

Occupational allergy to weeping fig in plant keepers

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Plant keepers take regular care of green plants in public buildings and offices. One of the most common green plants in Scandinavia is weeping fig (*Ficus benjamina*). We have previously reported on two plant keepers sensitized to this plant, one had asthma and the other allergic rhinitis. We now report a study of four plant-leasing firms employing 60 plant keepers and 24 less exposed. Positive RAST and skin tests in 16 of the plant keepers and two of the employees showed them to be sensitized. All sensitized subjects suffered from conjunctivitis and/or rhinitis and six had asthma. Handling of green plants is a new example of an occupation which may cause IgE-mediated allergy

Key words: allergy; asthma; *Ficus benjamina*; gardener; occupational disease; weeping fig.

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During recent decades green plants have come to be widely used in interior decoration, and weeping fig (*Ficus benjamina*) is one of the most popular green plants in Scandinavia. Firms specializing in the leasing of green plants undertake regular care of the plants, both in offices and greenhouses. Plants with many leaves, such as weeping fig (w-fig), are difficult to clean and dust, and dry components of the plant are usually removed by vigorous shaking. In this way plant-related allergens become airborne.

During the spring of 1984 we saw two patients, one with asthma and one with allergic rhinitis. Both worked as plant keepers and the symptoms were elicited by dust from w-fig. Extracts made from leaves and twigs gave positive skin and RAST tests in both patients (2). The finding prompted us to study the occurrence and clinical picture of this occupational allergy.

MATERIAL AND METHODS

Subjects

Four plant-leasing firms in Stockholm were selected for a study. They had a total of 86

employees (range 15-26 employees), 84 of whom volunteered to be examined. The workers were arbitrarily divided into three exposure groups. Those who worked daily with and came into close contact with w-fig (52 plant keepers and 8 greenhouse workers) were regarded as being highly exposed (Highexp.). Those who occasionally worked with the plant were regarded as moderately exposed (Modexp.). This group comprised eight salesmen, four directors and six florists. A low degree of exposure was assigned to subjects who never or seldom worked with the plant (Lowexp.). Six administrative personnel belonged to this group.

The investigation consisted of a clinical examination and an interview with questions regarding: heredity of allergy, personal history of earlier and present allergic symptoms, duration of employment and symptoms, relationship between symptoms and weeping fig exposure, work-place related symptoms, symptom relief during weekends and holidays, and smoking habits. Skin prick tests (SPT) were performed (see below) and a venous blood sample was taken for determination of total IgE and IgE antibodies to various allergens (see below). Sen-

sitized persons were subjected to bronchial or rhinoconjunctival challenge.

Atopics were defined as having a skin prick test reaction of 3+ or more and/or a RAST score of 2 (≥ 0.7 PRU/ml) or more to at least one common allergen.

Allergen extracts

Before extraction, leaves and twigs of w-fig were cut into small pieces. The sap (latex) was collected dropwise after cutting off twigs from the plant. Dust was collected by gently wiping the leaves with a smooth, dry rayon cloth. Extracts of plant material (1/10 w/v) and dust (1/15 w/v) were prepared overnight in physiological saline containing 0.03% phenol. The latex was thereafter diluted to 1/100 w/v with an unbuffered saline solution containing 0.03% human serum albumin (Albumin diluent®, Pharmacia). All extracts were sterilized by filtration through a 0.22 μm Millipore® filter before use in SPT and provocation tests.

Skin tests

SPT with extracts from w-fig and dust and a standard panel consisting of 14 common allergens (birch, timothy and mugwort pollen; dog, cat and horse dander; *D. pteronyssinus* and *farinae*; *Alternaria*, *Cladosporium*, *Penicillium notatum*, *Aspergillus* and soya-bean) was performed according to Pepys (7) using a disposable blood lancet. Scoring of test reactions was done according to the Nordic guidelines (8) with histamine chloride 1 mg/ml as the reference for 3+.

RAST

RAST was performed according to the manufacturer's instructions (Pharmacia Diagnostics AB, Uppsala) using the commercially available ^{125}I -labelled anti-IgE (Phadebas anti-IgE) and expressing the results in PRU/ml as derived from the Phadebas RAST Reference System (Pharmacia Diagnostics AB, Uppsala). Various kinds of w-fig discs were prepared by coupling 10 μl of allergen extract undiluted to each

CNBr-activated paper disc as previously described (5). The discs were tested against non-atopic serum samples with IgE levels of 10 to 4000 kU/l. There was a significant non-specific uptake which corresponded to approximately 0.4 PRU/ml at 4000 kU/l. Commercially available w-fig discs (*Ficus* spp, k81, Pharmacia Diagnostics AB, Uppsala) were also used.

Allergen provocation test

Bronchial provocation tests with extracts from w-fig sap were performed in sensitized subjects with bronchial asthma, defined according to the American Thoracic Society 1962 (1). All these subjects had a positive histamine inhalation provocation test, i.e. $\text{PC}_{20} < 16$ mg/ml. The aerosol was generated by a pressure-driven nebulizer (Aiolos, Medicinsk Teknik AB, Karlstad, Sweden) using air at 220 kPa, giving an output of 0.8 ml/min. The aerosol was delivered directly to a mouthpiece and 1 ml was inhaled during tidal breathing. In two patients (Nos. 1 and 15) bronchial provocation was performed according to the routine at the clinic with stepwise increasing allergen concentration every 20 min until an early asthmatic reaction occurred, defined as a fall in FEV_1 of 20% or more. Hourly PEF was then measured for at least 12 h to record any late asthmatic reaction. A late asthmatic reaction was defined as a fall in PEF of 20% or more between 3 and 12 h after the provocation. In four patients (Nos. 3, 5, 7 and 14) the provocations were performed when they were off work on Monday mornings. The allergen concentration was raised 10-fold every week until an early asthmatic reaction occurred. PEF and FEV_1 were measured before and immediately after allergen inhalation and repeated after 15, 30, 45 and 60 min. Hourly PEF was then measured for at least 12 h to record any late asthmatic reaction. Ten patients with rhinitis and/or conjunctivitis but without asthmatic symptoms were challenged with rhinoconjunctival provocation tests by dropping one drop of w-fig sap extract in stepwise increasing concentrations into the conjunctival sac and 0.2 ml into the nose.

Statistical analyses

The results were analysed by means of the Student's t-test and chi-square test.

RESULTS

In the Highexp. group 16 of 60, all of whom were plant keepers, and in the Modexp. group 2 of 18 were found to be sensitized to w-fig as judged by positive RAST and skin tests to latex extract. All RAST-positive subjects suffered from rhinitis and/or conjunctivitis and six had asthma. Of the 18 sensitized individuals seven were atopics and 11 non-atopics (Table 1), corresponding to an atopic occurrence of 39%. In the non-sensitized workers the occurrence of atopy was 21%. Neither this difference in occurrence nor the personal history of allergy was statistically significant between the groups, but heredity for allergy was over-represented in the sensitized ($P < 0.05$). Six of the 18 sensitized subjects could not relate their symptoms to w-fig exposure but two of them had experienced symptoms when working. The median exposure time to onset of symptoms was 12 months (range 1-60) and there was no significant difference between atopics and non-atopics. There was no significant difference in exposure time between sensitized and non-sensitized subjects.

Contact urticaria when getting sap on the skin was experienced by 13 of the sensitized and 17 of the non-sensitized subjects (Table 2). None of the eight greenhouse workers was sensitized, either in the airways or in the skin.

SPT with w-fig extracts in the sensitized

group was positive for leaf, twig and sap in 16, 16 and 18 subjects, respectively. All 18 sensitized persons had positive RAST to sap, 14 to twig and 11 to leaf (Table 3). SPT reactions in the RAST-negative group of 14 subjects were eight 1+, three 2+ and one 3+ to leaf extract. To twig extract there were six 1+, four 2+ and one 3+ reactions. To sap extract there were three 1+, one 2+ and one 3+ reactions. The single 3+ reaction to twig and sap extracts occurred in the same non-atopic subject, who also had w-fig exposure-related rhinoconjunctivitis.

Geometric means of the total IgE concentration were significantly higher in the sensitized group ($P < 0.001$), in sensitized atopics versus non-sensitized ($P < 0.001$) and in sensitized non-atopics versus non-sensitized atopics ($P < 0.005$). There were no significant correlations between smoking habits and total IgE concentration or risk of sensitization.

Bronchial provocation in the four patients challenged once a week elicited in two patients (Nos. 3 and 7) a single asthmatic reaction at low allergen concentration (1/100,000 w/v, 1/1,000,000 w/v, respectively) and then a dual asthmatic reaction when the concentration was raised 10-fold. In the other two patients (Nos. 5 and 14) a single early asthmatic reaction was elicited at concentration 1/1,000 w/v and 1/100 w/v respectively. The two patients (Nos. 1 and 15) challenged as usual both elicited single early asthmatic reactions at concentration 1/10,000 w/v. The nine patients challenged with rhinoconjunctival provocation test were all positive (range 1/100 - 1/1,000 w/v). Patient Nos. 8, 9 and 13 were not

Table 1

Occurrence of sensitization to weeping fig, as judged by positive skin and RAST tests, in 84 employees in four plant-leasing firms

Exposure group	n	Sensitized		Non-sensitized		% Sensitized
		Atopic	Non-atopic	Atopic	Non-atopic	
High	60	6	10	7	37	27
Medium	18	1	1	5	11	11
Low	6	0	0	2	4	0
Total	84	7	11	14	52	

Table 2
Clinical features in 18 subjects sensitized to weeping fig as judged by positive skin and RAST test (M = median)

Patient No.	Sex	Age (years)	Sensitized to (SPT $\geq$ 3 + and/or RAST $\geq$ 0.35 PRU/ml)				Atopy	Exposure time to onset of symptoms (months)	Noticed W-fg-related symptoms	Symptoms			
			pollens of birch and/or timothy and/or mugwort	animal dander	Dpt ¹	food allergen				contact urticaria	conjunctivitis	rhinitis	asthma
1	M	22	+	+	+	-	+	3	+	-	+	+	+
2	M	44	+	-	-	+	+	48	+	+	+	+	-
3	M	25	-	-	-	-	-	6	+	+	+	+	+
4	M	26	+	-	-	-	+	18	+	+	+	+	-
5	F	21	-	+	-	-	+	24	-	-	+	+	+
6	M	35	-	-	-	-	-	60	+	+	+	+	-
7	M	41	-	-	-	-	-	60	+	+	+	+	+
8	M	23	-	-	-	-	-	1	+	+	+	+	-
9	M	33	-	-	-	-	-	2	+	+	+	+	-
10	M	35	-	-	-	-	+	24	-	+	-	+	-
11	M	22	+	-	-	-	+	12	-	+	+	+	-
12	M	56	-	-	-	-	-	60	-	-	+	+	-
13	M	37	-	-	-	-	-	6	+	+	-	+	-
14	F	25	-	-	-	-	-	6	-	+	+	+	+
15	F	22	+	+	+	+	+	12	-	+	+	+	+
16	F	23	-	-	-	-	-	6	-	-	+	-	-
17	F	23	-	-	-	-	-	24	+	+	+	+	-
18	M	32	-	-	-	-	-	12	+	-	+	+	-
M = 29			7/18				M = 12 (range 1-60)		11/18	13/18	14/18	17/18	6/18

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challenged. The RAST-negative subject with 3+ reactions in SPT to twig and sap extract was challenged with rhinoconjunctival provocation. He experienced itching in the eyes and nose, but no objective symptom was noted. The provocation test was judged to be doubtfully positive.

DISCUSSION

In this study of employees at four plant-leasing firms it was found that 18 of 78 persons with a high or moderate degree of exposure to w-fig had developed asthma and/or rhinoconjunctivitis due to an IgE-mediated hypersensitivity to allergens from w-fig.

A main allergen source seemed to be the latex, since all sensitized subjects had positive SPT and RAST to latex. In addition, the SPT reactions were generally stronger and the RAST score for latex higher than for twig and

leaf. Furthermore, 13 subjects had experienced contact urticaria from the latex.

Macroscopically one can see that there is sap in the leaves as well as in the twigs when cutting them. Whether there are different allergens in the three w-fig extract preparations has yet to be elucidated.

We think that the main route for sensitization of the respiratory tract is by inhalation of airborne dust containing the allergens. Dust settles on the leaves and sap accumulates in the dry dust. The plant is usually cleaned by shaking it, and in that way the allergen-enriched dust becomes airborne and probably high exposure peaks occur. The fact that none of the eight highly exposed greenhouse workers was sensitized supports this hypothesis, because in greenhouses the air humidity is high and hence airborne dust is low. The fact that two patients (Nos. 9 and 10) both had negative SPT and RAST to leaf extract but a positive SPT

Table 3

Results of skin and RAST tests of weeping fig extracts and total IgE concentrations in 18 patients sensitized to weeping fig

Patient No.	SPT (No. of +)				RAST (PRU/ml)			Total IgE (kU/l)	PC ₂₀ (mg/ml)
	leaf 1/10 w/v	twig 1/10 w/v	latex 1/100 w/v	dust 1/15 w/v	leaf	twig	latex		
1	4	4	4	3	2.3	1.2	11.0	300	0.5
2	4	5	4.5	4	6.3	13.0	33	970	> 16.0
3	3	4	4	2	0.4	0.6	170	400	0.7
4	3	3	5	3	0.4	2.8	17	150	ND
5	4	4	4	2	0	0.6	3.2	380	3.0
6	4.5	5	3.5	4	2.3	1.8	12	90	ND
7	4	4	4	3	3.8	4.2	30	100	0.5
8	4	4.5	5	ND	0	0.4	1.7	37	ND
9	0	4	4	3	0	0	0.7	30	ND
10	0	0	2	2	0	0	0.4	1400	ND
11	4	0	4	4	1.0	0.7	2.4	64	ND
12	4	3	4	2	0.5	0	1.5	14	> 16.0
13	4.5	0	5	3	0.5	0.8	4.3	41	> 16.0
14	4	3.5	4	3	0	0	3.9	54	1.5
15	4.5	3	3	2	5.3	130	210	2000	12.0
16	2	2	3	3	0	1.3	2.4	170	ND
17	3	3	4	3	1.2	2.2	5.7	40	ND
18	4	5	4	3	0.7	14	14	41	ND
					M = 0.5 (range 1-6.3)	M = 1.0 (range 1-130)	M = 5.0 (range 0.4-210)	M = 95 (range 14-2000)	

Skin prick test with histamine chloride 1 mg/ml = 3+; ND = not done; M = median; PC₂₀ = Provocation concentration of histamine required to produce 20% fall in FEV₁

reaction to dust extract strongly indicates that the allergen in the dust does not derive from the upper surface of the leaves, but rather from the latex inside the leaves.

Another possible contributory route for sensitization could be the skin as 13 of the sensitized subjects suffered from contact urticaria when getting latex on the skin. They often also report itching on the hands and arms when working with the plant. Thus it is evident that the allergen can cross the skin barrier and also that it might be rather potent.

Surveys might underestimate the risk of sensitisation due to a so-called "healthy worker effect", i.e. sensitized subjects might have left their occupation because of symptoms.

We tried to evaluate whether this had occurred. In two of the firms, due to reorganization and technical problems, no information regarding previous employees could be obtained. In the other two firms with 34 employees, of whom 10 had been sensitized, only four subjects had quit their jobs during the last 3 years. As none of them had had allergic symptoms when they left their occupation, it is likely that the healthy worker effect in this case was of minor importance. However, during this study, and maybe as an effect of it, two patients (Nos. 14 and 16) were transferred to office work within the firm and one (No. 6) found other work. All three patients who changed their working conditions suffered from asthma, which by these patients was experienced as a more intolerable symptom than rhinitis.

In other occupational allergies where the exposure to the allergens is high, sensitization occurs both in non-atopic and atopic subjects; however, atopic individuals more readily get sensitized and more rapidly develop allergic symptoms (3).

In this study many (11 of 18) in the sensitized group were classified as non-atopic although four of them had heredity of atopy. This might depend on frequent high exposure peaks to rather potent allergens. None of the 11 sensitized non-atopic patients was sensitized to any of the 14 common allergens included in the SPT, and the personal history gave no hint of any other allergen precipitating their symp-

toms. Among the seven sensitized atopic patients, sensitization to any other common allergen could not be found. Sensitization to birch was found in five of these seven patients, however, in all but one the RAST scores were lower than to w-fig sap. These facts make it unlikely that there is cross-reactivity between w-fig allergens and any other common allergen. However, cross-reactivity to other plants of the genus *Ficus* could be expected to be extensive from our knowledge of tree pollen allergy.

The clinical picture of allergy to w-fig is often characterized by more or less chronic symptoms, possibly due to late allergic reactions and increased bronchial hyperreactivity. Some of the patients, therefore, do not identify their symptoms with exposure to w-fig. Usually conjunctivitis and/or rhinitis precede asthma. The patients experience relief of symptoms during weekends and holidays and hence give a hint that the offending allergen is work-place related. The clinical picture is rather consistent with other occupational allergies to respirable antigen such as the latex (gum-acasia)-induced printers' asthma, coffee workers' allergy and detergent enzyme (4, 6, 9).

The development and clinical picture of allergy to w-fig is illustrated by the following case report (patient No. 16): A 23-year-old non-atopic female who as a child once suffered from urticaria. She worked as a florist for 3 years and then as a plant keeper for 6 months. One week before allergological investigation in November 1984 she had experienced itching in the eyes 2 h after coming home from work, not understanding why but, when questioned, she recalled that she had worked extensively with w-fig that day. SPT and RAST were positive to w-fig but negative to other common allergens. It was therefore probable that exposure to w-fig-related allergens had precipitated a late conjunctival reaction. In January 1985 she also got rhinitis and in February periods with dyspnoea, cough and wheezing. Both rhinitis and symptoms of asthma developed mainly during evenings and nights. During weekends the symptoms decreased and on Sundays she usually had no symptoms at all. Five months later, in April 1985, allergological investigation was performed

again. The RAST values (PRU/ml) for leaf had risen from 0 to 1.7, for twig from 1.3 to 4.6 and for latex from 2.4 to 13. Bronchial provocation with latex extract from weeping fig was positive. (The patient is in this study classified as having only conjunctivitis.)

Green plants as indoor decoration are often recommended to patients with atopic allergy since such plants do not pollinate and do not have a strong smell. However, we have also occasionally seen low-exposed atopic patients with w-fig allergy.

We conclude that the risk of highly exposed plant keepers becoming sensitized to weeping fig is considerable, as 16 of 52 were sensitized. Handling of green plants is a new example of an occupation which may cause IgE-mediated allergy.

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