

Occupational dermatitis in Danish gardeners and greenhouse workers (III)

Compositae-related symptoms

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The clinical part of the study aimed at describing epidemiological and diagnostic aspects of occupational Compositae dermatitis. Patch testing with the sesquiterpene lactone (SL) and Compositae mixes, feverfew extract and supplementary allergens in 250 selected gardeners showed Compositae allergy in 25, 17 females and 8 males. 24 were possibly occupationally sensitized. The mean age was lower and the preponderance of women higher compared to classical Compositae dermatitis, and the distribution and course of the dermatitis most often did not differ from other occupational plant dermatoses. The Compositae mix detected 2× as many as the SL mix, and the overall detection rate with both was 76%, making aimed patch testing necessary. Chrysanthemum (*Dendranthema*), marguerite daisy (*Argyranthemum frutescens*) and lettuce (*Lactuca sativa*) were frequent sensitizers. Occupational type I allergy to Compositae comprised sensitization to *Gerbera*, chrysanthemum, lettuce, *Senecio cruentus* and *Aster*. Among 1657 respondents in the questionnaire part of the study, 824 had worked with Compositae, and 160 (19%) reported occupational Compositae-related symptoms of skin and mucous membranes. Possible risk factors for the development of these were assessed in a stepwise logistic regression model and a history of childhood eczema, hay fever and duration of exposure were significantly associated with Compositae-related irritant and allergic symptoms in both sexes.

Key words: plants; Compositae; contact dermatitis; sesquiterpene lactones; gardener; type I allergy; occupational; Compositae dermatitis. © Munksgaard, 1998.

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In the clinical part of a questionnaire-based study of occupational dermatitis in Danish floristry, we found a prevalence of Compositae sensitization of 10% among 250 patch tested gardeners and greenhouse workers (1, 2). Based on these patients, some epidemiological and diagnostic aspects of occupational Compositae dermatitis, as well as possible risk factors for the development of occupational Compositae-related symptoms in general, are presented.

Patients, Materials and Methods

The study design and details of patch test procedures have been presented previously (1, 2). Short ether extracts of chrysanthemum (*Dendranthema*) 3% pet., marguerite daisy (*Argyranthemum frutescens*) 3% pet., iceberg lettuce (*Lactuca sativa* var. *capitata*) 10% pet. and the sesquiterpene lactone co-

stunolide 0.1% pet. were prepared at our hospital pharmacy. The chrysanthemum extract tested negative in 29 consecutive eczema patients and positive in 1, probably reflecting a true Compositae allergy, and the marguerite daisy extract tested negative in 15 consecutive controls. Due to shortage of test material, the iceberg lettuce extract and the costunolide were not tested in controls. Compositae oleoresins from Hollister-Stier were tested under occlusion regardless of the vehicle.

Prick tests were performed with 10 common inhalant allergens and *Pityrosporum ovale*, commercial pollen extracts and plant parts as in selected patients. By scratch patch testing, water or a saline solution was applied to the plants.

Backward stepwise logistic regression was used to assess possible association between occupational Compositae-related symptoms and selected risk factors.

Results

824 persons, or approximately $\frac{1}{2}$ of the 1657 respondents in the questionnaire study, had worked with Compositae (1) and 160 (19%) reported occupational Compositae-related symptoms. 93 of these were examined, being included in the 253 attendants in the clinical part of the study (1, 2), and 92 were patch tested. 25 were sensitized to Compositae (2), 18 occupationally, 4 possibly occupationally and 3 nonoccupationally (Table 1). Only 1 of the nonoccupationally sensitized had not worked with Compositae. The Compositae-sensitive comprised 17 females (68%) and 8 males (32%) with a mean age of 34.6 and 38.0 years, respectively. In the group of occupationally sensitized the sex distribution was 11 females (61%) and 7 males (39%). The results of patch testing with the sesquiterpene lactone (SL) and Compositae mixes and other Compositae extracts and allergens appear in Table 2, 3. 2 women with weak positive reactions to the Compositae mix were excluded because the reactions were considered false-positive. On the

other hand, 3 persons with negative reactions were suspected of being sensitized: the 1st had several doubtful reactions probably because of low dose systemic corticosteroid, the 2nd was diagnosed as having lettuce allergy prior to the study and the 3rd claimed to have had a positive patch test reaction to a Compositae plant which was not included in the Compositae patch test battery. In addition, at least 10 persons who reported occupational Compositae-related skin symptoms in the questionnaire study were not examined further.

7 of the 25 Compositae-sensitized only had 1 positive Compositae reaction: 3 tested positive to the sensitizing (or closely related) species and the remaining 4 comprised the group of possibly occupationally sensitized persons. None of these reported Compositae dermatitis, but they all had symptoms of skin or mucous membranes suggestive of type I allergy or short-lived irritation from *Gerbera* or marguerite daisies and they were positive to either the SL or Compositae mix.

Irritant contact dermatitis from Compositae, especially chrysanthemum and marguerite daisy, was

Table 1. Source of sensitization, prevalence of occupational dermatitis and relevance of allergy in 25 Compositae-sensitive gardeners and greenhouse workers

	No. patients	Occupational Compositae dermatitis	Relevance of Compositae allergy	
			current/old	don't know
occupationally sensitized	18	18	18	
possibly occup. sensitized	4	0		4
non-occupationally sensitized	3	2	3	
	25	20	21	4

Table 2. Results of patch tests with the SL and Compositae mixes and individual ingredients of both mixes in 25^{a)} Compositae-allergic gardeners and greenhouse workers

Allergen/ ether extract	No. gardeners and greenhouse workers		
	tested to	positive to	% positive
SL mix 0.1% pet.	25	8	32%
Compositae mix 6.0% pet.	25	16	64%
SL and Compositae mix	25	5	20%
SL or Compositae mix	25	19	76%
alantolactone 0.1% pet.	8	1	
alantolactone 0.033% pet.	2	0	
costunolide 0.1% pet.	8	1	
costunolide 0.033% pet.	2	0	
dehydrocostus lactone 0.033% pet.	10	4	
chamomile 2.5% pet. (<i>Chamomilla recutita</i>)	19	11	58%
tansy 1.0% pet. (<i>Tanacetum vulgare</i>)	18	10	56%
feverfew 1.0% pet. (D) (<i>Tanacetum parthenium</i>)	10	7	70%
feverfew 1.0% pet. (DK) (<i>Tanacetum parthenium</i>)	25	11	44%
feverfew (D) or (DK)	25	13	52%
milfoil 1.0% pet. (<i>Achillea millefolium</i>)	19	7	37%
arnica 0.5% pet. (<i>Arnica montana</i>)	19	0	0%

D: feverfew grown in Germany.

DK: feverfew grown in Denmark.

^{a)} Including 3 non-occupationally sensitized, 1 of whom had not worked with Compositae.

Table 3. Selected results of patch tests with supplementary allergens, ether extracts and fresh plants from the Compositae family in 25^{a)} Compositae-sensitive gardeners and greenhouse workers

Allergen/ether extract/plant	No. patients tested	No. positive reactions
marguerite daisy 3.0% pet. (<i>Argyranthemum frutescens</i>)	17	11
marguerite 1.0% pet. (<i>Leucanthemum vulgare</i>)	2	0
chrysanthemum (D) 3.0% pet. (<i>Dendranthema</i>)	16	13
chrysanthemum (DK) 3.0% pet. (<i>Dendranthema</i>)	7	6
lettuce oleoresin 1:10 w:v alc. (<i>Lactuca sativa</i>)	8	5
iceberg lettuce 10% pet. (<i>Lactuca sativa</i> var. <i>capitata</i>)	6	1
lactucopicrin 1.0% pet.	7	0
chicory oleoresin 1:10 w:v alc.	1	1
lettuce as is	1	0
<i>Aster</i> oleoresin in pet.	3	0
<i>Gerbera</i> cultivar as is	2	0

D: plants grown in Germany.

DK: plants grown in Denmark.

^{a)} Including 3 non-occupationally sensitized, 1 of whom had not worked with Compositae.

Table 4. Test results in 12 gardeners and greenhouse workers with suspected contact allergy to lettuce

Patient no.	Patch test lettuce/other Compositae	S-P	SPT	Diagnosis (lettuce)
1	pos/neg	NT	NT	occup ACD + muc mem
2	pos/pos	neg	NT	occup ACD
3	pos/pos	neg ^{a)}	NT	occup ACD
4	pos chicory/neg	NT	NT	occup ACD
5	doubtful pos/pos	NT	NT	occup ACD
6	doubtful pos ^{a)} /neg	pos ^{a)}	NT	occup ACD
7	neg/pos	NT	NT	occup ACD
8	neg/neg	neg	NT	occup ICD
9	neg/neg	NT	NT	occup ICD
10	neg/neg	NT	pos	occup ICD + muc mem
11	pos/pos	NT	NT	non-occup ACD
12	pos/pos	NT	NT	non-occup ACD

S-P: scratch patch test with lettuce.

SPT: skin prick test with lettuce.

NT: not tested.

occup: occupational.

ACD: allergic contact dermatitis.

ICD: irritant contact dermatitis.

muc mem: symptoms of mucous membranes.

^{a)} In a previous test.

suspected in several persons. On the other hand, a diagnosis of occupational allergic contact dermatitis from lettuce was made in 4 persons with negative patch tests to this species in the present study

(Table 4, patient nos. 4–7). They all reported lettuce-related eczema and 3 had positive reactions to other Compositae species. Patient no. 10 developed a hand eczema of palms and finger webs and rhinitis when exposed to lettuce and the positive prick test may in fact suggest an allergic contact dermatitis rather than an irritant. The suspected primary sensitizers in the 18 patients with occupational Compositae dermatitis were marguerite daisy (8 persons), chrysanthemum (7 persons) and lettuce (6 persons).

The results of standard and supplementary patch tests are shown in Table 5: 10 of the 25 Compositae-allergic persons had no other contact allergy, 7 persons had 1 and 8 persons had 2 or more.

Prick and/or scratch patch tests with Compositae, including mugwort pollen in the 10 common inhalant allergens, were performed in 82 gardeners and greenhouse workers and 16 tested positive (Table 6). All of them had been occupationally exposed to Compositae and 13 reported symptoms. Only 1 of the 5 persons with positive prick tests to *Dahlia* had been occupationally exposed to this species and he did not report symptoms. Occupational type I allergy to Compositae was suspected in more patients than those tested, and even in the latter only 2 persons were tested further: they both had positive histamine release tests to *Gerbera*, suggesting true IgE-mediated allergy. The occupational eczema in patient no. 13 may have been allergic rather than irritant, due to repeated contact urticaria.

The clinical features of Compositae dermatitis in the 18 patients who were occupationally sensitized appear in Table 7. Most of the eczemas were localized to hands and forearms and only 1 had isolated facial dermatitis. Widespread eczemas were uncommon. Vesicular hand eczema was seen in 3 persons and suspected in 2. Besides, a woman had a palmar hand eczema that was strictly occu-

Table 5. Results of standard patch tests, pesticide patch tests and patch tests with plants as is other than Compositae in 25^{a)} Compositae-allergic gardeners and greenhouse workers

Allergens	No. positive reactions
nickel sulfate	7
thimerosal	5
captan	3
potassium dichromate, carba mix, thiuram mix, maneb	2 each
cobalt chloride, epoxy resin, fragrance mix, <i>p-tert</i> -butylphenol-formaldehyde resin, 2 plants as is	1 each

^{a)} Including 3 non-occupationally sensitized, 1 of whom had not worked with Compositae.

Table 6. Positive skin prick and/or scratch patch tests to Compositae in 82 gardeners and greenhouse workers

Patient no.	Positive to		Occupational symptoms from Compositae
	Compositae	other common inhalant allergens	
13	<i>Gerbera</i>	cat dander, grass pollen	CU, muc mem, ICD (<i>Gerbera</i>)
14	<i>Gerbera</i>	none	CU, muc mem (<i>Gerbera</i>)
15	mugwort, <i>Dahlia</i>	birch, grass pollen, dog, cat dander, house dust mites	none (marguerite daisies)
16	mugwort, chamomile	grass pollen	IR/CU, sneezing (marguerite daisies)
17	mugwort, chamomile	birch pollen	ICD (chrysanthemum, marguerite daisies)
18	mugwort	birch, grass pollen, dog, cat dander, house dust mites	don't know (<i>Tagetes</i>)
19	<i>Senecio</i> , mugwort, <i>Dahlia</i> , chamomile	birch, grass pollen	dermatitis, muc mem (<i>Senecio cruentus</i>)
20	chrysanthemum pollen	NT	muc mem (chrysanthemum)
21	lettuce	NT	CU (lettuce)
22	<i>Gerbera</i> pollen	NT	CU (<i>Gerbera</i> pollen)
23	<i>Aster</i>	none	CU (<i>Aster</i>)
24	mugwort	birch, grass pollen, house dust mite	IR/dermatitis (marguerite daisies)
25	<i>Aster</i> , <i>Dahlia</i> , chamomile	NT	CU (<i>Aster</i>)
3 ^{a)}	mugwort, <i>Dahlia</i> , chamomile	dog, cat dander	ACD (lettuce, marguerite daisy etc.)
26	mugwort	grass pollen	none (chrysanthemum, marguerite daisies)
10 ^{a)}	lettuce, mugwort, <i>Dahlia</i> , chamomile	birch, grass pollen, cat dander	ICD, muc mem (lettuce)

NT: not tested.

CU: contact urticaria.

muc mem: symptoms of mucous membranes.

ICD: irritant contact dermatitis.

ACD: allergic contact dermatitis.

IR/CU: short-lived irritation or contact urticaria.

IR/dermatitis: irritation or dermatitis.

^{a)} Patient nos. 3 and 10 from Table 3.

pational. Likewise, the majority of the 18 persons had strictly occupational eczemas without summer exacerbation.

The possible association between occupational Compositae-related symptoms and selected risk factors was assessed in a stepwise logistic regression model based on the questionnaires (Table 8). The parameter "sex" was retained in all reductions, to avoid missing any association between this allegedly important variable and Compositae dermatitis. A history of childhood eczema, hay-fever and the duration of time working with Compositae were significantly and positively associated with the occurrence of occupational Compositae-related symptoms in both sexes. On

the other hand, the prevalence of Compositae-related symptoms was inversely correlated with age in males only. Sex was not an independent risk factors. The 16 rejected risk factors were also jointly insignificant. The assumption of homogeneity was tested in an equivalent probit regression and could not be rejected, χ^2 with 5 degrees of freedom being 6.48.

Discussion

The frequency of positive Compositae patch test reactions is more than 2× as high as that seen in selected consecutive eczema patients (3), making the Compositae the most sensitizing plant family in this study. As previously pointed out, we attached importance to occupational symptoms caused by Compositae (1), and both the selection of gardeners and the screening for Compositae allergy with 2 mixes and a plant extract contribute to the high frequency. However, based on case records of those with negative patch tests and questionnaires of non-attendants, it seems that this is a minimum figure for prevalence, and this is also in accordance with the results of Hausen & Oestmann (4), who reported a minimum prevalence of 3.6% (24:675) compared to 1.2% (24:1958)

Table 7. Distribution of occupational Compositae dermatitis in 18 gardeners and greenhouse workers

Site of dermatitis	No. patients
face-neck+hands-arms	7
hands-arms	6
face-neck	1
face-neck+hands-arms+feet-legs	1
face-neck+hands-arms+trunc	1
face-neck+hands-arms+feet-legs+trunc	1
hands-arms+feet-legs	1

Table 8. Association between occupational Compositae-related symptoms and sex, age, personal or family history of atopy, training, seniority and duration of time working with Compositae in 808^{a)} persons

Selected multiple logistic regression equation			
	OR	CI	p-value
<i>Risk factor</i>			
S*age	0.720	0.55–0.94	0.0128
childhood eczema	1.657	1.01–2.71	0.0409
hay fever	1.902	1.11–3.27	0.0179
duration Compositae work	1.614	1.05–2.48	0.0253
sex ^{b)}	1.168	0.46–2.99	0.7421
<i>Rejected risk factors</i>			
age (years)			0.7386
S*skilled gardener			0.7516
S*personal atopy-hay fever			0.7175
family atopy-eczema			0.6194
personal atopy-asthma			0.5934
S*family atopy-eczema			0.5697
family atopy-hay fever			0.5229
seniority			0.4272
S*duration Compositae work			0.4508
family atopy-asthma			0.3593
S*seniority			0.3383
S*family atopy-hay fever			0.2968
skilled gardener			0.1009
S*personal atopy-asthma			0.0952
S*family atopy-asthma			0.1037
S*personal atopy-childhood eczema			0.0763

OR: "odds ratio" = exp.logistic coefficient.

CI: 95% confidence interval.

S*: interaction between sex and the variable in question.

The *p*-values for the rejected risk factors are the values at the point of rejection, listed in order of rejection.

^{a)} 16 persons were withdrawn because of information lacking in the questionnaires.

^{b)} Males were coded 1, females 0.

in our study. Likewise, Schubert (5) found that 34 of 201 (17%) of exposed gardeners were sensitized to chrysanthemum, which corresponds to a sensitization rate of 24 of 159 (15%) exposed in the examined group in the present study. The mean age of the Compositae-allergic is considerably lower than that of patients with classical Compositae dermatitis and this emphasizes the risk of close plant contact even in young persons. Likewise, the sex distribution differs from what is seen in consecutive Compositae-sensitive patients in our department, where more than 75% are women (3), indicating, as pointed out by Mitchell (6), that the sex ratio depends on frequency of exposure.

The Compositae mix detected 2× as many of the sensitized as the SL mix, but it seemed, on the other hand, to be more irritant, causing 2 false-positive reactions. It could be of importance that sensitization to alantolactone- and isoalantolactone-containing garden plants such as elecampane (*Inula helenium*) and *Telekia speciosa*, that would have elicited positive reactions to the SL mix, was

uncommon in these patients. The relatively frequent positive patch tests to dehydrocostus lactone of the SL and chamomile, tansy and feverfew of the Compositae mix are probably cross-reactions, and the 3 last-mentioned extracts seem to be important markers of Compositae allergy (if not primary sensitizers like feverfew) in both occupationally and non-occupationally exposed (3). Altogether, the results with relatively few persons who were positive to both mixes, a large minority who were negative to both and 7 persons with only 1 positive Compositae patch test point in the same direction: the young gardeners and greenhouse workers have been exposed to relatively few species, contrary to the multitude of cultivars that amateur gardeners are often exposed to in their herbaceous borders, and the sensitization of the former is proportionately limited. The overall detection rate with the 2 mixes was only 76% (Table 2), and this emphasizes the limitations of the mixes and the importance of aimed patch testing in persons with specific exposures.

10 of the 11 positive reactions to marguerite daisy were of current relevance, indicating an allergic potential and not just cross-reactions to other Compositae species. Marguerite daisy has not been described as sensitizing before, but it seems to be an important cause of Compositae dermatitis in both occupationally and non-occupationally exposed in Denmark (3). Likewise, the results confirm the position of chrysanthemum as a major sensitizer in Compositae dermatitis in Europe (4, 5, 7). Testing with oleoresins under occlusion implies a risk of false-positive reactions, but the reactions to lettuce and chicory were most often relevant and therefore considered truly allergic. However, several patients with negative patch tests were suspected of contact allergy to lettuce: some may have had an irritant contact dermatitis, but another possibility is that the patients, many of whom had a personal or family history of atopy, actually had a type I allergy to lettuce, eventually causing dermatitis. Protein contact dermatitis to lettuce sap with positive prick test, histamine release test and RAST, but negative patch test, has been reported by Alonso et al. (8), and cases of sensitization may have been missed in this study because prick and scratch patch tests were not performed routinely.

Compared to consecutive Compositae-allergic patients (9), the gardeners were less often sensitized to fragrance and colophony and more often to thimerosal. This could be due to a narrow range of sensitization in gardeners, making cross-reactions to more remotely related allergens in perfume and colophony less likely, and in the case of thimerosal the lower mean age in gardeners may offer

an explanation, since thimerosal allergy is more common in younger persons (10). The high prevalence of other contact allergies in Compositae-sensitive gardeners and the large minority with no other contact allergies may reflect the impact of strongly allergenic sesquiterpene lactones on particularly predisposed and particularly exposed persons, respectively.

Occupational chrysanthemum pollinosis has been described before (5, 11), whereas occupational type I allergy to *Gerbera* and *Aster* has rarely or ever been reported (12). The frequency of type I allergy to Compositae is a minimum figure for prevalence, since relatively few persons were properly tested with prick or scratch patch and even fewer with laboratory tests. Cross-reaction between chrysanthemum and mugwort pollen has been reported (5), but was not common in this study since only 3 of 9 persons with positive prick tests to mugwort had worked with chrysanthemum.

The localization and course of occupational Compositae dermatitis in most of the gardeners and greenhouse workers do not differ from that of plant dermatitis in general (13). The dermatitis disappears when the exposure is discontinued and most of the patients do not have summer flares. Likewise, vesicular hand eczema, which is so common among consecutive Compositae-sensitive patients (3, 14), was much more rarely seen in this study. However, the association between vesicular, palmar hand eczema and Compositae sensitization has not been established as causal; it may merely reflect a greater risk of sensitization to multiple contact allergens, including sesquiterpene lactones, in patients with chronic hand eczema, facilitated by the skin disease and/or enhanced individual susceptibility. Alternatively, the different clinical patterns may be a consequence of different degrees of sensitization, making the highly sensitized persons more apt to develop a widespread dermatitis with vesicular, palmar hand eczema.

Occupational Compositae-related symptoms include, among others, eczema, itching of the skin, short-lived skin irritation, contact urticaria and symptoms of mucous membranes. The results thus cannot be applied to Compositae dermatitis alone. The association between personal atopy and the response variable probably reflects a mixture of symptoms from skin and mucous membranes, including type I allergy. A possible misclassification could arise from Compositae-related rhinitis being registered as hay fever by the respondents. Sex was not an independent risk factor and, since eczema was the most frequent Compositae-related symptom, this supports the notion that differences in sex distribution in Compositae dermatitis are a

matter of frequency of exposure. The inverse correlation between age and Compositae-related symptoms in males may represent a selection through a "healthy worker effect"; on the other hand, self-employed gardeners, who were generally middle-aged males (1), had worked with Compositae longer than employees, but they may have been much less exposed than greenhouse workers thus accounting for a low prevalence of sensitization and irritation.

In conclusion, the Compositae are the most frequent cause of occupational allergic plant dermatitis in Danish gardeners and greenhouse workers, and important sensitizers are chrysanthemums, marguerite daisies and lettuce. In most occupationally sensitized persons, the clinical pattern and course is no different from that of other occupational plant dermatoses. Likewise, the sex distribution seems to reflect frequency of exposure rather than any inherently greater risk for either sex. Work-related contact with Compositae may cause a variety of allergic and irritant symptoms of both skin and mucous membranes, and the duration of exposure, as well as a history of childhood eczema or hay fever, seem to be significant risk factors for the development of Compositae-related symptoms.

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