$; for cat,

TABLE I. Baseline characteristics of urban and suburban homes in metro Detroit

Characteristic	Urban homes (N = 524)	Suburban homes (N = 473)	P value
Housing type,* n (%)			
Detached house or trailer	349 (74.1)	366 (80.8)	.020
Apartment/duplex/row house	121 (25.7)	85 (18.8)	
Basement	1 (0.2)	2 (0.4)	
Household income < \$40,000,† n (%)	243 (53.4)*	102 (24.2)	<.001
Household environment, n (%)			
Cigarette smoking‡	197 (37.6)	109 (23.0)	<.001
Mouse droppings§	26 (5.2)	5 (1.1)	<.001
Cockroach or cockroach stains	45 (9.0)	7 (1.5)	<.001

*N = 73 missing data.

†N = 121 missing data.

‡N = 45 missing data.

§N = 44 missing data.

TABLE II. Urban versus suburban differences in home allergen levels for 4 common indoor allergens

Allergen	Urban homes (N = 524)	Suburban homes (N = 473)	P value
Homes with detectable* allergen level, n (%)			
Dust mite (Der f)	188 (36.0) n = 523	184 (39.2) n = 470	.30
Cockroach	63 (12.2) n = 515	19 (4.2) n = 454	<.001
Dog	288 (55.1) n = 523	307 (65.0) n = 472	.001
Cat	385 (73.6) n = 523	383 (81.3) n = 471	.004
Among homes with detectable allergen levels (µg/g dust)			
Geometric mean† (95% CI)			
Dust mite (Der f)	0.11 (0.09-0.14)	0.12 (0.09-0.16)	.91
Cockroach	0.04 (0.03-0.06)	0.03 (0.01-0.08)	.23
Dog	0.13 (0.11-0.17)	0.28 (0.21-0.38)	.002
Cat	0.18 (0.15-0.22)	0.63 (0.48-0.82)	<.001

*Lower level of allergen detection for cockroach was 0.04 µg/g, Der f 0.05 µg/g, cat 0.016 µg/g, and dog 0.01 µg/g. The χ^2 test was used to compare percent detectable between urban and suburban homes.

†Geometric means presented because of skewness of the data. Wilcoxon rank sum tests were used to compare distributional differences between urban and suburban homes in detectable allergen levels.

48.7% vs 67.3%, $P = .042$). However, none of these characteristics was found to alter the relationship between urban/suburban dwelling and allergen levels (data not shown).

We recognize that having a single dust sample at the age of 1 year from the child's bedroom might not be truly representative of the environment and whether samples taken from different areas of the house would provide different information.

In summary, there was no difference in rates of having detectable dust-mite allergen levels between urban and suburban homes. Although more suburban homes had detectable dog and cat allergen levels, this was at least partially attributable to pet-keeping behaviors. As expected, in metropolitan Detroit, detectable cockroach allergen levels were more common in urban

homes than in suburban homes. However, we were surprised to find that the rate of detectable cockroach allergen level was only 12.2% in urban residences, which is low when compared with that in other inner-city populations such as New Orleans (44%),⁷ with Baltimore, Boston, New York, and St Louis having detectable cockroach allergen levels of 40%.⁸ We speculate that this may reflect the predominance of single-family dwellings in our urban sample compared with high-density residential structures that are present in many large cities. However, like many inner cities, asthma morbidity and mortality is high among the urban population.⁹ On the basis of these data, we suggest that although cockroach exposure may partially explain high urban asthma morbidity, it seems unlikely that cockroach allergen exposure is the sole or even the major contributor to the high asthma burden in Detroit children as has been suggested from other studies and cities.¹⁰ Our data also emphasize the potential importance of accounting for regional variation in key environmental allergen exposures when designing optimal intervention strategies directed toward different US urban populations.

Laura Veras, MD^a
Ganesa Wegienka, PhD^a
Suzanne Havstad, MA^a
Haejin Kim, MD^a
Christine Johnson, PhD^a
Dennis Ownby, MD^b
Edward Zoratti, MD^a

From ^aHenry Ford Hospital, Detroit, Mich, and ^bGeorgia Regents University, Augusta, Ga. E-mail: lauraveras@hotmail.com.

This research was supported by grants from the National Institute of Allergy and Infectious Diseases (grant no. AI051598) and the Fund for Henry Ford Hospital.

Disclosure of potential conflict of interest: D. Ownby is a board member for the Merck Childhood Asthma Network. D. Ownby, E. Zoratti, G. Wegienka, S. Havstad, H. Kim, and C. Johnson have received research support from the National Institutes of Health (AI089473, AI50681, AI051598, AI90052, HL113010 and HL092412). L. Veras declares that she has no relevant conflicts of interest.

REFERENCES

1. Aligne CA, Auinger P, Byrd RS, Weitzman M. Risk factors for pediatric asthma: contributions of poverty, race and urban residence. *Am J Respir Crit Care Med* 2000;162:873-7.
2. Togias A, Fenton MJ, Gergen PJ, Rotrosen D, Fauci AS. Asthma in the inner city: the perspective of the National Institute of Allergy and Infectious Diseases. *J Allergy Clin Immunol* 2010;123:540-4.
3. Rosenstreich D, Eggleston P, Kattan M, Baker D, Slavin RG, Mitchell H, et al. The role of cockroach allergy and exposure to cockroach allergen in causing morbidity among inner-city children with asthma. *N Engl J Med* 1997;336:1356-63.
4. Carlsen C, Dimich-ward H, Becker AB, Ferguson A, Chan HW, Dybuncio A, et al. Indoor allergen exposure, sensitization and the development of asthma in a high-risk birth cohort. *Pediatr Allergy Immunol* 2010;21:740-6.
5. Wisniewski JA, Agrawal R, Minniccozi S, Xin W, Patrie J, Heymann PW, et al. Sensitization to food and inhalant allergens in relation to age and wheeze among children with atopic dermatitis: clinical mechanism in allergic disease. *Clin Exp Allergy* 2013;43:1160-70.
6. Sporik R, Holgate ST, Platts-Mills TA, Cogswell JJ. Exposure to house dust mite allergen (Der P) and the development of asthma in childhood. *N Engl J Med* 1990;323:502-7.
7. Rabito FA, Carlson J, Holt EW, Iqbal S, James MA. Cockroach exposure independent of sensitization status and association with hospitalizations for asthma in inner-city children. *Ann Allergy Asthma Immunol* 2011;106:103-9.
8. Wood R, Bloomberg GR, Kattan M, Conroy K, Sandel MT, Dresen A, et al. Relationships among environmental exposure, cord blood cytokine responses, allergy and wheeze at one year of age in an inner city birth cohort (Urban Environmental and Childhood Asthma study). *J Allergy Clin Immunol* 2011;127:913-9, e1-6.
9. Wasilevich E, Lyon-Callo S, Rafferty A, Dombkowski K. Detroit: the epicenter of asthma burden in asthma in Michigan 2010: a blue print for action. Available at: <http://getastmahelp.org/reports.aspx>. Accessed October 1, 2014.

10. Simons E, Curtis-Brosnan J, Buckley T, Breyse P, Eggleston PA. Indoor environmental differences between inner-city and suburban homes with children with asthma. *J Urban Health* 2007;84:577-90.

<http://dx.doi.org/10.1016/j.jaci.2014.08.035>

Intact IL-12 signaling is necessary for the generation of human natural killer cells with enhanced effector function after restimulation

To the Editor:

Natural killer (NK) cells are lymphocytes that are important for host defense against viral and bacterial infections, as well as malignant transformation. They have the capacity to kill target cells and produce cytokines on activation without previous sensitization. Although NK cells have been traditionally categorized as members of the innate immune system, recent studies have shown that NK cells have the ability to modify their effector function based on previous cytokine stimulation, activating receptor-mediated stimulation, or both.¹⁻³ The first evidence that NK cells can remember came from studies showing that they mediated recall responses to haptens in mice lacking T and B cells using a contact hypersensitivity model.⁴ NK cell memory has also been demonstrated in viral infections by using murine models.³ In these models NK cells acquired long-lived memory to influenza A, vesicular stomatitis virus, and HIV antigens.⁵ Additionally, development of long-lived NK cell memory to mouse cytomegalovirus infection was shown to be dependent on IL-12-mediated signals.^{3,6} Even without exposure to specific antigens, *ex vivo* short exposure of mouse and human NK cells to activating cytokines, such as IL-12, IL-15, and IL-18, elicits "memory-like" properties that are defined as enhanced effector functions after restimulation.^{1,7,8}

In this study we tested the role of IL-12-mediated signals in the *in vitro* generation of human NK cells with enhanced effector function after restimulation. In our opinion the best method to address this issue would involve the use of PBMCs from patients with a deficiency in IL-12 or IL-12 receptor (IL-12R) because we could then exclude that the NK cells used in the experiments had been activated at any time *in vivo* by IL-12. We have previously described a 19-month-old patient with an IL-12Rβ1 deficiency caused by a complex mutation at exon 14 in the *IL12RB1* gene (c.1623_1624delinsTT; p.Q541X).⁹ We showed that IFN-γ production was markedly decreased after stimulation of PBMCs with PHA or PHA plus IL-12 and that there was diminished signal transducer and activator of transcription 4 phosphorylation after IL-12 stimulation.⁹ Here we specifically tested whether the NK cells from this patient responded to IL-12 stimulation. Flow cytometric analyses showed this patient's NK cells did not produce IFN-γ when they were stimulated with IL-12 plus IL-15 or IL-12 plus IL-18 (Fig 1). On the other hand, approximately 20% of the NK cells from the age-matched healthy control subject produced IFN-γ when they were stimulated with IL-12 plus IL-15, and 85% of the NK cells produced IFN-γ when they were stimulated with IL-12 plus IL-18 (Fig 1). When NK cells were stimulated with a combination of the 3 cytokines, almost all NK cells from the healthy control subject produced IFN-γ, whereas only 12% of the NK cells from the patient