

A new indoor allergen from a common non-flowering plant

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Ficus benjamina or weeping fig (w-fig) is one of the most common indoor non-flowering green plants in northern Europe. We have previously reported that occupational exposure to w-fig in plant keepers, both atopic and non-atopic, gives rise to IgE-mediated allergy with airway symptoms. About one-fourth of the plant keepers had become sensitized. We now report a study of sensitization in non-occupationally exposed persons comprising 395 patients, consecutively referred for allergological investigation, and 107 employees from two offices decorated with an abundance of w-figs. Of the patients, 56% were found to be atopic and more than half of them reported exposure to w-fig. Sensitization, as judged by a positive skin prick test and positive RAST, was found in 13 of the patients and in three of the employees. All of them suffered from rhinitis and/or asthma and were atopics and sensitized to one or several common allergens. We conclude that sensitization to w-fig is not uncommon and that in Sweden it is of the same magnitude as sensitization to the most common mould, *Cladosporium herbarum*. The risk that subjects with a genuine atopic constitution exposed to w-fig will become sensitized is about 6%. In approximately half of the patients the sensitization was considered to be clinically important.

Key words: allergy; *Ficus benjamina*; weeping-fig.

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The decoration of homes, office premises and public buildings with green plants is not new, but has become more widespread in recent decades.

Most indoor pot plants originate from subtropical or tropical regions. The characteristics of plants that become popular are that they can thrive indoors, are easy to care for and are decorative. New species and varieties that better fulfill these criteria are continuously being introduced on the market.

Ficus benjamina or weeping fig (w-fig) is one of the most common indoor plants in northern Europe. The plant is also known as Java willow, Ceylon willow and Bali fig tree. W-fig is a non-flowering green plant with numerous small leaves, and indoors it is often cultivated into a small tree. The pollen of w-fig is situated in small red fruit bodies, and in the plant's

natural habitat pollination is carried out by hymenoptera (Chalcididae).

We have found that dust from green plants, particularly w-fig, can induce sensitization and give rise to allergic asthma and rhinitis in occupationally exposed subjects (1, 2). This finding gave reason to consider whether sensitization to w-fig might occur in subjects less exposed, e.g. in offices or their homes.

MATERIAL AND METHODS

Allergy clinic patients

Three hundred and ninety-five consecutive patients, referred for allergological consultation at the Division of Allergy of the Department of Thoracic Medicine, Karolinska Hospital,



Fig. 1. A *Ficus benjamina* (Weeping fig) with a height of 1.6 m and approx. 1800 leaves, corresponding to a total upper leaf area of approx. 3.6 m².

between October 1, 1984 and May 9, 1985, were investigated. The majority of the patients had symptoms of airways allergy. The investigation consisted of a clinical examination and an interview including questions regarding: hereditary of allergy, personal history of previous and present allergic symptoms, and any w-fig-related symptoms. The patients were arbitrarily divided into four exposure groups: 1) no known exposure to w-fig (N-exp), 2) w-fig at home (H-exp), 3) w-fig both at home and at workplace (HW-exp) and 4) w-fig at workplace (W-exp). Patients Nos. 7 and 8 have been excluded from all frequencies given in per cent of sensitization to w-fig allergens, as they were referred on request after reading a newspaper article about w-fig allergy. 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).

Office workers

Office A was a local department of the National Health Insurance (*Försäkringskassan*, Jakobsberg) with 63 employees of whom 62 volunteered to be investigated. The office was open-planned with an area of 693 m² covered with wall-to-wall carpeting. Ever since the office was built in 1970 the only green plants used for decoration were 15 w-figs about 2 m high. The investigation consisted of a questionnaire regarding hereditary of allergy, personal history of previous and present allergic symptoms, duration of employment, and any workplace-related symptoms. SPT was performed (see below). A venous blood sample was taken for determination of total IgE and IgE antibodies to w-fig latex extract and allergens positive in SPT.

Office B was an official department of statistics (*Statens Statistiska Centralbyrå*), located in a 134,000 m² large building and shared with four other official departments. The total area of the premises was 23,239 m², most of which was covered with wall-to-wall carpeting. About 3,300 m² was an open-plan office. Both the offices and public areas inside the building were richly decorated with green plants, predominantly w-fig.

In the autumn of 1983 a questionnaire regarding allergy and hypersensitivity was distributed to all 823 employees, 738 of whom answered. Of these respondents, 107 replied affirmatively to the question "Do you suffer from hay fever and/or asthma?". Forty-five of these 107 subjects volunteered to undergo an allergological investigation performed as in office A.

The atopic status of all investigated subjects was assessed, atopics being defined as subjects having an SPT reaction of 3+ or more and/or a RAST score of > 2 (> 0.7 PRU/ml) to at least one common allergen.

Allergen extracts

Before extraction, leaves and twigs of w-fig were cut into small pieces (1-2 mm). The sap (latex) was collected dropwise after cutting twigs. Extracts of plant material (1/10 w/v)

were prepared overnight in physiological saline with 0.3 % phenol. The latex was then diluted to 1/100 w/v with an unbuffered saline solution containing 0.03 % human serum albumin (Albumin diluent®, Pharmacia, Uppsala). All three extracts were sterilized by filtration through a 0.22 µm Millipore® filter before use in SPT and provocation tests.

Skin tests

The patients were skin prick tested with the extracts from w-fig and a standard panel consisting of 14 common allergens; birch, timothy and mugwort pollen; dog, cat and horse dander; *D. pteronyssinus* and *farinae*; *Alternaria alternata* and *Cladosporium herbarum* (Pharmalgen, Pharmacia, Uppsala); *Penicillium notatum* and *Aspergillus fumigatus*; feather; and soybean protein (ALK, Copenhagen). The subjects in offices A and B were skin prick tested with birch, timothy, mugwort, cat, *D. pteronyssinus* and the w-fig latex extract.

The SPT was performed as described by Pepys (5), using a disposable blood lancet. Test reactions were scored according to the Nordic guidelines (6), 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 ¹²⁵I-labelled anti-IgE (Phadebas RAST); the results are expressed 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 (4). 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 corresponding to approximately 0.4 PRU/ml at 4000 kU/l. In addition, commercially available w-fig discs (*Ficus* spp, k81, Pharmacia Diagnostics AB, Uppsala) were used.

In the group of patients RAST was per-

formed to the respective allergen when SPT was positive (≥ 1+) and to additional allergens as indicated by the case history. In the group of officeworkers RAST was tested against w-fig sap in all subjects and against the allergens positive at SPT.

Statistical analyses

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

RESULTS

Allergy clinic patients

Of the 395 patients with respiratory symptoms, 221 (56 %) were found to be atopics. The frequencies of sensitization to three common allergens and to w-fig sap extract are shown in Table 1.

Twelve patients were sensitized to w-fig, as judged by positive SPT and RAST to the sap extract. Another patient was sensitized only to leaf extract (SPT: 4+; RAST: 4.1 PRU/ml). A rhinoconjunctival provocation test to leaf extract 1/100 w/v was positive. All 13 patients had positive RAST tests to other allergens also and were classified as atopics. Positive SPT reactions to w-fig extracts were also found in many RAST-negative patients without symptoms related to w-fig (Table 2).

Sixty-two per cent of all patients reported some exposure to w-fig, most of them in their homes (H-exp 45 %, HW-exp 8 % and W-exp 9 %). No signi-

Table 1
Occurrence of sensitization of three common allergens and weeping fig sap extract as judged by unequivocally positive RAST (≥ 0.7 PRU/ml) in 221 consecutive atopic patients visiting an allergy clinic

Allergen	Number of patients	Percent
Timothy	106	48
<i>D. pteronyssinus</i>	31	14
<i>Cladosporium herbarum</i>	8	3.6
Weeping fig sap	8*	3.6

* Two patients were excluded, as they were referred on request after reading a newspaper article about weeping fig allergy.

ficant difference in exposure was found between atopic (60 %) and non-atopic (64 %) subjects. However, exposure was significantly more common (12/13; $P < 0.05$) among sensitized patients than among non-sensitized subjects. The mean age of the sensitized patients (37 years) was significantly higher ($P < 0.05$) than that of the non-sensitized atopics (31 years). Some clinical features of sensitized patients are presented in Table 3.

The geometric mean of the total IgE concentration was significantly higher ($P < 0.025$) in the sensitized (467 kU/l) than in the non-sensitized group of atopics (188 kU/l). The results of SPT and RAST to w-fig extract and the total serum IgE

concentrations in the 13 sensitized patients are summarized in Table 4.

Ten of the sensitized patients (Nos. 3-10, 12 and 13) who had w-fig at home got rid of their plants. Five of these patients (Nos. 4, 7, 8, 10 and 13) reported diminishing symptoms after eliminating the plants.

The following three case reports illustrate patients with sensitization of clinical importance:

Patient No. 10, a 48-year-old woman with atopic eczema, rhinoconjunctivitis and asthma, who was sensitized to deciduous trees and grass pollens, several food allergens and moulds. She had two large w-figs at home and one at work and had

Table 2

Distribution of skin prick test (SPT) results for various weeping fig preparations among patients with positive SPT but negative RAST to weeping fig. Skin reactions were found in 98 patients, of whom 74 were atopics

Allergen preparation	0	1 +	2 +	≥ 3 +	Total No. skin reactions
Leaf	302	54	19	7	80
Twig	329	36	16	1	53
Sap	373	6	3	0	9

Table 3

Clinical features in 13 atopic patients sensitized to weeping fig (w-fig) as judged by positive skin and RAST tests

Patient No.	Sex	Age (years)	Sensitized to (positive RAST)					Symptoms			
			pollens of birch and/or timothy and/or mugwort	animal dander	Dpt ¹	Food allergen	Exposure to w-fig	Noticed w-fig-related symptoms	conjuncti-vitis	rhinitis	asthma
1	M	55	+	+	-	+	N-exp	-	+	+	+
2	F	25	+	+	-	+	H-exp	-	+	+	-
3	F	21	+	+	+	+	H-exp	-	+	+	-
4	F	48	-	+	-	+	H-exp	-	-	-	+
5	F	22	+	-	-	-	H-exp	-	+	+	+
6	M	28	+	+	-	+	H-exp	-	-	-	+
7	F	43	+	+	-	-	H-exp	-	-	-	+
8	F	30	+	+	-	+	H-exp	-	+	+	+
9	M	36	+	+	-	+	H-exp	-	+	+	-
10	F	48	+	+	-	+	HW-exp	+	+	+	+
11	F	40	+	+	-	+	HW-exp	-	-	+	+
12	F	41	+	+	-	-	HW-exp	-	+	+	-
13	F	44	-	-	-	+	HW-exp	+	-	+	-
$\bar{M} = 37$			11/13	11/13	1/13	10/13		2/13	8/13	10/13	8/13

¹ *D. pteronyssinus*.

suspected that w-fig caused her airway symptoms. After elimination of the plants the symptoms diminished.

Patient No. 13, a 44-year-old woman, had suffered twice from urticaria after eating shellfish. RAST was positive for shrimp and crab. She had had w-figs both at home and at work for several years and had had increasing symptoms of rhinitis which she suspected were precipitated by w-fig. After getting rid of the plants her rhinitis cleared.

Patient No. 7, a 44-year-old woman, had had steroid-dependent bronchial asthma for many years and was sensitized to birch and animal dander. She had cultivated two large w-figs at home for 10 years and had noted home-related symptoms. RAST for sap was 69 PRU/ml and her total IgE concentration was 100 kU/ml. Her asthma has slightly improved 1 year after she had got rid of the plants.

Office workers

In office A 13 of 62 subjects were classified as atopics. The mean duration of employment for all subjects was 7.3 years.

One employee of office A was allergic to w-fig. She was a 59-year-old atopic woman with rhinoconjunctivitis and asthma who was sensitized to birch and timothy pollens and had positive SPT (4+) and RAST (11 PRU/ml) to w-fig sap extract. She had chronic symptoms varying in intensity and had noticed workplace-related symptoms in spite of the fact that she had had a w-fig about 1.5 m high at home for 10 years. Her symptoms diminished markedly after she got rid of the plant at home.

Among the 45 “selected” subjects from office B, 24 were classified as atopics. The mean duration of employment for all subjects was 10.8 years. In office B two employees were allergic to w-fig.

One 56-year-old atopic woman with rhinitis and asthma sensitized to grass pollens had positive SPT (3+) and RAST (1.9 PRU/ml) to w-fig. Her total IgE concentration was 1800 kU/l. She had had two w-fig plants, 1.5–2 m high, at home for 10–15 years and had noticed home-related symptoms, which diminished after elimination of the plants.

Another 64-year-old atopic woman with rhinoconjunctivitis and hand eczema, who was

Table 4
Results of skin and RAST tests for weeping fig extracts and total IgE concentrations in 13 atopic patients sensitized to w-fig

Patient No.	Skin prick test (No. of +)			RAST (PRU/ml)			Total IgE (kU/l)
	leaf 1/10 w/v	twig 1/10 w/v	sap 1/100 w/v	leaf	twig	sap	
1	2	1	1	0.5	0.6	0.5	620
2	3	4	3	6.1	3.9	4.1	1500
3	0	1	1	11	5.5	13	4200
4	1	2	2	1.1	0.5	3.4	1000
5	0	2	2	0	0	2.6	230
6	2	2.5	2	0.7	0	0.6	1100
7	3	3.5	3.5	1.4	42	69	110
8	3	3	5	5.4	44	86	970
9	4	0	0	4.1	0	0	210
10	3	4	5	1.0	8.7	9.0	2200
11	3	3	4	2.8	4.8	7.8	43
12	3	3	3	0	3.7	6.8	270
13	2	3.5	3.5	0	0.6	1.2	87
				M = 1.1 (range 0–11)	M = 3.7 (range 0–44)	M = 4.1 (range 0–69)	M = 620 (range 43–4200)

Skin prick test with histamine chloride 1 mg/ml = 3+; M = median

sensitized to birch, had positive SPT (3+) and negative RAST to w-fig. Her total IgE concentration was 17 kU/l. She had cultivated w-figs at home for 10 years and had two plants about 2.5 m high and three plants 0.5 m high. She had symptoms at home and in spite of the negative RAST the positive SPT was considered as evidence of sensitization. She reported no change in her symptoms after elimination of the plants.

The three sensitized officeworkers all had more or less chronic symptoms and none of them had noticed w-fig-related symptoms.

DISCUSSION

The degree of exposure to allergens is of great importance in the sensitization of a population. High-grade exposure leads to a high proportion of sensitized subjects, while low-grade exposure leads to sensitization in a proportion of atopic subjects. This was exemplified in the present investigation, where all subjects sensitized to w-fig were found to be atopic. This finding contrasts with the observations in a study on occupational exposure to this plant showing that only seven of 18 sensitized subjects were atopic (2). The higher total IgE concentration in sensitized atopics indicates that these persons also had an increased tendency to give an IgE response.

Since 12 of the 13 sensitized subjects reported exposure to w-fig and a statistically significant difference between the proportions of sensitized and non-sensitized subjects was found, it is evident that low-grade exposure can lead to sensitization, at least in atopic subjects.

Surprisingly, we found no evidence of sensitization in office workers exposed at work only. All three sensitized office workers had w-fig at home. These facts indicate that significant exposure occurs when w-fig is cultivated at home. The reason for this may be not only that most people spend more time at home than at work, but that when they handle the plants and clean their homes, exposure peaks might occur as the allergens become airborne. At the two offices investigated the plants were handled by plant keepers and the premises were cleaned by charwomen.

Since the sensitized subjects were atopics with, in most cases, several allergies, the clinical evaluation of symptoms due to w-fig allergy was difficult. However, in some of the patients the clinical importance was obvious, e.g. in patient Nos. 10 and 13.

Patients with a clinically important w-fig sensitization have more or less chronic symptoms, as with other dust-borne allergies. Examples of patients with sensitization of little or no clinical importance are Nos. 1, 3 and 6. They all had comparatively high total IgE concentrations and low RAST scores for w-fig, and were sensitized to several other allergens giving typically allergic symptoms. The sensitization to leaf extract in patient No. 9 was probably also of minor importance.

Provocation tests might have helped in the clinical evaluation. However, in a previous study (2) of occupationally exposed plant keepers, there was a strong correlation between positive SPT, RAST and provocation tests in sensitized subjects. That is the reason why in this study we performed only one rhinoconjunctival provocation test with the leaf extract.

It is likely that the leaf extract contains specific allergens that were not found, or were found in very low concentrations, in the sap. The fact that patient No. 9 was sensitized only to leaf (4.1 PRU/ml) but not to sap extract supports this possibility. In patients with positive SPTs but negative RAST, most positive SPTs referred to the leaf extract. Some of these positive SPTs might represent a low-grade sensitization, but we believe that the majority are due to a non-specific irritant effect. With the sap extract, in spite of a lower concentration (1/100 w/v), the SPT reactions were generally stronger and the RAST scores higher. Furthermore, the sap extract gave only one 3+ reaction in SPT in a subject with negative RAST among the 502 investigated subjects. This 3+ reaction occurred in an atopic subject with a total IgE concentration of 17 kU/l and was judged to be a true sensitization. A similar relation between leaf and sap extract was found in the study of occupational allergy in plant-keepers (2) and supports the view that the major allergens emanate from the sap. The sap extract should there-

fore be used in both SPT and RAST for the diagnosis of w-fig allergy.

The occurrence of w-fig sensitization could not be considered unusual, at least not in the Stockholm area. Eight per cent of the exposed atopic subjects were shown to have specific IgE antibodies, an incidence equalling that of the most common mould allergy in Sweden, *Cladosporium herbarum*.

A striking observation in the sensitized patients was the high prevalence of food intolerance. Ten of the 13 were RAST positive to various food allergens, six of them to soy-bean protein. At our allergy clinic the proportion of atopic patients with food intolerance is 10–15%. Cross-reactivity between sap extract and food allergen is unlikely as no common specific food allergen was found among the patients. This finding is unexplained and requires further investigation.

The significantly higher mean age in sensitized than in non-sensitized patients (37 vs. 31 years) is also difficult to explain. Large w-figs are expensive, and most sensitized patients had cultivated their w-figs at home for many years and hence might have been exposed for a longer period. The interest in cultivating plants probably increases with age and green plants are probably not a first priority when young people are starting a home.

It is difficult to understand how sensitization to sap constituents takes place. We suggest the following hypothesis: All water taken up by the roots of the plant and not used in the photosynthesis will be evaporated by the leaves. About 6–8% (valid for birch) evaporates by diffusion through the surface epithelial cells and the rest via the stomatal apertures that are situated on the underside of the leaves. The amount of water evaporated by diffusion is considerably greater if the total area of the leaves is large, the ambient air humidity low, and the temperature high. For example on a sunny day the evaporation by diffusion from a birch tree with 2×10^5 leaves is some 60–70 l, increasing on particularly hot and dry days to about 400 l (6). W-fig has small but numerous leaves. The area of a leaf is about the size (20 cm²) of a birch leaf. A 2-m high thriving w-fig has about

1500–2000 leaves giving a large total leaf area of 3–4 m². The relative air humidity in most modern apartments in Sweden is low, 20–30%, especially in the winter because of the central heating, and the temperature is about 20–22°C. When the water diffuses, soluble allergens will accompany the water by osmosis and deposit on the surface of the leaves when the water evaporates. However, if dust accumulates on the leaves, the allergens will be absorbed by the dust, and thus become airborne.

This hypothesis is supported by the following facts: In the study of occupationally exposed plant keepers (2) none of the eight workers in the greenhouses, where air humidity is high and the concentration of airborne dust is low, was sensitized, while 16 of 52 plant keepers working in the dry indoor air of the premises, were sensitized. Our patients live in modern apartments with a dry atmosphere. Furthermore, two of the sensitized plant keepers had negative SPT and RAST to extract made from leaves but positive SPT reactions to extract made from dust collected from w-fig leaves.

This hypothesis may explain why sensitization to w-fig is not reported from the plant's natural habitat, where the air humidity is high, the dust content low and the plant's leaves are regularly cleaned by rainfall. It could also be expected that a lower frequency of sensitization will be found in geographical areas where the indoor climate has a high air humidity and a low dust content.

There are several other species of the genus *Ficus* that are fairly common as indoor plants. In a preliminary study we have found extensive cross-reactivity. However, w-fig is probably the biggest producer of allergenic dust, owing to its large total leaf area and the practical problem of keeping the leaves dust-free.

We conclude that proven atopics exposed to w-fig, particularly in home surroundings, run a definite risk of becoming sensitized. If only unequivocally positive RAST results are accepted, the risk figure is 6%, approximately half of which is considered clinically important. Non-occupational exposure at work places seems to be of minor importance for sensitization, but may induce symptoms in sensitized individuals.

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REFERENCES

1. Axelsson, G., Skedinger, M. & Zetterström, O.: Allergy to weeping fig. A new occupational disease. *Allergy* 40, 461-464, 1985.
2. Axelsson, G., Johansson, S. G. O. & Zetterström, O.: Occupational allergy to weeping fig in plant keepers. *Allergy* 42, 161-167, 1987.
3. Bonner, J. & Galston, A.: Principles of plant physiology, pp. 224-226. Freeman and Co., San Francisco, 1952.
4. Johansson, S. G. O., Bennich, H. & Berg, T.: In vitro diagnosis of atopic allergy. III. Quantitative estimation of circulating IgE antibodies by the radioallergosorbent test. *Int. Arch. Allergy Appl. Immunol.* 41, 443, 1971.

5. Pepys, J.: Skin tests in diagnosis. In Gell, P. H. G., Coombs, R. R. A. & Lackman, P. J. (eds.): Clinical aspects of immunology, pp. 55-80. Blackwell Scientific Publ., Oxford, 1975.
6. Proceedings of symposium at Northern Congress of Allergology: Allergy diagnostic and allergen extracts. Northern standardization report II. *Acta Allergol.* 29, 222-240, 1974.

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