
Occupational asthma due to exposure to iroko wood dust

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Background: Occupational asthma (OA) from iroko wood has been reported primarily in case reports.

Objective: To improve understanding of the pathogenesis of OA induced by iroko wood dust.

Methods: Three groups of woodworkers were included in this study: 9 workers who had clinically proven OA from iroko; 10 asymptomatic woodworkers; and 10 woodworkers with asthma. All patients underwent the following tests: a skin test with an iroko aqueous extract, specific IgE determination, and an iroko bronchial provocation test (IBPT). An eosinophil count was determined before and after the IBPT, and a methacholine inhalation test was performed after avoidance of exposure to iroko. Patients were asked to monitor their peak expiratory flow rates during a week at work followed by a week's vacation.

Results: In all patients with a personal history predictive of OA from iroko, a reduction of the peak expiratory flow rate and positivity to the IBPT while working with iroko were present. The latter test result showed a dual response, with a decrease in forced expiratory volume in 1 second from 25% to 32% at 10 minutes and a further decrease from 35% to 43% at 8 hours; at 24 hours, the eosinophil count was higher ($P = .046$). In 4 patients, the intradermal test results with iroko extract were positive, whereas the skin prick test result and the specific IgE determination were negative in all patients. The methacholine test result was also positive. In the control groups, all the test results with iroko extract were negative.

Conclusions: Our data suggest that OA due to iroko wood may be induced by immunologic mechanisms other than IgE-mediated immediate hypersensitivity reactions.

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INTRODUCTION

Occupational asthma (OA) is the most common cause of work-related respiratory disease in most industrialized countries.¹ It can be induced by many agents, approximately 250 having been identified to date.² This figure will probably increase because new materials are continually being introduced in the workplace. Among these materials are various types of woods, such as western red cedar,³ obeche,⁴ imbuia,⁵ ash,⁶ ramin,⁷ oak,⁸ ako,⁹ and iroko.¹⁰

The iroko (*Chlorophora excelsa*) is a large tree (50 m in height, 2 m in diameter) of the Moraceae family, originally from western Africa where it is known by different names such as “Kambala,” “Sanga-sanga,” “Semli,” “Lusanga,” “Odum,” “Mvule,” “Intule,” “Rokko,” “Moreira,” and “Tek.” Its trunk, without the sapwood, is long-lasting and resistant to fungi, insects, and humidity; therefore, it is widely used in hydraulic and naval constructions, joinery, and flooring, often instead of teak (*Tectona grandis* L.).¹¹

After occupational exposure to iroko wood dust, clinical manifestations of asthma and rhinitis have been reported¹² in conjunction with allergic contact dermatitis (sometimes airborne) due to type IV hypersensitivity reactions.^{13,14} The pathogenesis of asthma and rhinitis remains undetermined. In

this study, we report our experience with a group of patients who had asthma after occupational exposure to iroko wood.

PATIENTS AND METHODS

Study Participants

Three groups of patients participated in this study. Group A included 9 woodworkers (6 male nonsmokers, 1 male smoker, and 2 female nonsmokers) between 34 and 65 years old (mean age, 47.3 years), who usually worked with pine, chestnut, iroko, and walnut and who reported coughing, dyspnea, and wheezing after exposure to iroko wood dust only. These symptoms, which became evident after 6 months of working with this type of wood, diminished after treatment with an inhaled β_2 -agonist and did not occur on weekends or during vacation. Group B consisted of 10 woodworkers (6 male nonsmokers, 2 male smokers, 1 female nonsmoker, and 1 female smoker) between 18 and 60 years old (mean age, 47.33 years), who did not report respiratory symptoms while working with any type of wood. Group C included 10 woodworkers with asthma (5 male nonsmokers, 2 male smokers, and 3 female nonsmokers) between 22 and 69 years old (mean age, 41.7 years). Patients with perennial allergies were excluded from the study.

All these workers were given a Mini-Wright peak flow meter (Menarini, Florence, Italy) to monitor the peak expiratory flow rate (PEFR) during a week at work followed by a week on vacation. They were asked to monitor PEFR every 2 hours from waking in the morning to retiring to bed at night, to report what they had been doing during the day, and

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Table 1. Characteristics of Woodworkers Included in the Study and Results of in Vivo and in Vitro Tests*

Feature	Group A†	Group B‡	Group C§
Sex (M:F)	7:2	8:2	7:3
Age, y (mean ± SD)	47.33 ± 10.57	47.33 ± 13.42	41.7 ± 12.50
Smokers	1 yes, 8 no	3 yes, 7 no	2 yes, 8 no
PEFR, L/s (mean ± SD)			
Off work	8.44 ± 0.01	8.40 ± 0.01	...
At work with iroko	6.10 ± 0.01	8.29 ± 0.01	...
At work with other wood	8.31 ± 0.02	8.29 ± 0.01	...
Inhalant SPT positive	1 yes, 8 no	3 yes, 7 no	8 yes, 2 no
Iroko SPT positive	9 no	10 no	10 no
Iroko IDT positive	4 yes, 5 no	10 no	10 no
IgE detected			
Total	3 yes, 6 no	3 yes, 7 no	4 yes, 6 no
Inhalant	1 yes, 8 no	4 yes, 6 no	8 yes, 2 no
Iroko wood	9 no	10 no	10 no
FEV ₁ , L (mean ± SD)			
Pre-IBPT	4.38 ± 0.01	...	...
Post-IBPT (10 min)	3.25 ± 0.009	...	...
Post-IBPT (8 h)	0.1 ± 0.01	...	...
Eosinophils (×10 ⁶ /L) (mean ± SD)			
Pre-IBPT	112.11 ± 23.63	164.1 ± 59.10	151.0 ± 43.29
Post-IBPT	213.77 ± 29.98	169.4 ± 54.26	156.2 ± 45.78
PC ₂₀ FEV ₁ , μg (mean ± SD)	461.11 ± 190.02	...	520.0 ± 326.76

* Abbreviations: FEV₁, forced expiratory volume in 1 second; IBPT, iroko bronchial provocation test; IDT, intradermal test; PC₂₀FEV₁, provocative concentration causing a 20% decrease in FEV₁; PEFR, peak expiratory flow rate; SPT, skin prick test.

† Woodworkers with occupational asthma from iroko wood dust.

‡ Asymptomatic woodworkers.

§ Woodworkers with asthma.

whether use of a β_2 -adrenergic agent (salbutamol) had been necessary.

Skin Tests

All patients underwent skin prick tests with the most common inhalant allergens (ALK-Abelló, Milan, Italy) and with 1:10 (wt/vol) iroko aqueous extract (provided by ALK-Abelló) on the volar aspect of the forearm with use of allergy pricker lancets (ALK-Abelló lancets). Histamine (10 mg/mL) and saline solution were used as positive and negative controls, respectively.

Intradermal tests with the iroko extract were also performed on the volar aspect of the forearm at a concentration of 1:1,000 (wt/vol). If the results were negative, the tests were continued, first with the concentration of 1:100 (wt/vol) and then with 1:10 (wt/vol) at 20-minute intervals. Results of intradermal tests were considered positive if the diameter of the wheal was at least 7 mm at 30 minutes after intradermal injection.

Total and Specific IgE Determinations

Total serum IgE levels and specific serum IgE levels for the most common inhalant allergens were measured by means of a radioallergosorbent test (Pharmacia Diagnostics, Milan, Italy).

Iroko IgE Determination

Paper disks were activated with cyanogen bromide and coupled with iroko wood extract, as described by Ceska et al.¹⁵

Iroko disks were incubated overnight with the patient's serum and, after washing, with approximately 100,000 counts per minute of ¹²⁵I-mouse anti-human IgE monoclonal antibody HE-2.¹⁶ *Lolium* disks and 4 dilutions of a grass-specific serum pool, calibrated against the Pharmacia Phadebas radioallergosorbent test system, were used as reference.

Eosinophil Count

Blood was anticoagulated with heparin (Sigma Chemical, St. Louis, MO), diluted 10 times, and stained with an eosin-formalin solution (2.5 mL of formalin and 25 mL of 1% eosin for 250 mL of distilled water). Eosinophils were morphologically identified and counted by using a Buerker chamber. This test was performed 24 hours before and 24 hours after the specific bronchial provocation test with iroko extract (IBPT).

Bronchial Provocation Tests

The specific IBPT was performed in all the study groups as previously described,¹⁷ after all woodworkers had stopped working for 4 weeks, during a period outside the pollen season. A baseline forced expiratory volume in 1 second (FEV₁) equal to or greater than 80% of predicted values was required, and a control challenge with phosphate-buffered saline was performed before antigen provocation. The IBPT was begun with 1:100,000 (wt/vol) iroko extract and, if the result was negative, was continued with 1:10,000, 1:1,000,

1:100, and 1:10 (all wt/vol). The aerosolized iroko extract was inhaled from a DeVilbiss 646 nebulizer (DeVilbiss, Somerset, PA) at tidal breathing for 2 minutes. After exposure, FEV₁ was measured at 1, 5, 10, 15, 30, and 60 minutes, then hourly for 10 hours, and at 24, 48, 72, and 96 hours. In patients with a positive IBPT result, a methacholine inhalation test (Lofarma, Milan, Italy) was performed after they had avoided exposure to iroko wood for 6 months, as described by Parker et al.¹⁸ by using a DeVilbiss 646 nebulizer with an output of 0.28 mL/minute. The results were expressed as the provocative concentration causing a 20% decrease in FEV₁.

RESULTS

As shown in Table 1, in the 9 group A patients, who had OA from iroko, the result of the skin prick test with iroko extract was negative, and the skin prick test result with the most common inhalant allergens was positive for grass in 1 patient only. In contrast, results of intradermal tests with the iroko extract were positive in 4 patients. One patient had a positive reaction at the concentration of 1:1,000 (wt/vol), another at the concentration of 1:100 (wt/vol), and the other 2 at the concentration of 1:10 (wt/vol). Nevertheless, iroko wood-specific IgE was not detected in any patient, whereas grass-specific IgE (28.9 IU/mL) was found in the patient with a positive skin prick test result for these pollens.

All the skin test results with the iroko wood extract and the iroko-specific IgE were negative both in the asymptomatic woodworkers from group B and in the group C patients with asthma. Woodworkers in group A, with OA from iroko, showed a significant decline in PEFR while exposed to iroko wood (Fig 1), which continued even after working hours and necessitated inhalation of salbutamol. The IBPT result was positive in this group of patients, with a decrease in FEV₁ of more than 25%. In contrast, group B woodworkers had no respiratory symptoms while working with iroko wood and no significant change of PEFR (Fig 2).

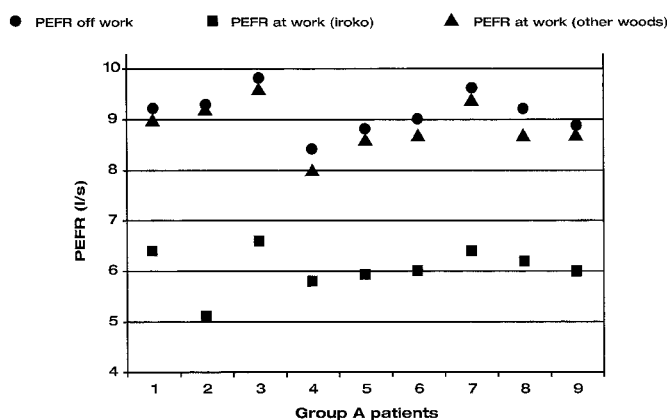


Figure 1. Peak expiratory flow rates (PEFRs) in 9 patients with asthma while working with iroko wood monitored off work and at work while using iroko wood or other woods.

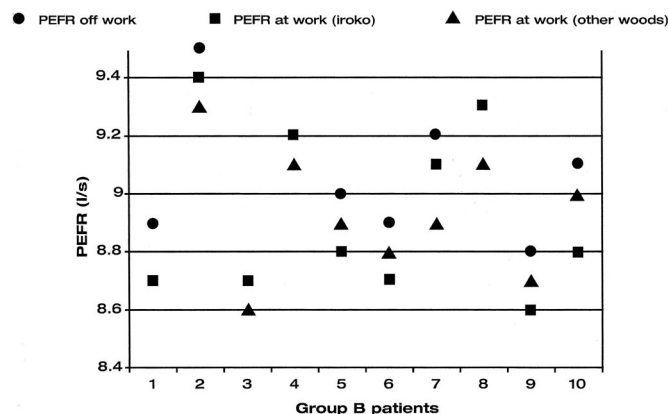


Figure 2. Peak expiratory flow rates (PEFRs) in 10 asymptomatic woodworkers monitored off work and at work while using iroko wood or other woods.

The aforementioned patient from group A, with a positive skin test result at the higher dilution, already had a positive IBPT at the concentration of 1:10,000 (wt/vol), whereas all the other patients reacted at the concentration of 1:1,000 (wt/vol). The bronchial challenge in all cases induced a dual asthmatic response, with a decrease in FEV₁ of 25% to 32% at 10 minutes and a further decrease from 35% to 43% at 8 hours. The patients were then given salbutamol by inhalation, which caused an initial rapid improvement of FEV₁ and a slow return to baseline during the next 3 days. After the IBPT, all patients from group A showed an increase in the blood eosinophil count (Fig 3) that, even if at the limit of statistical significance ($P = .046$), was not present in the control groups, in which the IBPT result was negative. The methacholine inhalation test result was positive in all group A and group C patients, with a decrease in FEV₁ of 20% (Fig 4).

DISCUSSION

Worldwide, 2 million workers are regularly exposed to wood dust in the workplace.¹⁹ To our knowledge, many patients have OA from hard wood or soft wood dust and have been

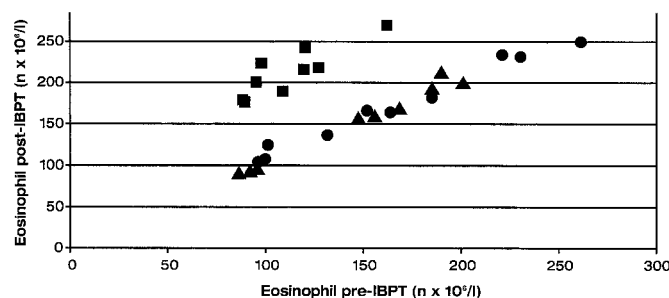


Figure 3. Eosinophil counts in patients in groups A, B, and C. Group A patients (■), who had asthma while working with iroko wood, showed a significant increase of the eosinophil count after the iroko bronchial provocation test (IBPT) compared with asymptomatic woodworkers from group B (●) and woodworkers with asthma from group C (▲).

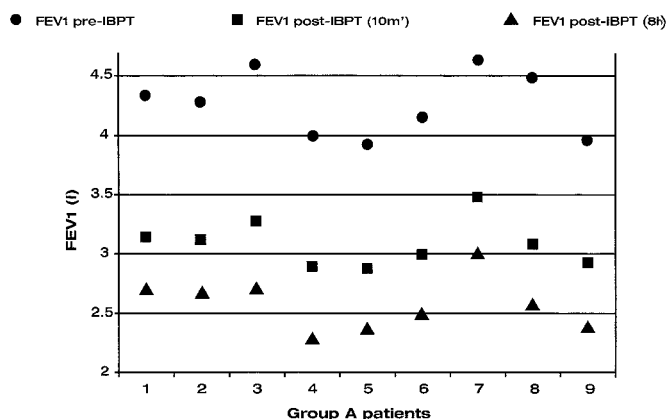


Figure 4. Forced expiratory volume in 1 second (FEV₁) in patients with asthma while working with iroko wood before the iroko bronchial provocation test (IBPT) and 10 minutes and 8 hours after the IBPT.

described primarily in case reports, with the exception of OA due to western red cedar, which has been studied in depth. In fact, OA attributable to western red cedar is known to be caused by plicatic acid, a low-molecular-weight compound (440 Da) unique to this wood, which is probably able to involve immunologic mechanisms other than type I hypersensitivity.²⁰

The first case of asthma from iroko was reported together with one of the first cases of asthma from western red cedar.²¹ In that case report as well as in others,^{10,12,22} the diagnosis of OA due to iroko wood was based on the clinical history and on the IBPT (the pathogenetic mechanism had not yet been clarified). In fact, although a positive skin prick test result for iroko wood was shown by Pickering et al,²¹ the skin test results in the articles by Colas et al²² and Azofra and Olaguibel¹⁰ were negative. Nevertheless, obtaining good quality, standardized occupational allergens is difficult. The number of patients with iroko OA evaluated in our study is the largest reported in the literature thus far. In all our patients, the skin prick test result and the specific iroko IgE test result were negative, whereas the intradermal test results were positive only in some patients. Because the relevant material may not have been extracted from the wood, further studies are necessary. In the case of western red cedar, for example, it was necessary to couple the plicatic acid with human serum albumin to achieve an effective hapten-carrier conjugate.²⁰

That reactions to intradermal tests were irritants can be excluded because these test results were negative in some patients with a positive history of OA due to iroko and in all patients in the control groups. Thus, we can hypothesize that non-IgE-mediated mechanisms are involved and that OA from iroko is a form of low-molecular-weight OA, similar to that found with western red cedar, and not a high-molecular-weight form in which one would expect to find specific antibodies against the wood or some component thereof.

Our data also show that OA due to iroko wood caused a systemic phlogistic reaction in our patients because an in-

crease of the eosinophil count after the IBPT occurred in all of them, even if the values were not statistically significant because of the small number of patients. The increase in the eosinophil count is considered a phlogistic index in other types of OA as well, eg, OA due to toluene diisocyanate.²³ Furthermore, our patients have several analogies with other cases of OA; like patients with OA due to toluene diisocyanate or western red cedar, they are mostly nonsmokers and without atopy, and they have a high degree of airway responsiveness to methacholine as well as a frequent late or even dual response to the IBPT.^{24,25} Our patients also show some analogies with other cases of iroko OA reported in the literature; in fact, Colas et al²² and Azofra and Olaguibel¹⁰ reported a dual response to the IBPT (the latter investigators observed this response even after premedication with cromoglycate and beclomethasone), whereas in the cases reported by Pickering et al²¹ and De Zotti and Gubian,¹² a late response occurred. Dual or late reactions to IBPT are reportedly more frequent in patients with OA than in patients with asthma due to common inhalant allergens.²⁶ Because it is not yet clear how the iroko extract causes early- and late-phase bronchospasm, further studies should be conducted. It could be of interest to follow the course of the studies performed in reference to western red cedar.

In the patients we studied, dual reactions occurred in all patients from group A but in none of the control subjects. This finding favors the hypothesis of an immunologic mechanism and excludes an irritant or toxic one. Furthermore, the patients' histories confirm this relationship because in all cases symptoms appeared 6 months after the initial exposure to iroko wood and disappeared on weekends and during vacation. Of note, in our study the IBPT result was positive at the concentration of 1:1,000 (wt/vol) in all group A patients, who had OA from iroko, except in 1 patient with positive results at the concentration of 1:10,000 (wt/vol). This result may be explained as a possible synergistic effect between immunologic and irritant mechanisms. This patient, in fact, demonstrated a high reactivity, being the only one in the group to react to the intradermal test at the concentration of 1:1,000 (wt/vol), to have a greater reduction in PEFR while working with iroko wood, and to show a nonspecific bronchial hyperreactivity even at the concentration of 150 µg of methacholine. On the contrary, 2 woodworkers with asthma from control group C with a positive result of the methacholine test at the concentration of 150 µg did not have a decrease in FEV₁ after challenge with iroko extract, whereas the methacholine bronchial provocation test result was positive in patients with OA due to iroko wood even 6 months after avoiding contact with this wood. Furthermore, we should emphasize that after interruption of work with iroko wood, all our patients no longer had any symptoms of asthma or a decline in PEFR at work. These data further confirm the diagnosis of OA due to iroko wood based on the patients' histories, on the monitoring of PEFR at work and on vacation, on the positive reaction to the inhalation challenge with iroko

extract, and on the positive results of skin tests (in 4 patients only).

Of note, none of the woodworkers in the population we studied with OA due to iroko wood exposure had a clear history of OA confirmed by PEF data followed by a negative challenge test result. Therefore, in our opinion, elicitation of a case history and measurements of PEF alone may be sufficient to make a diagnosis without requiring any inflammation challenge.

CONCLUSION

Our data suggest that the pathogenesis of OA due to iroko could be attributable to the low-molecular-weight compounds of this wood, which could induce immunologic mechanisms other than IgE-mediated immediate hypersensitivity reactions.

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