

Allergic contact dermatitis to plants in a Spanish dermatology department: a 7-year review

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To investigate the incidence of allergic contact dermatitis (ACD) to plants in our area, we reviewed the records of the patients that were studied in the Allergic Contact Unity of our hospital in the last 7 years (2248 patients). We found 69 cases of positive patch tests to plant allergens, representing 3% of all the patients in that period. Diallyl disulfide was the most frequent allergen (47 cases), involving mainly middle-aged housewives with chronic hand eczema. Positive tests to sesquiterpene lactone mix (SL mix) were found in 11 patients, mostly middle-aged rural workmen with an airborne clinical pattern. Other allergens detected were lichens, primin, tulipalin A and wood. These results show a high incidence of ACD to diallyl disulfide that, in our opinion, should be tested in all housewives or cooks with chronic hand eczema. The predominance of the classical airborne pattern of allergy to SL in our study may be because the airborne way of allergen exposure in our area, with a high percentage of rural population, is the most frequent, and it makes it important to remember this possibility in the differential diagnosis of photosensitivity.

Key words: allergic contact dermatitis; diallyl disulfide; lichens; plants; primin; sesquiterpene lactones; tulipalin A; wood. © 2006 The Authors. Journal compilation © 2006 Blackwell Munksgaard.

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The incidence of allergic contact dermatitis (ACD) to plants is unknown. This fact is partially due to the difficult diagnosis of this clinical problem in the community, and even when it is suspected, the identification of the species implicated can be very difficult, and the lack of appropriate purified allergens in some cases does not make possible the confirmation.

The purpose of this study was to investigate the global incidence of ACD to plants in the patients tested in the Allergy Contact Unity (ACU) of our hospital in a 7-year period and to describe the most remarkable epidemiological, aetiological and clinical features of this dermatosis in our area. We also tried to identify the occupational and non-occupational groups at risk and evaluate the impact of the ACD.

Patients and Methods

A retrospective study was performed. We reviewed the records of patients that were studied in the ACU of our department between January 1998 and December 2004, representing a total number of 2248 patients. All were referred by dermatologists and came from the Health

Service Area of Santiago de Compostela, in the north-west of Spain (that covers a population of 500 000 habitats, mostly employed in primary and services sector).

In all cases, a general and specific clinical interview was performed, and also patch test with the standard series of the Spanish Research Group in Contact Dermatitis (GEIDC), which includes the sesquiterpene lactone (SL) mix 0.1%. We also included other allergens in our standard series as primin, part of the standard series of the European Environmental Contact Dermatitis Research Group (EECDRG) but not present in the standard series of the GEIDC. When an ACD to plants was suspected, we supplemented our standard series with specific allergenic series of plants (Table 1) and lichens and wood (Table 2). When no specific allergen was available, we used small samples of the flower and leaf of suspect plants or sawdust in alcoholic, hydro-alcoholic or saline solution, applied as is. Reagents were applied in Finn Chambers[®] on Micropore[®] tape. Readings were made after 2 and 4 days according to International Contact Dermatitis Research Group (ICDRG) criteria.

Table 1. Plants series (Chemotèchnique®)

Allergens	Concentration (%) (petrolatum)
<i>Chamaemelum nobile</i>	0.1
Diallyl disulfide	1.0
<i>Arnica montana</i>	0.5
<i>Taraxacum officinale</i>	2.5
<i>Achillea millefolium</i>	1.0
Propolis	10.0
<i>Chrysanthemum cinerariifolium</i>	1.0
Sesquiterpene lactone mix	0.1
Alpha-methylene-gamma-butyrolactone (Tulipalin A)	0.01
<i>Tanacetum vulgare</i>	1.0
Alantolactone	0.1
Lichen acid mix 0.3% (atranorin 0.1%, evernic acid 0.1%, D-usnic acid 0.1%)	0.3

In those patients with a distribution of cutaneous lesions or history of sun aggravation that suggested photosensitivity, phototest and photopatch tests were performed. The minimal erythema dose (MED) for ultraviolet B (UVB) was determined with an UV-800 unit lamp with fluorescent bulbs (285B350 nm) (Philips TL 20 W/12; Waldmann, Villingen/Schwenningen, Germany). Irradiation output was measured using a UV spectrometer (Waldmann). Photopatch tests were performed in these patients with the plants series (Table 1), and in those cases with possible involvement of other photoallergens, we used the Scandinavian Photopatch series (Table 3), but testing only those substances that were considered possibly to be involved in each case. 2 sets of tests were applied on the back. Afterwards, one set was shielded from light, whereas the other one was irradiated with 10 J/cm² of UVA (PUVA unit lamp Waldmann UV 200 AL). Readings were made at 48 and 96 h.

Results

During the 7 years of the study, 69 patients (51 female and 18 male) of the 2248 studied (3%) had positive patch tests to some plant allergen. Because only 1357 patients tested during this period showed any positive patch test, these 69 individuals represented 5.1% of them. 57 of 69 positive patch tests (82.6%) were clinically

Table 2. Lichens and wood series

Allergens	Concentration (%) (pet.)
Atranorin	0.1
Usnic acid	0.1
Evernic acid	0.1
Wood mix (pine, teak, fir, birch)	20

Table 3. Scandinavian photopatch series (Chemotèchnique®)

Photoallergens	Concentration ^a (%)
Trichlorcarbanilide (ITC)	1
Prometazine (HCL)	1
4-aminobenzoic acid (PABA)	5
Trybromsalicylanide (TBS)	1
Chlorpromazine HCL	0.1
Musk ambrette	1
6-Methylcoumarine	1
Bithionol	1
Fenticlor	1
D-Usnic Acid	0.1
Atranorin	0.1
Wood mix	20
Evernic acid	0.1
Balsam of Peru	25
Tetrachlorsalicylanilide (TCS)	0.1
Hexachlorophene	1
Chlorexidine digluconate	0.5
Triclosan	2
Diphenhydramine (HCL)	1
Fragrance mix	6

^aAll agents in pet., except chlorpromazine.

relevant. Mean ages at diagnosis were 48 and 51 years for female and male, respectively, and 65% were comprised in a range between 30 and 60 years old. In 21 cases (30.4%), an occupationally related exposure was found. The occupations most frequently involved are detailed in Table 4.

Chronic hand eczema (49 patients, 71%) was the most common clinical pattern identified, mainly because of the high frequency of allergy to diallyl disulfide. The simultaneous involvement of exposed areas of hands, forearms and face was found in 10 patients (14.5%), 6 with allergy to SL. Table 5 reflects other clinical patterns found in the positive group, which are individualized in each allergenic group in Table 6.

Table 7 summarizes the allergens associated with ACD to plants in our study. Diallyl disulfide was the most common allergen identified in this series, with 47 confirmed cases in the 276 patients (17%) patch tested with this allergen during this period (68% of all ACD to plants and 2% of all patients studied in this period). Middle-aged women (89%) were predominantly involved,

Table 4. Occupations associated with allergic contact dermatitis (ACD) to plants.

	Number of patients
Non-occupationally exposed	48 (69.6%)
Occupationally exposed	21 (30.4%)
Agricultural workers	33.3%
Cooks, restaurant employees	23.8%
Carpenters, wood industry	19.1%
Florists	14.3%
Building workers	9.5%

Table 5. Clinical patterns in allergic contact dermatitis (ACD) to plants

Clinical patterns	%
Chronic hand eczema	71
Face plus forearms plus hands (exposed areas)	14
Hands plus forearms/arms	6
Face	6
Generalized	1
Feet	1
Feet plus calf/thigh	1

with ages ranging from 18 to 78 years and a mean age of 50 years, mostly non-occupationally exposed (81% of cases, involving predominantly housewives). Cooks and restaurant employees were the occupations most frequently related (5 cases), followed by agricultural workers (4 cases). The most frequent clinical picture was a chronic hand eczema (91%), with a frequent specific involvement of the thumb, index and middle finger of the non-dominant hand (Fig. 1). We found a concomitant allergy to nickel in 40% of these patients.

SL mix was the second most frequent allergenic group involved with 11 cases (16% of all ACD to plants and 0.49% of all patch tested patients). We found a male predominance (8 cases), with ages ranging from 23 to 79 years and a mean age of 49 and 43 years for male and female, respectively. 5 cases were occupationally exposed (3 farmers and 2 building workers in rural areas). We found positive reactions to

Table 6. Clinical patterns in groups with different plant allergies

Group	Sites of dermatitis	Number of cases
DAS	Hands	43
	Others	4
SL plus Compositae ^a	ABCD	7
	Hands	3
	Generalized	1
	Face	1
	Others	1
Lichens	Hands	2
	ABCD	2
	Face	1
	Lower limbs ^b	1
Primin	Upper limbs ^c	2
	Hands	1
	Others	1
Tulipalin A	Hands	3
Wood	Hands	1
	Upper limbs ^c	1
	ABCD	1

DAS, diallyl disulfide.

ABCD, airborne contact dermatitis.

^aThree of these 13 patients were also positive to lichens and 2 to fragrances (see Table 9).

^bFeet plus calf/thigh.

^cHands plus forearms/arms.

Compositae extracts in 8 of the 139 patients (5.8%) patch tested with the plants series (11.6% of all ACD to plants and 0.36% of all patch-tested patients). Most showed multiple sensitizations to different extracts of Compositae (Table 8). In 2 cases, we found positive results to Compositae extracts, although SL mix 0.1% included in the standard series was negative, so the total number of Compositae-sensitive patients raised up to 13. Both cases were associated with concomitant sensitization to other plant allergens: a florist with simultaneous allergy to tulipalin A and *Tanacetum vulgare*, and a carpenter with sensitization to teak, *Taraxacum officinale* and *Arnica montana*. On the other hand, 5 of 11 patients sensitized to SL mix showed no positive reactions to Compositae extracts. Concomitant allergy to lichen acid mix and fragrance mix in Compositae-sensitive patients was found in 3 and 2 patients, respectively (Table 9).

The most frequent clinical pattern in Compositae-sensitive patients was an airborne contact dermatitis (ABCD, 7 cases) involving mainly the face (Fig. 2) and upper extremities. Some patients showed clinical features of chronic actinic dermatitis (Fig. 3). Other clinical pictures, as chronic hand eczema (3 cases), were less common.

Sensitization to lichen allergens was present in 6 of the 154 patients (3.8%) patch tested during this period (allergens from lichens were included not only in the plants series but also in the lichens and wood series). They represented 8.7% of all ACD to plants and 0.27% of all patch-tested patients. There was also a slight male predominance (4 cases). Their ages ranged from 23 to 51 years, with a mean age of 38 years. 4 cases were classified as occupational dermatoses (2 sawmill workers, 1 building worker and 1 carpenter). 2 had been diagnosed with atopic dermatitis. The localizations most frequently involved were hands, face and upper extremities (in an airborne clinical pattern), face, and lower extremities. 3 of these patients were positive to lichen acid mix 0.3% (patients tested with the plants series), and all these cases were associated to allergy to SL mix 0.1%. In 2 of these 3 patients, a simultaneous sensitization to fragrance mix was proved. Positivity to atranorin and evernic acid was present in 2 and 1 patients, respectively (patients tested with the lichens and wood series). In one patient sensitized to evernic acid, a concomitant allergy to balsam of Peru was found. In another patient, with allergy to atranorin, a positivity to wood sawdust of *Fagus sylvatica* and *Erythropheum ivorense* was also proved.

4 patients (5.8% of all ACD to plants and 0.18% of all patch-tested patients) were

Table 7. The frequency of positive plant test reactions

Allergens	Number of positive patch tests	Number of patients tested	% of total plant positives	% of total patients tested
Diallyl disulfide	47	276	68.1	2.09
Sesquiterpene lactone mix	11	2248	15.9	0.49
Compositae extracts	8	139 ^a	11.6	0.36
Lichens	6	154 ^b	8.7	0.27
Primin	4	2248	5.8	0.18
Tulipalin A	3	139 ^a	4.3	0.13
Woods	3	25	4.3	0.13
Wood mix	1			
Sawdust ^c				
<i>Tectona grandis</i> (Teak)	1 ^d	2	1.4	0.04
<i>Apuleia leiocarpa</i> (Grapia)	1	1	1.4	0.04
<i>Fagus sylvatica</i> (European beech)	1	1	1.4	0.04
<i>Erythrophleum ivorense</i> (Tali)	1 ^e	1	1.4	0.04

^aPatients tested with our plants series (Table 1) that contained Compositae extracts and Tulipalin A.

^bPatients tested with our plants series (Table 1), and lichens and wood series (Table 2), because both contained lichen allergens.

^cApplied as is in saline solution.

^dAlso positive to wood mix.

^eAlso positive to European beech.

sensitized to primin. They were all females with ages ranging from 33 and 72 years (mean age 53 years). 3 were housewives, and all cases were considered as non-occupational dermatoses in hobby gardeners. Clinical patterns of lesions in these patients were (i) hand and forearm (2 cases); (ii) hand (1 case) and (iii) hand, forearm, arm and upper trunk (erythema multiforme-like lesions, 1 case).

Tulipalin A allergy was present in 3 of the 139 patients (2.2%) patch tested with the plants series (4.3% of all ACD to plants and 0.13% of all patch-tested patients). They were also all females with ages ranging from 31 and 51 years (mean age 42 years), and all were working in floral

shops at the time of diagnosis. All patients showed chronic eczematous lesions in most of fingertips (Atulip fingers $\equiv$, Fig. 4), and in one case a weak positivity to *T. vulgare* was present.

Sensitization to wood allergens was proved in 3 of the 25 cases (12%) patch tested with the lichens and wood series, representing 4.3% of all ACD to plants and 0.13% of all patch-tested patients during this period. However, as specific extracts of the suspect wood were not available, we used sawdust of the suspect plants in saline solution applied as is under occlusion. All patients were males with ages ranging from 34 and 51 years (mean age 41 years), and all were considered as occupational dermatoses (2 carpenters and 1 sawmill worker). Clinical patterns were hands (1 case), with allergy to extracts of *F. sylvatica* (European beech) and *E. ivorense* (Tali) and concomitant allergy to atranorin; hands, forearms and arms in 1 case, with sensitization to extracts of *Apuleia leiocarpa* (grapia); ABCD pattern (1 case), in a patient sensitized to *Tectona grandis* (teak) who also presented a weak positivity to *A. montana* and *T. officinale*.

5 patients underwent phototesting and photopatch-testing, because the distribution of eczema or history of sun aggravation suggested photosensitivity. 2 had abnormal phototest results, with lower thresholds for UVB wavelengths. Both were males, aged 44 and 79 years, bricklayer and farmer, respectively. In the first case, allergy to SL mix 0.1% and Compositae extracts was found, and in the second case, concomitant sensitization to SL mix 0.1%, extracts of Compositae, lichen acid mix and fragrance mix



Fig. 1. Chronic hand eczema involving fingertips of thumb and index.

Table 8. Distribution of reactions in 13 Compositae-sensitive patients

Patient number	SL mix	<i>Achillea millefolium</i>	<i>Tanacetum vulgare</i>	<i>Chamaemelum nobile</i>	<i>Arnica montana</i>	<i>Taraxacum officinale</i>	<i>Chrysanthemum cinerariifolium</i>
1	pos.	pos.	pos.	—	—	—	—
2	pos.	—	—	—	—	—	—
3	pos.	pos.	pos.	—	—	—	—
4	pos.	pos.	pos.	pos.	pos.	—	pos.
5	—	—	pos.	—	—	—	—
6	pos.	—	—	—	—	—	—
7	pos.	pos.	pos.	pos.	—	—	—
8	pos.	—	—	—	—	—	—
9	pos.	pos.	—	—	—	—	—
10	pos.	—	—	—	—	—	—
11	pos.	pos.	pos.	—	—	—	—
12	—	—	—	—	pos.	pos.	—
13	pos.	—	—	—	—	—	—

pos., positive reaction.

was present. In this patient, photopatch-testing also showed an increased reaction to lichen acid mix in the set that was irradiated with UVA compared with the one that was shielded from the light. No photoaggravation of reaction to Compositae extracts was seen in these patients.

Discussion

The results of this study reflect the geographical distribution of the allergenic species and are also linked to the decorative, culinary or therapeutic uses of them in our area. This point is emphasized by comparing our results with those reported by Cook et al. (1) in a series of 68 Australian patients with positive patch tests to plants, in a 17-year period. The plants producing ACD most frequently in this study were *Grevillea* spp., very uncommon species in our country. On the other hand, diallyl disulfide allergy was reported as a minor cause of ACD, probably due to a less frequent culinary use of garlic than in Spain.

High frequency of allergy to diallyl disulfide in Spain was previously reported by other authors (2). In our case, this allergen was not included in our standard series, as it is not part of the standard series of the GEIDC, so it was only tested when a clinical diagnosis was suspected. Even so, the incidence of positives was very high (2% of all the patients studied in the ACU during this period). As it was expected, most positives were seen in middle-aged housewives, with chronic hand eczema often involving the thumb, index and middle finger of the non-dominant hand.

Sensitization to SL mix 0.1% was found in 0.49% of the patients patch tested during this period. This incidence, lower than the 1.1% reported in last multicentric European studies of the EECDRG (3), is higher than the 0.28% reported by the GEIDC in previous statistics

Table 9. Concomitant lichen and fragrance allergies in plant sensitive patients

Group	Number of patients	Other sensitizations
SL mix + , Compositae extracts +	6	Lichens (LAM): 2 cases Fragrance mix: 1 case
SL mix + , Compositae extracts -	5	Lichens (LAM): 1 case Fragrance mix: 1 case
SL mix - , Compositae extracts +	2	Teak: 1 case Tulipalin A: 1 case
Lichens	6	SL mix and/or Compositae: 3 cases Tali and European beech: 1 case Fragrance mix: 2 cases ^a

^aBoth were positive for SL mix and 1 for Compositae.

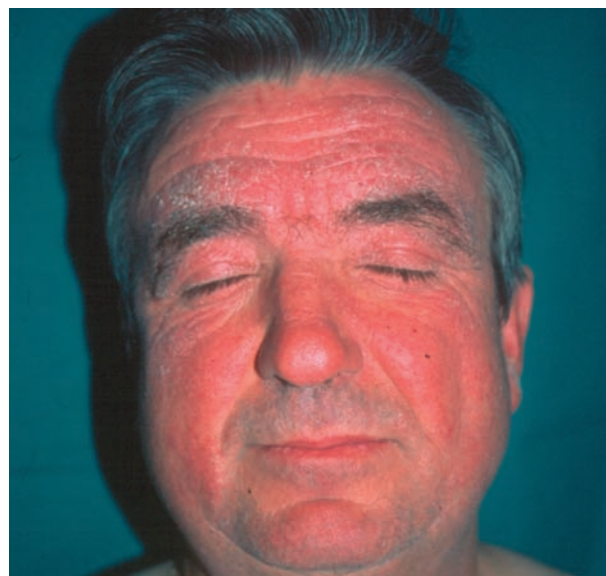


Fig. 2. Erythema and scaly lesions in face in a patient with allergy to Compositae. Note the involvement of upper eyelids.



Fig. 3. Lichenification and cutaneous thickening in photo-exposed areas in a patient with chronic actinic dermatitis.

(4), probably because of the high rate of rural population of our area, occupationally more exposed to allergenic species of Compositae. In a previous multicentre study of the EECDRG (5), the involvement of face/neck and hands/fingers and/or forearms/arms was the most frequent clinical pattern in patients with positive reactions to SL mix. Our study shows the predominance of the classical airborne clinical pattern in



Fig. 4. Chronic eczematous lesions involving fingertips of both hands (tulip fingertips).

Compositae-sensitive patients, instead of the chronic hand eczema that was the most frequent clinical presentation in other reports (6, 7), mainly in female hobby gardeners. The concomitant allergy to lichens and/or fragrances in some of the Compositae-sensitive patients in our series could also explain the high proportion of the airborne clinical pattern. The male predominance also contrasts with the equal sex distribution or female predominance reported by other authors (5, 7–11).

Because Compositae extracts were not included in the standard series, our study does not allow us to compare the sensitivity of SL mix 0.1% and Compositae mix. However, we found 2 patients with reactions to Compositae extracts, although SL mix 0.1% failed to detect the sensitization. In both cases, a current relevance could be established. On the other hand, 5 cases of reactions to SL mix 0.1% showed negative results to Compositae extracts in our plants series. Nevertheless, in 3 of these cases, the relevance of the reactions to SL mix 0.1% was doubtful. These results emphasize, in our opinion, the importance of adding Compositae extracts to the standard series or at least supplement SL mix 0.1% with a series of Compositae extracts in aimed patch testing to improve the detection of Compositae allergy, as it was remarked in other studies (8–11). Although it has been proved that Compositae mix is significantly more sensitive than SL mix, the higher risk of irritancy and active sensitization of Compositae mix versus SL mix speaks against the possibility of adding it to the European standard series (11); so, aimed patch testing using Compositae extracts at a phyto-regional level can be the most appropriate option, as locally grown Compositae may vary across different geographical areas.

Relationship between chronic actinic dermatitis (CAD) and Compositae sensitivity has been studied in previous reports (7, 12–15). The incidence of allergy to Compositae in patients with CAD has been estimated in 85% by Frain-Bell et al. (12), using unpurified plant extracts (that may result in false-positive results). 2 series of 80 and 44 patients with CAD from St John's Institute of Dermatology who were patch tested with SL mix, found, respectively, an incidence of 36% (14) and 25% (15) of positive results. Nevertheless, another series of 9 North American patients diagnosed of CAD (16) showed no clear significant association (only 1 case of positivity to *T. vulgare*), so the significance of this relationship remains unknown.

On the other hand, CAD appears like an associated condition in 22% (7) and 17% (15)

of SL-sensitized patients in previous reports, a proportion similar to our series (2 cases in the 11 positives to SL mix, 18%). The mechanism for photosensitivity in patients allergic to Compositae is unknown. It has been suggested that chronic contact dermatitis from Compositae allergens could stimulate the skin's immune system by promoting recognition of endogenous neoantigens induced within the skin by irradiation alone (17). The presence of sensitizations to other allergens, like lichens or fragrances, in patients with clinical features of photodermatitis, has also been previously reported (18, 19), and they could also play a role in the development of CAD. The presence of phototoxic polyacetylenes in Compositae plants has also been used to explain the unclear connection between abnormal reactions to UV light and Compositae allergy (20).

Because of the localization and seasonal occurrence of ABCD, its clinical picture may be wrongly confused with CAD. Clinical features that allow the differentiation between these 2 entities are the involvement of the upper eyelids, retroauricular areas (Wilkinson's triangle) or V of the neck that is present in ABCD and usually spared in photodermatitis. However, the differential diagnosis can be often difficult, so patients with allergy to Compositae and a clinical pattern of ABCD or partial involvement of exposed areas, and a personal history of photosensitivity, should undergo photobiological tests. And, on the other hand, sensitization to Compositae and other allergens (lichens, fragrances, rubber chemicals) should be tested in all patients with clinical features of CAD (14).

Sensitization to lichen allergens appears in our series like occupational dermatoses in wood industry workers, building workers of rural areas and carpenters, sometimes producing chronic eczematous lesions in hands, sometimes resulting in an airborne contact dermatitis. As reported in literature (21–24), multiple concomitant sensitization in these patients (particularly with *Frullania* and Compositae) is very common: three of our patients sensitized to lichen acid mix had also positive patch tests to SL mix 0.1%, and 2 to fragrance mix, probably as a cross reaction due to the presence of lichen allergenic components such as usnic acid, evernic acid and atranorin in male fragrances. Interestingly, both patients had a clinical pattern of ABCD that seems to be the result of an airborne exposure to common environmental allergens that are present in rural areas, in addition to an increased individual susceptibility. The photoaggravation of lichen-induced reaction that was seen in one

of our patients has been also previously reported (25, 26).

Although primin is not part of the standard series of the GEIDC, we included it in our standard series expecting that the wet weather conditions of our geographical area, which promotes the growth of *Primula obconica*, would result in a higher incidence of primin allergy. However, the 0.18% of all patients tested during 8 years is still far from the 0.7% reported in last European multicentre study (3). Eczematous lesions were the most frequent morphologic pattern, followed by erythema-multiforme like lesions that have been already described in the literature (27). No cases were seen in florists. Interestingly, in contrast to primin, the three cases of tulipalin A allergy were detected in florist women, with chronic hand eczema involving mainly fingertips, who referred worsening of cutaneous lesions after contact with *Alstroemeria* spp., that have been reported to be, in addition to Compositae, the most important allergenic species in the pathogenesis of occupational ACD in floral shop workers (28, 29).

ACD to wood allergens, according to literature, is an infrequent occupational dermatosis reported mainly in carpenters or wood industry workers, caused usually by contact with wood from tropical species used in building construction or furniture. Species involved in our 3 cases were *A. leiocarpa* (grapia); *T. grandis* (teak); *F. sylvatica* (European beech) and *E. ivorense* (Tali) in the last one. ACD to grapia has been occasionally previously reported (30), and teak seems to be an important allergen in occupational allergic dermatitis caused by wood dusts (31). In our teak-sensitized patient, simultaneous allergy to *T. officinale* and *A. montana* could also contribute to the ABCD clinical pattern he presented (this patient came from a rural area and worked as a carpenter but also in brickworks).

In conclusion, our review has shown a high incidence of ACD to diallyl disulfide that should be tested in all housewives or cooks with chronic hand eczema. Allergy to Compositae showed a predominance of the classical clinical pattern of airborne contact dermatitis, probably because the airborne allergen exposure still remains the most frequent way of sensitization to Compositae species in a mostly rural population like ours, instead of the direct plant exposure in hobby gardening that usually results in chronic hand eczema, maybe the most important way of sensitization in urban areas. Because testing with the SL mix does not detect all Compositae allergic patients, probably supplementary routine testing with extracts of Compositae would result in

higher incidence rates of allergy to this plant family.

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