

Contact allergy to the Asteraceae plant *Ambrosia artemisiifolia* L. (ragweed) in sesquiterpene lactone-sensitive patients in southern Sweden

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Ambrosia artemisiifolia L. a classical cause of ragweed dermatitis in North America, is also found in Europe. 17 patients with contact allergy to sesquiterpene lactone (SL) mix were recalled for patch testing with extracts of North American and Swedish ragweed, the latter harvested in summer and autumn. 8/17 patients were test-positive to the American extract, 14/17 to the Swedish summer extract and 15/17 to the autumn extract. All patients except 1 were found to have a chronic hand eczema of the pompholyx type. 5/16 hand eczema patients had a flare-up of their pompholyx at patch testing. We concluded that patients with SL mix allergy are allergic to American as well as to Swedish ragweed. Pompholyx seems to be a frequent clinical picture in patients with SL mix allergy.

Key words: *Ambrosia artemisiifolia* L.; Asteraceae; Compositae; flare-up, hand eczema; patch test; pompholyx; ragweed; sesquiterpene lactone. © Blackwell Munksgaard, 2002. © Blackwell Munksgaard, 2002.

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In North America, it is well known that *Ambrosia artemisiifolia* L. (ragweed, Fig. 1) is a species causing Type I allergic rhinitis and asthma (1). The high-molecular, water-soluble allergens are borne and spread by pollen. The plant proper, however, also produces an oleoresin containing low-molecular contact allergens of sesquiterpene lactone (SL) structure (2). Consequently, a Type IV allergic contact dermatitis has repeatedly been described, particularly in male farmers, involving the face, neck and arms (3). Occasionally, both types of immunological states can occur in one and the same individual (4, 5), but usually there is no such correlation.

When *Ambrosia artemisiifolia* L. first reached Europe as a ballast weed, it was for a long period of time restricted to the European ocean ports (6). For several decades the plant has been spreading in central and southern Europe. It is now dispersed from 2 main nuclear areas, a small one in the Rhone valley near Lyon, and a larger one in Hungary. From there, it is rapidly spreading, e.g. to northern Europe, by way of the intercontinental trade in cereals (6).

Because of recent frequent findings of *Ambrosia artemisiifolia* L. in southern Sweden, there is growing concern about an increase in allergic diseases due to this plant, primarily of the hay fever type, but also with regard to allergic contact dermatitis. In the present paper, we have looked for contact allergy to American as well as Swedish ragweed in patients with contact allergy to SL.

Materials and Methods

Patients

Patients, previously patch tested in the Malmö Department with the European standard series and found to be positive to SL mix, were recalled for testing with extracts of *Ambrosia artemisiifolia* L. (ragweed). Only patients from Malmö city proper were approached; otherwise there was no selection. 17 patients accepted, 12 females and 5 males, 34–76 years of age (mean 57.5 years). With 1 exception, all patients had been patch tested because of long-standing eczema and suspected contact allergy. 1 patient had attended for a melanoma check and been sent for patch testing because of an ec-



Fig. 1. *Ambrosia artemisiifolia* L. (ragweed).

zematous reaction on the foot caused by adhesive tape. There were no subjects with occupational contact with SL-containing plants, such as farmers, gardeners or florists. Atopy, defined as an atopic disease in self or first-degree relatives, occurred in 5 of the patients. All patients had been found to be patch test positive to other contact allergens besides SL mix. The reaction pattern was, however, similar to that in other patch-tested patients in our clinic.

Preparations of extracts

A 1.0% w/w petrolatum (pet.) preparation of an acetone extract of American ragweed was obtained from Dr Jere D. Guin, Little Rock, AR, USA. One Swedish plant was harvested in the summer and kept in a freezer, another in the autumn. The plant was identified by one of the authors (ÅS) who is an experienced field botanist. Pieces of the frozen and fresh plant, respectively, were put in glass beakers and diethyl ether was added just to cover the pieces. 30 s later the solvent was poured into a weighed round bottle. The diethyl ether procedure

was repeated 2 ×. In order to avoid contamination of peroxides ethanol-stabilized diethyl ether in a freshly broken bottle was used. The solvent was evaporated in a rotary evaporator and acetone was added to the residue giving a 10% w/v stock solution.

Patch testing

Patients were tested with SL mix 0.1% pet., the American extract 1.0% pet., and Swedish extracts (summer and autumn) in 10-fold serial dilutions 1.0–0.0001% acetone. The SL mix, obtained from Chemotechnique Diagnostics, Tygelsjö, Sweden, contained alantolactone, dehydrocostus lactone and costunolide. The test materials were applied on the back with Finn Chambers (Epitest OY, Tuusula, Finland) on Scanpor tape (Norgesplaster A/S, Vennesla, Norway) and removed after 48 h. Test reading was performed on day (D)3 and D7 according to ICDRG recommendations (7). As controls, 5 other patients, without SL sensitivity and referred for patch testing, were tested with the 2 Swedish allergen extracts, all at 1.0%.

Results

Clinical findings

It was found that all 17 patients except 1 (see above) had hand eczema, with a mean duration of 13 years (range 3–30 years). Furthermore, in all cases the hand eczema was of the pompholyx type (vesicular palmar eczema). 2 patients had additional eczema of the dorsal aspects of the hands.

Out of the 16 patients with hand eczema, 5 experienced a flare-up reaction, including increased itch and appearance of new vesicles of their pompholyx, during the patch test procedure.

Laboratory findings

Renewed patch testing with SL mix was positive in all cases (Fig. 2). A positive test to the American ragweed preparation was obtained in 8/17 patients, in 14/17 patients to the Swedish summer extract, and in 15/17 patients to the Swedish autumn extract. In addition, as can be seen in Table 1, positive reactions were observed to serial dilutions in 7/17 patients.

The ragweed patch tests were negative in all 5 controls. The difference against the results with the Swedish extracts as above (14/17 and 15/17 positive tests) was significant ($P < 0.01$) using the Fisher's exact test, two-sided.

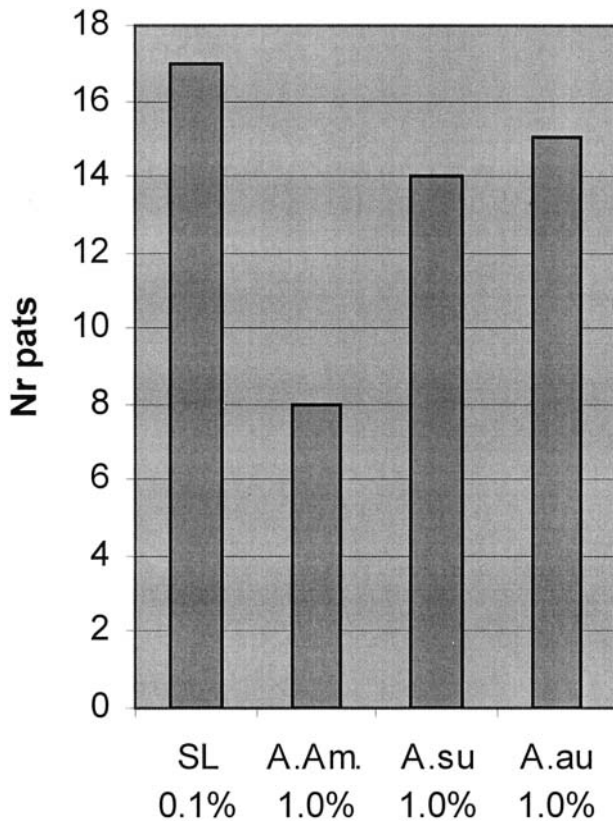


Fig. 2. Positive patch tests to SL mix and to extracts of American and Swedish ragweed in 17 patients. SL = SL mix; A.Am = American extract; A.su = Swedish summer extract; A.au = Swedish autumn extract.

Discussion

In the present study, patients were included because of a previous positive patch test to SL mix. At retest, all patients were again found to be positive and, in most cases, the test reactions were strong. The continued and strong contact allergy may be explained by repeated, accidental exposures since these particular allergens from the environment are difficult to avoid. SL allergens are ubiquitous, occurring in wild as well as cultured Asteraceae (Compositae) plants including many weeds. Patients with occupational contact with SL, such as gardeners and florists, may sometimes need to change to another occupation presumed to have less SL contact, but among our patients none were thus exposed.

Patch testing with plant extracts yielded positive reactions in almost all patients, though more to the Swedish extracts than to the American one (Fig. 2). This may possibly be explained by the difference in extraction solvent (acetone/diethyl ether). Furthermore, there might be qualitative and quantitative differences with regard to the allergen contents.

Since all our patients with SL mix allergy re-

Table 1. Patch test results to SL mix, to extracts of American and Swedish (summer and autumn) ragweed

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
SL-mix 0.1% pet.	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
A. American 1.0% pet.	-	+	-	+	-	+	-	+	+	+	+	+	+	+	+	+	+
A. summer 1.0% ac.	-	+	-	+	-	+	-	+	+	+	+	+	+	+	+	+	+
A. summer 0.1% ac.	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
A. summer 0.01% ac.	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
A. summer 0.001% ac.	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
A. summer 0.0001% ac.	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
A. autumn 1.0% ac.	+	+	-	+	+	-	+	+	+	+	+	+	+	+	+	+	+
A. autumn 0.1% ac.	-	+	-	(+)	-	-	-	-	-	+	-	+	+	+	+	+	+
A. autumn 0.01% ac.	-	-	-	-	-	-	-	-	-	+	-	+	+	+	+	+	+
A. autumn 0.001% ac.	-	-	-	-	-	-	-	-	-	+	-	+	+	+	+	+	+
A. autumn 0.0001% ac.	-	-	-	-	-	-	-	-	-	(+)	-	+	+	+	+	+	+
Eczema	0	P	P	PA	P	P	P	PD	P	PD	PA*	NT	NT	NT	NT	NT	NT

SL = SL mix; A. American = American extract; A. summer = Swedish summer extract; A. autumn = Swedish autumn extract; ac. = acetone; P = pompholyx; PA = activated pompholyx; PD = pompholyx + dorsal eczema; NT = not tested; *even once before when patch tested.

acted to the ragweed extracts (from stem, leaves and flowers) this plant must also be considered important as a cause of SL contact dermatitis in Europe. Unfortunately, current agricultural politics support the spread of this and other weeds when cultivated land is laid fallow (6).

The clinical picture of ragweed dermatitis as reported from North America is usually a chronic dermatitis in exposed skin areas, such as the hands, arms and face, with a peak intensity in late summer and early autumn (3). In Europe, several eczema locations have been registered among patients with SL allergy. Contact dermatitis located to the hands has been reported in 44–94% (8–13). In our present study hand eczema was found in 16/17 patients (94%). It should be pointed out that the patients were recalled for the present study with limited selection, the inclusion criterion being a positive patch test to SL mix.

In one earlier report (11), 65% of the SL mix-positive patients had a clinical picture of vesicular hand eczema. All our 16 patients with hand eczema had the same type of eczema, i.e. pompholyx.

Pompholyx may be an expression of a systemic contact dermatitis. We have, however, no indication in our patients of systemic exposure to SL antigens. Still, it is noteworthy that 5/16 pompholyx patients had a flare-up of their dermatitis on patch testing, which might be explained by percutaneous absorption at the test site and haematogenous spread. In the experimental animal, a flare-up of allergic contact dermatitis at a distant site can be elicited by topical application of the antigen (14). There are several casuistic reports of an eczematous flare-up at patch testing, though this could not be confirmed in a controlled study (15). In her thesis on Compositae dermatitis, Paulsen (16) attempted oral provocations in patients with SL allergy. Provocation with the suspected allergen (feverfew leaves, chamomile tea and lettuce) did not, however, give any positive results. Thus, so far there have been no indications that systemic exposure to the allergen can elicit clinical reactions in SL contact allergy (16).

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