

Contact and photocontact sensitization in chronic actinic dermatitis: a changing picture

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Background: Patients with chronic actinic dermatitis (CAD) frequently have positive patch or photopatch tests. In our previous study (period 1987–1992), the most prominent contact allergen was the sesquiterpene lactone mix (36% of patients with CAD).

Objective: To assess whether contact allergy profiles in CAD patients between 2000 and 2005 have changed in respect to our previous data (1987–1992).

Patients and Methods: Fifty CAD patient records from 2000 to 2005 for patch and photopatch testing were retrospectively analysed and data were compared with that from 86 patients seen between 1987 and 1992.

Results: Thirty-two (64%) and 64 (74%) patients had positive patch or photopatch tests in 2000–2005 and 1987–1992, respectively. The allergen profile has altered. A decline in sesquiterpene lactone mix positive reactions was noted: 29 (36%) patients were positive in 1987–1992 and 10 (20%) patients in 2000–2005, but this was not significant ($P = 0.08$). Reactions to non-fragrance consumer allergens (i.e. *p*-phenylenediamine and preservatives) had risen from 7 reactions (1987–1992) to 21 reactions in 13 individuals (2000–2005) ($P < 0.001$). Of these allergens, *p*-phenylenediamine was the most common (12%; $P = 0.004$).

Conclusions: A significant rise in positive patch tests to non-fragrance consumer allergens, particularly *p*-phenylenediamine, was seen in CAD patients in 2000–2005. We speculate this alteration of allergen profile may be partly due to changes in exposure patterns.

Key words: Chronic actinic dermatitis; patch test; *p*-phenylenediamine; photopatch test; sesquiterpene lactone. © John Wiley & Sons A/S, 2010.

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Background

Chronic actinic dermatitis (CAD) is an immune-mediated photodermatosis characterized by increased photosensitivity leading to an eczematous rash affecting light-exposed areas (1). The main diagnostic features consist of a persistent eczematous eruption on sun-exposed skin and reduced minimum erythema doses (MED) to ultraviolet B (UVB), ultraviolet A (UVA) light, and/or visible light.

A relationship between CAD and allergic or photoallergic contact dermatitis has been identified, although the nature of the relationship remains

unclear (2). In a previous study, we have shown that over 70% of patients with CAD have positive patch tests or photopatch tests, suggesting that there may be an association between the development of a cutaneous allergy and the expression of photosensitivity presenting as CAD (3). However, a proportion of patients with CAD do not have positive patch test findings, which means that there is either an absence of skin sensitization or that a cutaneous allergen has been missed. Importantly, most patients who have contact allergy or allergic contact dermatitis to the same allergens never go on to develop CAD.

Objectives

The purpose of this study was to provide an updated assessment of the allergen profile in patients newly diagnosed with CAD, comparing the present profile with that of our previous cohort. We have assessed whether contact allergy profiles in more recent CAD patients seen (2000–2005) has changed with respect to previous data (1987–1992).

Patients and Methods

The records of CAD patients diagnosed at St John's Institute of Dermatology, St Thomas' Hospital, between 2000 and 2005, were retrospectively studied, and the results compared to previous data of CAD patients seen by us between 1987 and 1992 (3). Patients were identified by manual and electronic search of our in-house photobiology database for this period, and clinical information was obtained by review of the patient case records.

Diagnostic criteria for CAD included a history of photosensitivity, clinical features of a chronic eczematous or pseudolymphomatous skin changes in a photodistribution, coupled with abnormal responses to UVB or UVA (and sometimes visible light) on monochromatic phototesting.

Phototesting

Photoprovocation testing was performed using a single exposure of a small area of unaffected skin to radiation from a 1 kW xenon arc solar simulator (Oriel, Stratford, CT). One day after exposure, patients with CAD had developed eczematous responses from low doses of radiation. Monochromatic irradiation testing was performed with an Oriel monochromator with wavelengths of 300 (± 5), 307.5 (± 5), 320 (± 5), 340 (± 10), 360 (± 10), 380 (± 10), 400 (± 10), 500 (± 20), 600 (± 20), and 700 (± 20) nm; patients with CAD had low MED in the UVB and usually UVA ranges, and sometimes also the visible range.

Table 1. Allergens for photopatch testing ('light series') used in the study period

Allergen	Concentration in petrolatum (%)
Butyl methoxydibenzoylmethane	10
Isoamyl methoxycinnamate	10
Ethyl dimethyl aminobenzoate	10
Musk ambrette	5
Ethylhexyl methoxycinnamate	10
Phenyl benzimidazole sulphonic acid	10
PABA	10
Benzophenone-3	10
Benzophenone-4	10
3-(4-Methylbenzylidene) camphor	10

Patch and photopatch testing

Patients investigated for CAD also underwent patch and photopatch testing with an extended European baseline series and a 'face and light' series (containing cosmetic and UV filter allergens) (Table 1) on an unaffected area of the upper back. Trolab® (Hermal, Reinbeck, Germany) allergens were used. Patch tests and photopatch tests were applied using 8 mm Finn Chambers® under Scanpor® tape. Patches were removed at D2 and readings were performed at D2 and D4. Photopatch tests were applied in duplicate, one set being irradiated with 5 J/cm² UVA (or 2.5 J/cm² in very photosensitive patients) at D2 whilst the other remained non-irradiated.

Patch test reactions were interpreted according to the ICDRG guidelines (4). Photopatch tests were interpreted as positive if a positive reaction was seen in irradiated skin with a corresponding negative reaction in the un-irradiated control.

The frequency of patch test positive reactions to the test substances was recorded and compared to the data from our 1987–1992 (86 patients) study using the chi-squared test.

Results

Demographics

In the study period, 50 newly diagnosed patients with CAD were identified. There was no significant difference in age or sex between the two periods (2000–2005: $n = 50$, 72% male, mean age 63 years; 1987–1992: $n = 86$, 78% male, mean age 65 years).

In the 2000–2005 cohort, 38 (76%) were Caucasian (skin type I–III), 8 (16%) were Asian (Indian or Sri Lankan; skin type V), and 4 (8%) were Afro-Caribbean (skin type VI). In 1987–1992, 80 (90%) of patients were Caucasian (skin type I–III), 1 was of mixed Asian/European origin (skin type IV), 6 (7%) were Asian (skin type V), and 2 (2%) were Afro-Caribbean (skin type VI).

Occupation and hobbies

In 2000–2005, 26 (52%) had outdoor hobbies, compared to 38 (44%) in 1987–1992. The majority in both periods were keen gardeners (44% in 2000–2005). The majority of patients were retired [69% in 1987–1992 (3); 58% in 2000–2005 (Table 2)]. Of those still working, 6/23 (26%) had an outdoor occupation in 2000–2005 (Table 2) and 5/28 (18%) in 1987–1992 (3).

Patch and photopatch tests

Thirty-two patients (64%) had positive patch or photopatch tests. Twenty-seven patients (54%) had

Table 2. Occupation of patients at presentation (2000–2005)

29	(58%)	Retired	1	(2%)	Housekeeper
3	(6%)	Music student	1	(2%)	Finance officer
2	(4%)	Social worker	1	(2%)	Builder
2	(4%)	Housewife	1	(2%)	Painter
1	(2%)	Industrial chemist	1	(2%)	Farmer
1	(2%)	Machine fitter	1	(2%)	Secretary
1	(2%)	Meter reader	1	(2%)	Caterer
1	(2%)	Lollipop man	1	(2%)	Fitter
1	(2%)	Genealogist	1	(2%)	Driver

positive patch tests alone, 4 patients (8%) had both positive patch and photopatch tests and 1 patient (2%) had only positive photopatch tests. This was similar to the previous study, although the total number of patients who had positive patch or photopatch tests had decreased slightly (64 patients; 74%) (Table 3). Of those who were patch test positive, all had more than one positive reaction. The median number of positive patches was 3 [interquartile range (IQR) 2–5].

Reactions to non-fragrance consumer allergens (i.e. *p*-phenylenediamine and preservatives) had risen to 21 allergen reactions in 13 individuals in the period 2000–2005, compared to seven allergen reactions in the period 1987–1992 ($P < 0.001$). Of these allergens, *p*-phenylenediamine was the most common, accounting for 6 (12%) of all positive patch tests, which is a significant increase ($P = 0.004$) (Table 4, Fig. 1). In these six patients, *p*-phenylenediamine was of current relevance in four, old relevance in one and of unknown relevance in one.

A decline in sesquiterpene lactone mix positive reactions was noted: 29 (36%) patients were positive in 1987–1992 and 10 (20%) patients in 2000–2005, but this change did not reach statistical significance ($P = 0.08$). Of these 10 patients, only 3 had simultaneous positives to a non-fragrance consumer allergen. Of the 10 sesquiterpene lactone mix positive

Table 3. Comparison between number of positive patch or photopatch tests in the periods 1987–1992 and 2000–2005

	1987–1992		2000–2005	
Total number of patients undergoing patch and photopatch testing	86		50	
No. of patients with positive patch or photopatch tests	64	(74%)	32	(64%)
No. of patients with positive patch tests alone	54	(63%)	27	(54%)
No. of patients with positive photopatch tests alone	2	(2%)	1	(2%)
No. of patients with positive patch and photopatch tests	8	(9%)	4	(8%)
No. of patients with positive patch/photopatch tests to two or more agents	56	(65%)	31	(62%)

Table 4. Number of patients sensitive to non-fragrance consumer allergens

Non-fragrance consumer allergens	Dilution (%) ^a	1987–1992	2000–2005
<i>p</i> -Phenylenediamine	1	0	6
Methyldibromoglutaronitrile	0.2	0	2
Quaternium-15	1	0	2
2-Bromo-2-nitropropane-1,3-diol	0.5	1	1
Imidazolidinyl urea	2	2	3
Diazolidinyl urea	2	0	3
Formaldehyde	1 (aq.)	1	2
Paraben mix	16	0	1
Methylisothiazolinone (and) methylchloroisothiazolinone	0.01 (aq.)	1	1
Thiomerosal	0.1	1	0
Ethylenediamine	1	1	0
Total		7/86	21/50

^aDilutions were in petrolatum, unless otherwise stated.

reactions, 9 were of current relevance and 1 of old relevance.

Other notable allergens in the 1987–1992 period included fragrance mix I (21%), colophonium (20%), and rubber chemicals (thiuram mix, mercaptobenzothiazole, and mercapto mix) (14%). In 2000–2005, fragrance mix I and rubber chemicals were still prominent, being positive in 9 (18%) patients and 8 (16%) patients, respectively. Colophonium had a non-significant fall in frequency to 8% ($P = 0.1$). Nickel sulfate and cobalt chloride remained steady (14% and 12% in 2000–2005).

Discussion

We have previously studied 86 patients with CAD at our institution and found a high incidence of contact and photocontact allergy, particularly to plant-derived allergens (3). Whilst the percentage of CAD patients who had positive patch or photopatch tests has remained relatively constant (64% and 74% in 2000–2005 and 1987–1992, respectively), our present study has shown that the allergen profile has changed.

Previously, sesquiterpene lactone mix (containing alantolactone, costulonide, dehydrocostus lactone each at 0.03% pet.) was noted to be an important allergen, not only in our previous study but in other reports (3, 5). In the present study, whilst still remaining prominent, we saw a decline in sesquiterpene lactone mix positive reactions: 29 (36%) patients were positive in 1987–1992 and 10 (20%) patients in 2000–2005, but this was not significant ($P = 0.08$). As gardening remains a popular hobby amongst CAD patients, perhaps

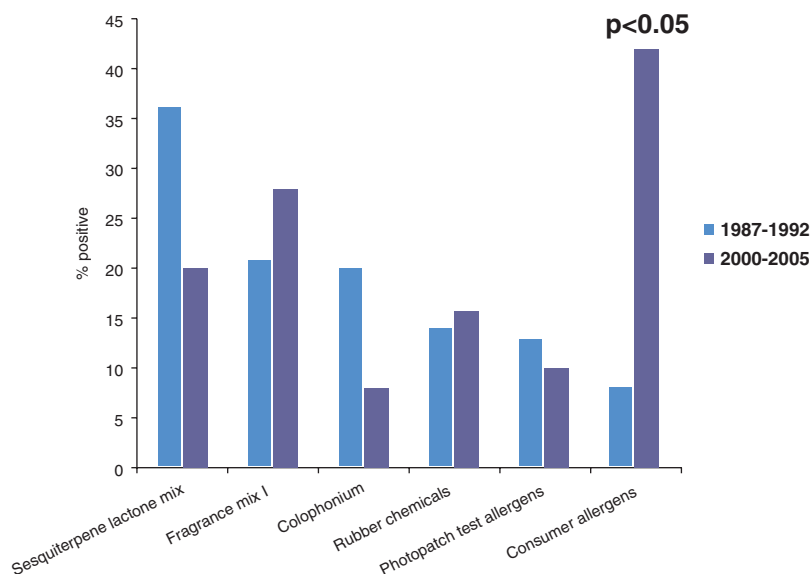


Fig. 1. Percentage Positive patch and photopatch tests in CAD patients in the periods 1987–1992 and 2000–2005.

plants of the *Compositae* family have decreased in popularity amongst hobbyist gardeners. We have no information as to whether the quality of the sesquiterpene lactone mix changed over the periods of the study.

A notable finding in this study is the prominence of non-fragrance consumer allergens in CAD patients: 21 allergen reactions in 13 individuals (2000–2005, 50 patients) compared to 7 allergen reactions (1987–1992, 86 patients) ($P < 0.001$). This represents a significant change compared to the previous cohort and the reason for this is unclear. *p*-phenylenediamine featured strongly, accounting for 12% of positive patch tests. *p*-phenylenediamine is not a new allergen: it is an aromatic amine which has served as a marker for hair dye sensitivity for over 50 years as part of a standard series for patch test screening. Interestingly, five out of the six *p*-phenylenediamine positives were male. Three of the *p*-phenylenediamine positive patients were of Indian extraction, which also may influence matters. Hair dyeing practices are thought to be increasingly popular amongst Asian men, and Southern Asians have previously been shown to have an increased incidence of *p*-phenylenediamine allergy (6). Two of the *p*-phenylenediamine patients were also positive to sesquiterpene lactone mix, which may be the main contributor to their CAD; however, the remaining four *p*-phenylenediamine positive patients cannot be explained in this way. Interestingly, although *p*-phenylenediamine and sesquiterpene lactones are chemically unrelated, a recent paper has suggested the possibility of cross-reactivity between the two substances (7). As fashions change and hair dye use becomes more common in men, it will be interesting to see how

p-phenylenediamine prevalence in CAD changes in future.

Other notable allergens in the 1987–1992 period included fragrance mix I (21%), colophonium (20%), and rubber chemicals (14%). In 2000–2005, fragrance mix and rubber compounds were still prominent, being positive in 9 (18%) patients and 8 (16%) patients, respectively. Colophonium had a non-significant fall in frequency to 8% ($P = 0.1$). Nickel sulfate and cobalt chloride remained steady (14% and 12% in 2000–2005).

Conclusions

A significant rise in positive patch tests to non-fragrance consumer allergens was seen in our cohort of CAD patients in the period 2000–2005. Although part of this may be explained by multiple reactions within individuals, closer analysis revealed that the allergen profile has altered, in comparison with previous data. In particular, *p*-phenylenediamine is featured strongly, accounting for 12% of positive patch tests in CAD patients. We speculate that the reasons for this altered allergen profile are that either exposure patterns have changed, namely, more people are dyeing their hair, perhaps at a younger age, and/or patients are being patch tested at a different, earlier stage of their CAD compared to 1987–1992.

We feel finally that allergic contact dermatitis is significantly important in much CAD causation in chronically sun-exposed subjects, although not all (8). Such dermatitis is a delayed-type hypersensitivity reaction, as also is CAD, the latter apparently against endogenous ultraviolet radiation-induced antigen, perhaps sometimes resembling DNA (9). Thus, the heightened cutaneous immune reactivity

of allergic contact dermatitis when present may well predispose to later CAD development, with the nature of the allergen being irrelevant, as long as the dermatitis is sufficiently severe and widespread, and probably also mainly on sun-exposed sites. There may be shared elements of the regulatory response to the contact allergen and ultraviolet light exposure (10, 11). In addition, or alone in CAD not associated with contact sensitivity, chronic photodamage may conceivably impair normal photo-induced cutaneous immunosuppression, further promoting the delayed-type hypersensitivity of CAD.

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