

Letters

OCCUPATIONAL RHINITIS AND ASTHMA DUE TO CABREUVA WOOD DUST

Several wood dusts have been associated with respiratory symptoms in exposed workers, but with the exception of occupational asthma (OA) caused by Western red cedar (*Thuja plicata*),¹ most publications are case reports. Several mechanisms have been proposed as causes for wood-induced asthma, but the origin of this asthma still remain unclear. Cabreuva (*Myrocarpus frondosus*) is a hardwood-flooring Amazonian tree that belongs to the Fagaceae family. One case of hypersensitivity pneumonitis² and 1 case of OA associated with a toxic reaction to cabreuva wood (CW)³ have been reported. We are unaware of any report of occupational rhinitis (OR) with or without OA due to CW.

We report the case of a 53-year-old atopic man employed as a parquet floor layer for 40 years. Four years after he started working with CW, he experienced ocular and nasal itching, nasal obstruction, and rhinorrhea, and 4 years later he developed chest tightness, dyspnea, and dry cough. Symptoms occurred exclusively 6 to 7 hours after exposure to CW and not while handling other woods or during wood painting. Symptoms worsened during the evening and night and improved during weekends and holidays (positive stop/resume test result). He first sought treatment with us in November 2007, 1 year after the last exposure to CW.

The results of skin prick and specific IgE tests performed for common inhalants, tree pollens, molds, latex, and legumes were positive to grass (1.35 kU/L). Skin prick tests with decreasing dilutions (1:1,000, 1:100, 1:10, and 1:1) of CW dust extract (10% wt/vol in phosphate-buffered saline; protein concentration, 1.3 mg/mL) produced negative results. Basal forced expiratory volume in 1 second (FEV₁) was 3.23 L (99% predicted), results of a bronchodilator test were negative, and a methacholine challenge test result was positive (provocation dose that caused a decrease in FEV₁ of 20% [PD₂₀], 448 µg). A specific inhalation challenge (SIC) with CW sawdust by the occupational method for 60 minutes (cumulative exposure) in a 7.46-m³ inhalation challenge room elicited moderate ocular and nasal itching, rhinorrhea and mucosal edema (anterior rhinoscopy), and a reduction in peak nasal inspiratory flow from 100 to 0 L/min after 45 minutes of exposure. A 20% FEV₁ decrease immediately after the end of exposure and a 21% FEV₁ decrease after 6 hours were registered. The PD₂₀ decreased to 131 µg/24 h after SIC. No FEV₁ change or nasal reaction was shown on a control challenge with lactose (the day before SIC). Induced sputum (IS) and nasal secretion (NS)⁵ samples collected before and after exposure both on the control day and during SIC showed a post-SIC increase in IS total cell count, which was mostly significant for lymphocytes (2.4% [1.98 × 10⁴/mL] before and 6.6% [29.37 × 10⁴/mL] after SIC). Most lymphocytes were identified with flow cytometry as CD4⁺ cells both before and after SIC. No change was found in post-SIC NS cell count. No significant change was registered in body temperature and blood leukocyte count assessed before and after SIC to rule out hypersensitivity pneumonitis. A basophil

activation test performed on peripheral blood with CW extract showed a 39.3% CD63 expression and a stimulation index (percentage of CD63 expression with CW extract/percentage of CD63 expression with wash buffer) of 24.6 (Figure 1A). The negative SIC result with CW extract in an atopic control and the negative basophil activation test result in 2 atopic and 2 nonatopic controls (mean [SD] CD63 expression, 3.0% [1.3%]; mean [SD] stimulation index, 1.4 [1.3]) excluded a nonspecific response.

Peripheral blood mononuclear cell proliferation with CW extract determined a stimulation index (proliferation with CW extract/proliferation with medium alone) of 4 for the patient and 0.5 for a healthy control. Immunoblotting performed with CW extract and patient's serum revealed an IgE reactivity toward a 75-kDa protein (Figure 1B).

A diagnosis of OA and OR due to CW dust was made.⁴⁻⁶ The presence of a latency period, the positive stop/resume test result, the onset of rhinitis before bronchial symptoms, the absence of symptoms in the patient when exposed to other woods, and the negative SIC result in the control subject suggest the development of specific hypersensitivity to CW. The dual bronchial response to SIC, which is frequently reported in OA due to other woods,¹ the increase in CD4⁺ lymphocytes after SIC, as reported for other high-molecular-weight and low-molecular-weight agents,⁷ and peripheral blood mononuclear cell proliferation to CW extract are consistent with an immunologically mediated hypersensitivity. The observed lack of increase in IS and NS eosinophils after SIC may be accounted for by the long period elapsed between the last exposure to CW and the clinical evaluation. Patient IgE reactivity toward a 75-kDa protein and BAT with CW extract strongly suggest a role of IgE and basophils in CW-induced respiratory allergy, whereas the BAT result in control subjects excludes the possibility of basophil acti-

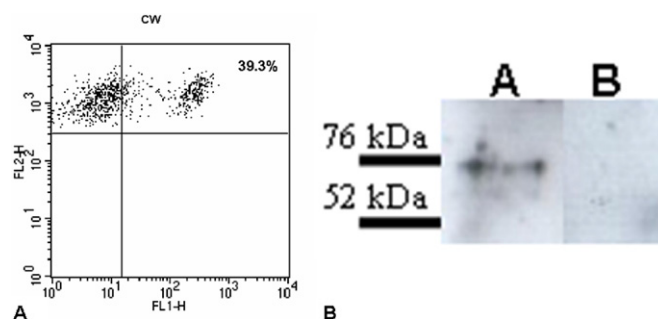


Figure 1. Results of a basophil activation test and immunoblotting. A, CD63 expression on the patient's basophils after in vitro stimulation with cabreuva wood (CW) extract. Heparinized blood was preactivated at 37°C for 10 minutes with interleukin 3 and then incubated with CW extract for 20 minutes. Reaction was blocked on ice, and the expression of fluorescein isothiocyanate (FL1-H) CD63 was assessed. Basophils were gated from blood leukocytes through a phycoerythrin (FL2-H) polyclonal antibody. On the upper right quadrant, the patient's CD63⁺ basophils are shown; on the upper left quadrant, the CD63⁻ basophils are shown. B, Lane A: CW extract run on 12% sodium dodecyl sulfate–polyacrylamide gel electrophoresis, blotted on nitrocellulose membrane, and incubated with patient's serum and with anti-human IgE. Lane B: healthy control's serum.

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vation caused by endotoxin contamination of the extract.⁸ In conclusion, our data show that CW is able to induce both OR and OA in exposed workers and suggest an underlying immunomediated mechanism.

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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.^{1,2} 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.^{3,4}

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.^{5,6} 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).⁵ 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.^{5,7} 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 schoolchildren 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 (≥ 1 positive skin prick test result)⁷ 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

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