

Asthma due to Central American walnut (*Juglans olanchana*) dust

R. K. BUSH and D. CLAYTON

Allergy Section, William S. Middleton Veterans Hospital, and University of Wisconsin Clinical Sciences Center, Madison, Wisconsin, U.S.A.

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Summary

The purpose of our study was to describe a case of asthma due to Central American walnut (*Juglans olanchana*) dust and to ascertain whether an IgE antibody mechanism was implicated. The subject was a 48-year-old man who developed asthma following exposure to Central American walnut dust. Although intradermal testing with an aqueous extract of walnut dust produced no response, inhalation challenge with the extract produced significant bronchoconstriction. Another asthmatic person exposed to the wood dust had a positive skin test, but did not respond to the bronchial challenge. A direct radioallergosorbent test (RAST) on both subjects showed no evidence of serum IgE antibodies to Central American walnut dust. Consequently, the mechanism responsible for the sensitivity to the walnut dust remains unknown.

Introduction

We report the first known case of asthma due to Central American walnut dust. Although the number of persons exposed to exotic wood dusts is not known, such woods are increasingly being used in furniture production and for decoration. Wood dust exposure is known to provoke lower respiratory symptoms, including asthma (Sosman *et al.*, 1969; Bush, Yunginger & Reed, 1978; Pickering, Batten & Pepys, 1972) and extrinsic allergic alveolitis (Howie, Boyd & Moran, 1976). The mechanisms that produce such symptoms, though not completely defined, are thought to have an immunological basis. In previous work, we found an IgE antibody involved in asthma provoked by zebra wood dust inhalation (Bush *et al.*; 1978). Although plicatic acid, a constituent of western red cedar dust, has been shown to activate the classical complement cascade *in vitro* (Chan-Yueng, Giclas & Henson, 1980), it is not known if this mechanism is responsible for western red cedar

Correspondence: Dr Robert K. Bush, University Hospital, H6/367 CSC, 600 Highland Avenue, Madison, Wisconsin 53792, U.S.A.

asthma. The mechanisms whereby other wood dusts precipitate asthma have yet to be identified.

Case report

A 48-year-old man developed rhinorrhea and episodes of cough, wheezing and dyspnoea. Although asthmatic in childhood, he had since been asymptomatic. He associated the onset of present respiratory symptoms with exposure to Central American walnut dust at work. He began to wheeze with exercise, exposure to cold air, and inhalation of irritants. When first evaluated 1 year after onset of symptoms, his absolute eosinophil count was $628/\text{mm}^3$. A spirogram revealed an FEV_1 of 3.4 litres, which decreased to 2.6 litres after one breath of methacholine, 5 mg/ml. A diagnosis of bronchial asthma was made. The patient was advised to avoid further exposure to the wood dust. Asthma and rhinitis symptoms improved with bronchodilators and antihistamines. Although the patient no longer works directly with the wood dust, he is still occasionally exposed to it and requires maintenance bronchodilator therapy to control asthma symptoms.

Materials and methods

Preparation of wood dust extracts

Fine dusts of Central American walnut were obtained by sanding the wood. A 1:20 (w/v) extract of the wood dust was prepared in Coca's solution. After the dust was extracted for 72 hr, the solids were removed by centrifugation and the supernate was sterilized by Millipore filtration. Fresh serial dilutions of this extract were made for intradermal and bronchial challenges.

Skin testing and precipitin tests

Intradermal skin testing was performed using 0.02 ml of ten commercially available, common inhalant antigens (grass, ragweed, tree, and mixed-Autumn pollens; *Alternaria*, *Hormodendrum*, *Aspergillus*, cat and dog dander, and house dust; 1000 PNU/ml, Greer Laboratories, U.S.A.), as well as the Central American walnut wood dust, serially diluted from 1:100 (w/v) to 1:1000 (w/v). Antigens capable of eliciting a 6–8 mm weal were considered positive. Skin tests were performed on the affected patient, an asthmatic control exposed to Central American walnut dust, a non-exposed asthmatic, and a non-atopic individual.

Double-diffusion immunoprecipitin tests in agarose were performed by the method of Flaherty *et al.* (1974). Sera from the affected patient and the asthmatic were tested against a panel of mold, (*Aspergillus* species and *Alternaria*, Hollister-Steir, U.S.A.) and thermophilic actinomyces antigens (Marshfield Clinic Laboratory, U.S.A.) as well as the wood dust extract, at 1:20 (w/v) and 1:50 (w/v).

Radioallergosorbent testing (RAST)

Modifications of the direct RAST as previously described (Bush *et al.*, 1978) were used to explore the possibility of an IgE-mediated reaction. Cyanogen-bromide-activated filter paper discs were incubated with a 1:20 (w/v) extract of the wood dust in 0.05 M Tris HCl buffer, pH 8.0. After the coupling procedure, unreacted sites were blocked with 0.9 M ethanolamine. The discs were washed three times with Phadebas RAST buffer (Pharmacia, U.S.A.) and then incubated overnight with 50 μl of

patient serum, exposed asthmatic control serum, and non-exposed control serum. The discs were again washed three times with Phadebas RAST wash solution and incubated overnight with 50 μ l of ^{125} I-antihuman IgE (36 000 ct/min, Pharmacia). After a final wash, the discs were counted in a gamma counter. IgE binding of 200% of negative control was considered a positive response.

Bronchoprovocation testing

Bronchial challenges were conducted using methods previously described (Bush *et al.*, 1978). Extracts were administered by a De Vilbiss No. 42 nebulizer powered by a De Vilbiss compressor at a flow rate of 11 l/min. Vital capacity inhalations were made through the open mouth, with the nebulizer held approximately 2 in away. Pulmonary function tests were recorded on a Vitalograph Model 122000 Spirometer. Bronchodilators were withheld for 12 hr prior to testing. Following baseline measurement of FEV₁ and forced vital capacity, the affected patient and exposed asthmatic inhaled three breaths of Coca's solution. Spirometry was repeated 10 min later. Challenges with serial dilutions of the wood dust were performed at 10-min intervals and the pulmonary function tests repeated. A fall of 15% or greater in FEV₁ was considered a positive response. Spirometry was repeated at 2.5 and 3.5 hr after a positive response.

The following challenges were performed on the affected patient: inhalation of Central American walnut dust extract in stepwise fashion using 1:10 000–1:1000 (w/v); and, on a separate day, repeated inhalations of Coca's solution. An exposed asthmatic was tested with: wood dust extract, 1:10 000 (w/v), 1:1000 (w/v), and 1:100 (w/v), in stepwise fashion; on a separate day, inhalations of the same wood dust extracts, followed by shifting the dust from one pan to another for 1- and 5-min intervals, similar to the methods described by Pepys and Davies (1978).

Results

The affected patient demonstrated positive skin test reactivity only to the ragweed antigen extract (8-mm weal). Skin testing with serial dilutions of the wood dust extract from 1:1 000 000 (w/v) to 1:100 (w/v) did not produce a positive response. The exposed asthmatic control subject had negative skin tests to common inhalant antigens. However, this subject had a 6-mm weal in response to testing with the wood dust extract at 1:100 (w/v). A non-exposed asthmatic and a non-exposed, non-atopic control showed no response to the wood dust extract up to 1:100 (w/v).

We could not detect specific IgE against the wood dust extract by the direct RAST. Serum from the affected patient and the exposed asthmatic control subject bound 126 and 127% respectively of the radioactivity compared to the serum of the non-exposed asthmatic individual. Precipitins were not demonstrated in the sera of exposed individuals when tested to the panel of fungal or wood dust extracts.

The affected patient demonstrated a positive response to bronchoprovocation (20.6% decrease in FEV₁ from 3400 to 2700 ml) after inhaling 1:1000 (w/v) of the Central American walnut dust extract (Fig. 1). After the patient's symptoms were reversed with aerosol isoproterenol, pulmonary function tests were repeated at 2.5 and 3.5 hr. A late-phase response was observed at 3.5 hr with a fall in FEV₁ by 15% from baseline.

Repeated inhalations of Coca's solution by the affected patient on a separate occasion did not result in a fall in FEV₁ over a 4 hr observation period. The exposed

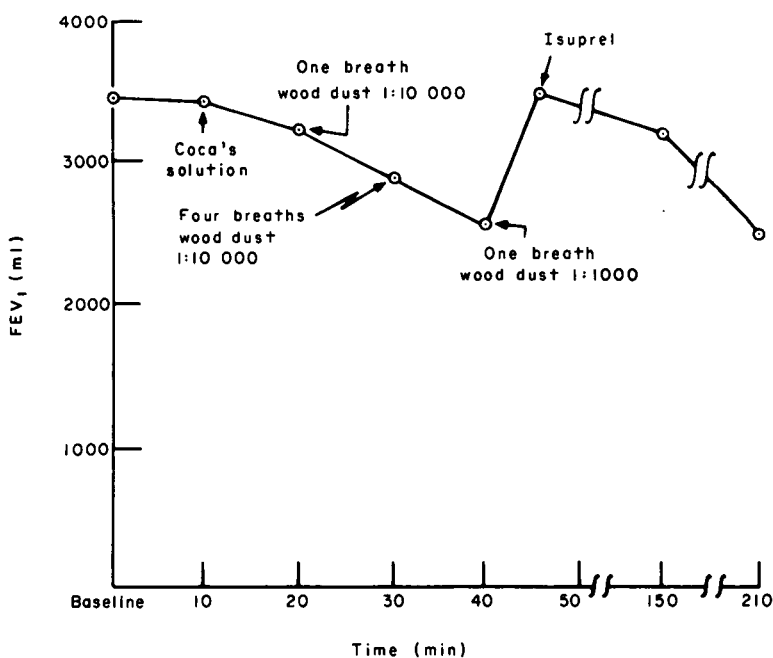


Fig. 1. Bronchial challenge of Central-American-walnut-sensitive asthmatic showing immediate fall in FEV₁ and late phase response. Arrows indicate the FEV₁ 5 min after administration of the aerosol.

asthmatic control subject was challenged with wood dust extract at 1:10 000 (w/v) and 1:100 (w/v), and shifting wood dust for 1 and 5 min. He showed neither an immediate nor a late-phase response.

Discussion

No cases of asthma due to *Juglans* dust sensitivity have been reported to date. Species of the *Juglandaceae* family, *J. regis* and *J. nigra*, are reported to cause dermatitis, possibly by sensitization to the xanthoquinone, juglone (Woods & Clanan, 1976). Juglone is found in the nutshells, roots and bark, but not in the wood itself. We do not know if juglone played a role in producing asthma in the affected patient in our study, although the patient was not known to be exposed to Central American walnut bark. Plicatic acid, the low molecular weight chemical which is the aetiological agent responsible for western red cedar sensitivity, has recently been shown to activate the serum complement cascade *in vitro* (Chan-Yueng *et al.*, 1980). However, the role of complement activation in the development of asthma in western red cedar sensitivity has yet to be established. We did not examine complement activation by walnut dust extract.

In contrast to zebra wood sensitivity (Bush *et al.*, 1978), an IgE antibody mechanism could not be demonstrated in the affected patient in our study. Although the patient responded negatively to a skin test of wood dust extract, he did exhibit an IgE response to ragweed antigen. Specific IgE antibodies to an extractable antigen were sought but not found in serum of the affected patient and the exposed control asthmatic. Thus, the mechanism for the development of sensitivity to Central American walnut dust in the affected patient remains speculative.

The affected patient's continuing asthma symptoms and need for bronchodilator therapy in spite of limited exposure to the wood dust are of interest. Late-phase asthmatic responses, as demonstrated by this patient, are known to increase nonspecific airway reactivity (Cockroft, Cotton & Mink, 1979) which may continue after exposure to the irritant ceases. It is therefore possible that the patient's intermittent exposure to wood dust is leading to non-specific airway reactivity, or that the increased non-specific reactivity induced by the initial exposure to the dust has become permanent.

As indicated by other authors (Woods & Clanan, 1976), skin testing was of little or no value in predicting sensitivity to the wood dust. The affected patient showed no response to intradermal testing with the wood dust extract, yet had a significant bronchoconstrictor response to the inhalation challenge. In contrast, a similarly exposed asthmatic showed a positive intradermal response to the concentrated wood dust extract, but did not respond to repeated bronchoprovocation with as great as 5 min exposure to the dust itself. Bronchial provocation using the suspected agent is the most reliable method of establishing wood dust sensitivity. The material in the walnut dust which produced a positive response was water soluble in this case. Sosman *et al.* (1969) found that in some cases of wood dust sensitivity only an alcoholic extract was capable of eliciting a positive clinical response. Therefore, it may be advisable to use an alcohol extract if an aqueous extract yields a negative challenge or skin test.

A number of exotic wood dusts which provoke respiratory symptoms have been reported: mahogany (Sosman *et al.*, 1969), Cedar of Lebanon (Sosman *et al.*, 1969), African zebra wood (Bush *et al.*, 1978), iroko (Pickering *et al.*, 1972), ramin (Howie *et al.*, 1976), obeche (Woods & Clanan, 1976), boxwood (Markin, 1930), western red cedar (Milne & Gandevia, 1969), California redwood (Chan-Yueng & Abbard, 1976), kejaat (Ordman, 1949), cocabolla (Eaton, 1973), abirucana (Booth, LeFoldt & Moffitt, 1976), and quillaja bark (Raghuprasad *et al.*, 1980). As importation of exotic woods for industrial and avocational purposes increases, more cases of wood dust sensitivity will no doubt be recognized.

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