

# Letter

## RISK OF ATOPY ASSOCIATED WITH MICROBIAL COMPONENTS IN HOUSE DUST

**To the Editor:** Several lines of evidence show that adequate microbial exposure in terms of quantity and diversity is crucial for the development of tolerance and maintenance of mucosal epithelial integrity and homeostasis.<sup>1,2</sup> Urbanization, sedentary lifestyle, and modern amenities and cleaning practices have, however, markedly reduced exposure to environmental microorganisms, which is considered to be 1 of the major reasons for the current asthma and atopy epidemics in the western world.<sup>3,4</sup>

Examination of house dust provides a practical approach to get clues about the composition of environmental microbiota. We recently found that house dust in Russian Karelia, an area with low occurrence of atopy and atopic diseases, was rich in gram-positive bacteria abundantly found in animals, composting soil, and fresh waters, whereas Finnish Karelian dust was characterized by lower bacterial content and the predominance of bacteria from the gram-negative lineage.<sup>5,6</sup> The difference between the areas in concentrations of muramic acid (abundant in gram-positive bacteria) was up to 20-fold, whereas these areas were negligible for lipopolysaccharide (indicative of gram-negative bacteria).<sup>5</sup> These areas, the eastern part of Finland (Finnish Karelia) and the northwestern part of Russia (Russian Karelia), are geographically adjacent, but because of the huge economic gap between them, the living conditions in Russian Karelia are simple and the lifestyle traditional. Our finding nonetheless raises the possibility that there might also be qualitative and quantitative differences in house dust microbiota between nonatopic and atopic children in a given area.

We examined whether there were differences in house dust microbiota using chemical analyses between nonatopic and atopic children and whether there was any association between the risk of atopy and exposure to microbial components in dust among Finnish Karelian children. Such an analysis is less meaningful among children in Russian Karelia because atopic diseases and atopy are uncommon in that area, and all Russian children, regardless of their atopy status, are heavily exposed to environmental microbiota.

The study area, participants, and methods have been described in detail elsewhere.<sup>5,7</sup> For the purpose of this study, 90 randomly selected house dust samples, which had been collected by the participating families from homes of nonatopic and atopic school-children by vacuuming floor dust according to written instructions,

were analyzed for muramic acid, lipopolysaccharide, and ergosterol (a marker of fungi) concentrations. These data were linked with data of atopy ( $\geq 1$  positive skin prick test result)<sup>7</sup> for each child. All dust samples were sieved, and only fine dust was used in the analyses. To assess the relationship between the risk of atopy and the richness of microbial components in dust, we created an index. The range of the concentration of each marker was divided into tertiles and categorized from lowest to highest as 0, 1, and 2. An index summing the category number of all the 3 markers together was given for each child. None of the potential confounders (parental atopy, having a dog or cat, exposure to tobacco smoke, concentration of each chemical marker separately) showed a significant effect in univariate or multivariate analyses.

Study participant and housing characteristics are presented in eTable 1 (online only). A tendency to a higher ergosterol concentration (median, 11.8 vs 7.8. ng/mg) in dust from the homes of nonatopic children was found; however, the differences in none of the 3 markers achieved significance in this limited material (Table 1). By contrast, regression analysis revealed an inverse dose-dependent association between the risk of atopy and the index of microbial components in dust. This analysis showed that exposure even to relatively low levels of microbial components in dust can significantly reduce the risk of atopy among children and that a heavy exposure (exposure to dust very rich in such components) reduces the risk of atopy to an odds ratio of 0.23 (Figure 1).

Families who have an atopic child may clean their homes more thoroughly than other families. However, analysis of bacterial DNA in a randomly selected subgroup of these dusts did not reveal differences in numbers of 16S ribosomal RNA copies between dust samples from the homes of nonatopic and atopic Finnish children (data not shown), suggesting that the differences in house dust from the homes of atopic and nonatopic children may be largely qualitative and related to diversity.<sup>8</sup> In addition, we measured marker concentrations (not loads), which are not necessarily linked with cleaning practices but rather with the composition of environmental microbiota. Finally, floor dust instead of mattress dust was examined because the former has been shown to better differentiate among various environments.<sup>9</sup>

In conclusion, we found that house dust rich in diverse microbial components is associated with tolerance and strongly reduced risk of atopy. Further studies in larger populations are highly warranted.

## ACKNOWLEDGMENT

This research was supported by grants from the Sigrid Juselius Foundation, the Allergy Foundation, and the Academy of Finland (grants 111 177 and 122 117).

**Disclosures:** Authors have nothing to disclose.

© 2010 American College of Allergy, Asthma & Immunology.

Published by Elsevier Inc. All rights reserved.

doi:10.1016/j.anai.2010.01.008

Table 1. Median (Range) of Muramic Acid, Lipopolysaccharide, and Ergosterol Concentrations in House Dust by Atopy Status of the Child

| Chemical marker                       | Nonatopic           | Atopic             | P value<br>(Mann-Whitney test) |
|---------------------------------------|---------------------|--------------------|--------------------------------|
| Muramic acid, ng/mg                   | 19.5 (6.0-65.4)     | 17.1 (2.1-178.7)   | .15                            |
| Lipopolysaccharide (C10-C16), nmol/mg | 0.020 (0.004-0.054) | 0.019 (0.007-0.06) | .36                            |
| Ergosterol, ng/mg                     | 11.8 (2.6-58.1)     | 7.8 (2.4-45.1)     | .09                            |

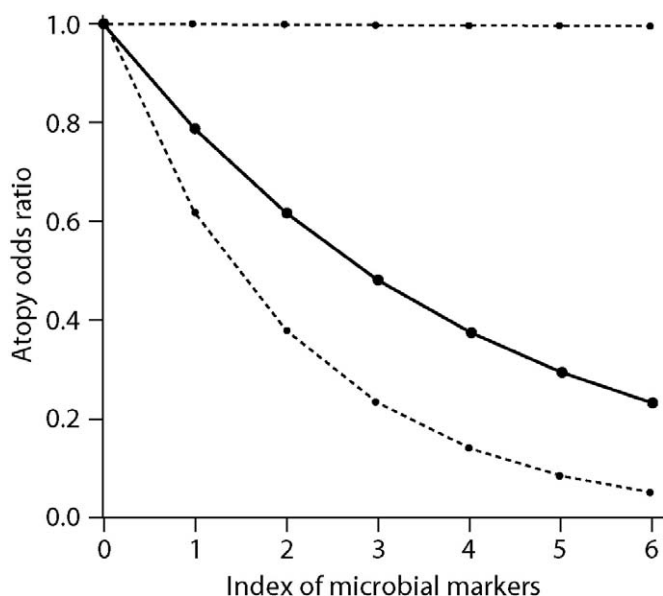


Figure 1. Association between index of microbial components in dust and the risk of atopy (solid line) with 95% confidence intervals (dotted lines) in Finland. Index indicates the sum of tertiles (numbered from lowest to highest as 0, 1, and 2) of the 3 marker concentrations together, created for each child separately.

We are indebted to statistician Risto Sippola, National Public Health Institute, Helsinki, Finland, for statistical analyses, to Katja Saarnio, National Public Health Institute, Kuopio, Finland, for skillful technical assistance in performing marker analyses, and to Christina Pehrson, University of Lund, Lund, Sweden, for analyzing samples with gas chromatography–mass spectrometry.

The Karelia Allergy Study Group: T. Haahtela, L. von Hertzen, P. Jousilahti, T. U. Kosunen, T. Laatikainen, M. J. Mäkelä, and E. Vartiainen.

LEENA VON HERTZEN, PhD, MPH\*

ANNE HYVÄRINEN, PhD†

TIINA LAATIKAINEN, MD, PhD‡

MIKA J. MÄKELÄ, MD, PhD\*

AINO NEVALAINEN, PhD†

ERKKI VARTIAINEN, MD, PhD‡

TARI HAAHTELA, MD, PhD\*

\*Skin and Allergy Hospital

Helsinki University Central Hospital

Helsinki, Finland

†Department of Environmental Health

National Institute for Health and Welfare

Kuopio, Finland

‡Department of Health Promotion and Chronic

Disease Prevention

National Institute for Health and Welfare

Helsinki, Finland

leena.vonhertzen@kolumbus.fi

## SUPPLEMENTARY DATA

Additional table accompanies the on-line version of this article (available at <http://www.annallergy.org>).

1. Rakoff-Nahoum S, Paglino J, Eslami-Varzaneh F, Edberg S, Medzhitov R. Recognition of commensal microflora by Toll-like receptors is required for intestinal homeostasis. *Cell*. 2004;118:229–241.
2. Hedl M, Li J, Cho JH, Abraham C. Chronic stimulation of Nod2 mediates tolerance to bacterial products. *Proc Natl Acad Sci U S A*. 2007;104:19440–19445.
3. von Mutius E. Allergies, infections and the hygiene hypothesis: the epidemiological evidence. *Immunobiology*. 2007;212:433–39.
4. Garn H, Renz H. Epidemiological and immunological evidence for the hygiene hypothesis. *Immunobiology*. 2007;212:441–452.
5. Pakarinen J, Hyvärinen A, Salkinoja-Salonen M, et al. Predominance of Gram-positive bacteria in house dust in the low-allergy risk Russian Karelia. *Environ Microbiol*. 2008;10:3317–3325.
6. von Hertzen L, Haahtela T. Disconnection of man and the soil: reason for the asthma and atopy epidemic? *J Allergy Clin Immunol*. 2006;117:334–344.
7. von Hertzen L, Mäkelä M.J, Petäys T, et al. Growing disparities in atopy between the Finns and the Russians: a comparison of 2 generations. *J Allergy Clin Immunol*. 2006;117:151–157.
8. Alenius H, Pakarinen J, Saris O, et al. Contrasting immunological effects of two disparate dusts: preliminary observations. *Int Arch Allergy Immunol*. 2008;149: 81–90.
9. Hyvärinen A, Roponen M, Tiittanen P, Laitinen S, Nevalainen A, Pekkanen J. Dust sampling methods for endotoxin: an essential, but underestimated issue. *Indoor Air*. 2006;16:20–27.

Table E1. Online Depository. Subject and housing characteristics among Finnish schoolchildren.

|                                                       | Nonatopic  | Atopic     |
|-------------------------------------------------------|------------|------------|
| <b>N</b>                                              | 43         | 47         |
| <b>Age, mean (sd)</b>                                 | 10.7 (2.4) | 11.5 (2.4) |
| <b>Sex, males (%)</b>                                 | 21 (50.0)  | 29 (63.0)  |
| <b>Parental history of atopic diseases* n (%)</b>     | 20 (51.3)  | 29 (65.9)  |
| <b>Occurrence of atopic disease, n (%)</b>            |            |            |
| Dg asthma                                             | 2 (4.9)    | 11 (24.4)  |
| Dg hay fever                                          | 1 (2.5)    | 10 (22.2)  |
| Dg atopic eczema                                      | 10 (23.8)  | 21 (45.7)  |
| Wheezing in 12 months                                 | 4 (9.8)    | 10 (21.7)  |
| <b>Pets in household (at any age 0-15 yrs), n (%)</b> |            |            |
| Cat                                                   | 22 (52.4)  | 17 (37.0)  |
| Dog                                                   | 23 (56.1)  | 29 (63.0)  |
| Other                                                 | 15 (37.5)  | 9 (20.5)   |
| <b>Parental farming (currently), n (%)</b>            | 6 (14.3)   | 3 (6.5)    |
| <b>Indoor exposure to tobacco smoke, n (%)</b>        | 3 (11.1)   | 1 (3.2)    |
| <b>Dwelling type, n (%)</b>                           |            |            |
| Single or semi-detached house                         | 31 (73.8)  | 42 (91.3)  |
| Apartment house                                       | 4 (9.5)    | 2 (4.4)    |
| Farm                                                  | 7 (16.7)   | 2 (4.4)    |

dg = physician-diagnosed

\* parental-reported asthma, hay fever or atopic eczema ever, one or more of these