

Short Communications

SDZ ASM 981 is the first non-steroid that suppresses established nickel contact dermatitis elicited by allergen challenge

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The macrolactam ascomycin derivative SDZ ASM 981, a selective cytokine-inhibitor, developed for treatment of human inflammatory skin disease, has been shown to be effective in the topical treatment of atopic dermatitis (1) and psoriasis (2). Pre-clinical studies have shown SDZ ASM 981 effective after topical application in allergic contact dermatitis of domestic pigs (3).

This provided the rationale to evaluate SDZ ASM 981 in 2 experimental cream formulations (creams F and G) in a randomized, vehicle- and 0.1% betamethasone-17-valerate cream-controlled, within-volunteer, multicenter study. Both cream formulations (creams F and G) were tested at 0.2% and 0.6% SDZ ASM 981 concentrations. In total, 66 healthy volunteers with previous positive patch tests to nickel, who had given their informed consent, were recruited. Dermatitis was induced on the back by 48-h challenge with 5% nickel sulfate in water patches. Thereafter, established allergic contact dermatitis was treated 2× daily with study medication for up to 12 days. Evaluations of erythema, induration and vesiculation were performed daily on a scale ranging from 0 to 3. The total symptom score (TSS) (ranging from 0–9) was defined as the sum of each of the 3 clinical signs.

Given that the disease spontaneously clears after several weeks, it was clear that end-point analysis would be inappropriate. To focus on the clinical assertion that therapeutic intervention should reduce the time until a test site attains a satisfactory outcome, time-to-event analysis was selected for primary efficacy assessment. Partial clearance of a test site was defined as a TSS of 0 or 1. To incorporate the within-patient nature of the data, a non-parametric method according to Schemper (4, 5) was selected to investigate the time-to-event data, with test sites not attaining partial clearance at the end of treatment censored in the usual way.

With regard to time until partial clearance (reduction of TSS from at least 6 to 1 or less), 0.6% SDZ ASM 981 in both cream formulations was significantly more effective than corresponding vehicles ($p=0.03$ (formulation F), $p=0.02$ (formulation G); Schemper pairwise test), showing a 1-day reduction on median time to partial clearance. Neither formulation at the 0.2% concen-

tration was significantly more effective than corresponding vehicle (at 10% level). No difference was observed between 0.06% SDZ ASM 981 in the 2 experimental cream formulations and 0.1% betamethasone-17-valerate cream with regard to time until partial clearance. Furthermore, with regard to reduction of total symptom score, the greatest therapeutic difference between active medication and placebo was observed after 3 days of treatment. 0.6% SDZ ASM 981 in both cream formulations was significantly more effective in suppressing the signs of inflammation than corresponding vehicles ($p=0.007$ (formulation F), $p=0.01$ (formulation G); paired t -test). The therapeutic effect of 0.6% SDZ ASM 981 (mean 32% on the TSS with both formulations) was comparable to 0.1% betamethasone-17-valerate (mean 32% on the TSS). At the end of the 12 days treatment, 30% of the betamethasone, 0.6% cream F and 0.6% cream G test sites completely cleared (TSS=0), whereas 21.5% and 18.5% placebo (F and G) test sites completely cleared. Local and systemic tolerability of SDZ ASM 981 in both cream formulations was excellent.

To our knowledge, this is the 1st time that a topical non-steroid has shown efficacy in this indication. A variety of treatments evaluated for topical use, such as cyclosporin A, have been tested and shown to be ineffective in this indication (6). Further clinical studies will be initiated to prove SDZ ASM 981 safe and effective in the treatment of allergic contact dermatitis.

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Patch testing for corticosteroid allergy using high and low concentrations

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Key words: corticosteroids; patch test method; concentration; budesonide; tixocortol pivalate; medicaments.
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This study was designed to assess whether a high, low or combination of concentrations should be used for patch testing for corticosteroid allergy when reading at day (D) 2 and 4. 2 corticosteroids were used, both of which are recommended for inclusion in the standard series: 1 potent and 1 weak in anti-inflammatory action. Previous reports had suggested that a low concentration gave more rapid onset of the allergic reaction (1–3), though dose-dependent inhibition of the corticosteroid allergic reaction had not been demonstrated (4).

Patients, Methods and Results

Tixocortol pivalate 1% & 0.001% pet. and budesonide 1% & 0.001% eth. were included in the standard series of 2 centres. Readings were taken at D2 and D4. 1122 patients were tested (Manchester 715; Leeds 407). The positive reactions are summarized in Table 1. There were 43 reactions to any corticosteroid. 30 reacted to tixocortol pivalate, all at the high concentration and only 9 at the lower. 13 reacted to budesonide, all at the high concentration and only 4 at the lower. 30 reactions overall were not detected by testing at low concentration. No additional reactions were detected by testing at low concentration. More rapid reactions were not apparent at low concentration.

Comment

This study suggests that a single high concentration of corticosteroid is the optimum for patch testing with tixocortol pivalate and budesonide with readings at D2 and D4. No advantage was gained by testing with an additional low concentration. In previous work, patients used for studying the time course of the corticosteroid allergic reaction (2) were obtained by screening with a 0.1% concentration. This might result in false-negative reactions and select individuals reacting at low concentration. This implies that the well-documented cases with reactions at low concentration (1, 3) are a rare event.

We did not test at 0.1% or 0.01% concentrations. However, the low concentration of 0.001% was chosen based on the concentration giving the highest yield at early time points in previous studies (1, 2). Whilst 1 of

Table 1. Positive reactions in 1122 patients (L=Leeds; M=Manchester)

Patient	Tixocortol pivalate (pet.)		Budesonide (eth.)	
	1%	0.001%	1%	0.001%
L1	++ & ++	+ & ++		
L2	- & +	- & ?+		
L3	- & +	- & -		
L4	- & +	- & -		
L5			?+ & ++	- & -
L6			- & +	- & -
L7			+ & ++	- & -
L8	+ & +	- & +	- & +	- & -
L9	++ & ++	- & +	- & +	- & -
M1	- & +	- & +		
M2	?+ & ++	- & ++		
M3	++ & ++	++ & ++		
M4	++ & ++	- & -		
M5	?+ & +	- & -		
M6	- & ++	- & -		
M7	++ & ++	- & -		
M8	- & ++	- & -		
M9	?+ & ++	- & -		
M10	+++ & ++++	- & -		
M11	- & ++	- & -		
M12	++ & ++	- & -		
M13	++ & ++	- & -		
M14	- & +	- & -		
M15	?+ & ++	- & -		
M16	- & ++	- & -		
M17	- & +	- & -		
M18	++ & ++	- & -		
M19	- & +	- & -		
M20	++ & ++++	- & -		
M21	- & +	- & -		
M22			++ & ++	+ & ++
M23			++ & ++	++ & ++
M24			- & +	- & +
M25			- & ++	- & -
M26			?+ & ++	- & -
M27	- & +	- & -	++ & ++	+ & ++
M28	++ & ++++	++ & ++	- & ++	- & -
M29	++ & ++	++ & ++	++ & ++	- & -

these studies did involve screening patients with different concentrations of budesonide, the highest concentration tested was 0.1% (2).

We continue to recommend testing with a 1% dilution of corticosteroid in eth. when testing for corticosteroid allergy (5). In rare instances, where clinical suspicion persists, the use of low concentrations (1, 3) or intradermal tests (6) for diagnosis may be indicated.

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Cheilitis due to nickel contact allergy in a trumpet player

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Key words: contact allergy; nickel; lip eczema; trumpet; musicians; allergic contact cheilitis © Munksgaard, 2000.

Case Report

A 32-year-old man presented with a several-month history of itching, dryness and sometimes scaling of the lips. Various emollients gave no relief. There was no occupational exposure to airborne irritants; no special recreational activities were reported except trumpet playing at weekends. There was no history of atopic diseases or prior allergic contact dermatitis. Examination revealed scaling and partly crusting cheilitis, particularly prominent on the median 1/3 of the lips (Fig. 1).

There were no reactions on prick testing with house-dust mite (*D. pteronyssinus*), cat dander or grass pollen. The patient was then patch tested with a standard series, and reactions to the fragrance mix (D2 +, D3 ++) and to nickel sulfate (D2 ++, D3 ++) were found.

Subsequent use of fragrance-free emollients did not ameliorate the condition. Re-assessment of the patch test results led to the suspicion that contact with his trumpet could be responsible for the cheilitis. Indeed, there was complete healing of the lip eczema following the use of a gold mouthpiece on his trumpet. For more than 1 year, there has been no recurrence of the condition.

Comment

Contact allergy to nickel may have unusual (1, 2) or systemic manifestations (3). The release of nickel from metal devices is favoured by friction, heat or galvanic factors (4). This may not only happen during cooking processes (5), but also on exposure to various bodily fluids. These include sweat exposure during work, effects of adjacent tissue on implant materials, or contact of saliva with orthodontic braces (2, 6). In the last situation, nickel release and subsequent antigen contact via

the alimentary tract prior to sensitization may even result in systemic immunologic tolerance (7). On the other hand, systemic T-cell hyper-responsiveness and TH₁-type mediator production in vitro are typical features in patients with systemically-induced nickel contact reactions (8).

The clinical features and patch test results in our patient led to the diagnosis of allergic contact dermatitis, probably caused by trumpet playing. As the eczema completely cleared after switching to a gold mouthpiece, nickel exposure due to contact with the previously-used mouthpiece was considered causative. This observation is in accordance with the previous report by Nakamura et al. (9) on nickel as elicitor of allergic contact reactions in a trumpet player. However, in the patient described here, the only manifestation of contact eczema was in the lip region. Thus, apart from the degree of sensitiza-



Fig. 1. Eczematous lesions in the lip area.

tion, factors such as occlusion, corrosion and epithelial barrier may also promote the elicitation of clinical symptoms in uncommon locations. This was apparent in the patient's hands remaining symptom-free despite continued contact with the instrument.

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Patch testing with budesonide in serial dilutions A multicentre study of the EECDRG

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Testing consecutive dermatitis patients with several corticosteroids revealed contact allergy frequencies between 2.9–4.9% (1–2). 1 substance used was budesonide (3): this was originally tested at 1.0%, but lately 0.10% has also been advocated, since strong reactions were seen with 1.0%. Concerning the vehicle, petrolatum (pet.) or ethanol (eth.) has given equivalent patch test results (4). In 1 study among 10 patients known to be allergic to budesonide (5), 0.002% picked up most patients. In another study, the majority reacted to 0.02% budesonide (6). Recently, within the EECDRG (7), 0.10 and 0.002% were compared and most patients reacted to 0.10%.

Materials and Methods

This survey took place from 1 January 1999 to 31 May 1999. Budesonide dispersed in petrolatum at 4 different concentrations (1.0, 0.10, 0.01, 0.001% w/w) was pur-

chased from Chemotechnique, Malmö, Sweden, added to the standard series of each clinic and consecutive dermatitis patients tested, each clinic using the test system that they had at the time. Patches remained on the back for 2 days and mandatory readings were performed on day (D) 3 or 4 and, if possible, consistently but voluntarily, on D7. Results were read in accordance with ICDRG guidelines (8). All information was compiled on a standardized form. Even if reactions were graded according to the strength of the separate reactions, in the final comparison, a reaction was regarded as either positive or negative and no attempt was made to compare the gradings from each centre.

Results and Discussion

Table 1 shows the number of tested and positive patients in each clinic. The test results are seen in Table 2. 2599 pa-

Table 1. The 14 clinics participating in the study, the number of patch tested patients, and the number of patients positive to at least 1 concentration of budesonide

Clinic	No. tested			No. positive
	total	male	female	
Modena	44	13	31	3
Bologna	397	149	248	1
Odense	128	41	87	0
Bordeaux	125	47	78	2
Amsterdam	196	64	132	1
Stockholm	71	40	31	1
Gentofte	326	118	208	4
Malmö	350	144	206	2
Dortmund	148	73	75	3
Almada	68	22	46	0
Amersham	238	97	141	0
Oulu	158	52	106	3
Leuven	257	73	184	6
Erlangen	93	41	52	0
total no.	2599	974	1625	26

tients were tested (2146 in 12 centres with the Finn Chamber system (Epitest Ltd Oy, Finland) and 453 in 2 centres with the van der Bend system (Brielle, The Netherlands)) and 22 reacted to at least 1 of the 4 preparations (0.8%) on D3 or D4. 20 reacted to budesonide 0.10 and 0.01%, 19 to 0.001% and 18 to 1.0% on D3 or D4. When also considering D7 readings, 26 patients reacted.

The study that compared 0.10 and 0.002% (7) showed a lower outcome for 0.002%. The present study also showed a lower outcome for 1.0%, and it seemed that 0.10 and 0.01% detected contact allergy to budesonide equally well. To minimize the risk of patch test sensitization (9, 10), the lowest possible concentration should be used, speaking in favour of 0.1%.

This study again showed that a low concentration of budesonide may be the sole tracer of contact allergy (pat. no. 11) (6). Furthermore, in the 8 centres that consistently read on D3 or D4 and D7, 28.6% of budesonide allergy would have been missed had not the D7 reading taken place (7).

Table 2. The yield of positive patients in the 8 centres that use D3 or D4 and D7 as mandatory reading occasions (patients 1–14) and in the 6 centres that use D3 or D4, and not D7 as the mandatory reading occasion (patients 14–26)

Test prep	Bud 1.0%		Bud 0.10%		Bud 0.01%		Bud 0.001%		Only D3 or D4	Only D7	Both D3 or D4 and D7
	D3	D7	D3	D7	D3	D7	D3	D7			
Patient no.											
1	+		+		+	+	+				+
2	+		+	+	+	+					+
3	+		+		+				+		
4		+		+		+	+	+			+
5		+		+		+		+		+	
6		+	+	+	+	+	+	+			+
7	+		+		+		+		+		
8		+	+	+	+	+		+			+
9		+		+		+				+	
10	+		+		+		+		+		
11							+		+		
12		+		+		+		+		+	
13		+		+		+		+		+	
14	+	+	+	+	+	+	+	+			+
total	6	8	8	9	8	10	7	7	4	4	6
15	+		+		+		+		+	na	na
16	+		+		+		+		+	na	na
17	+		+		+		+		+	na	na
18	+		+		+		+		+	na	na
19	+		+		+		+		+	na	na
20	+		+		+		+		+	na	na
21	+		+		+		+		+	na	na
22	+		+		+		+		+	na	na
23	+	+	+	+	+	+	+	+	+	na	na
24	+	+	+	+	+	+	+	+	+	na	na
25	+		+		+		+		+	na	na
26	+		+		+		+		+	na	na
total	12	2	12	2	12	2	12	2	12		
total whole material	18		20		20		19				

+ stands for a positive reaction seen for the respective concentration and reading occasion.

na: not applicable.

Therefore, based on this study and others (4–7), we suggest, that budesonide 0.01% pet. (w/w) is to be recommended for a standard series, and that a further reading should also be done after 1 week.

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The relevance of positive patch test reactions in chronic otitis externa

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Otitis externa is a multifactorial disease state, with both endogenous and exogenous causation (1–3).

Materials and Methods

We studied a group of 79 patients, 45 women (57%) and 34 men (43%), whose ages ranged from 3 to 85 years, during the period July 1995–July 1999. The 79 patients had chronic otitis externa that persisted for at least 4 months to over 30 years. 50 patients (63%) had been referred by an otorhinolaryngologist, because of lack of response to topical therapy.

The 79 patients were patch tested with the European standard series, a series of topical medicaments (Table 1), their own topicals, and additional series if appropriate (Table 2), using van der Bend patch test chambers, affixed with Fixomull Stretch tape. Tests were removed after 2 days (D) and the results read according to international guidelines at D2, D3, D4 and D7.

Results

35 patients (44.3%) showed positive reactions. 22 patients (27.8%) reacted to a topical aural preparation or its ingredients. 9 of these (11.4%) had used topical aural

preparations during the last 4 months before testing. 9 others (11.4%) had used these topical drugs in the outer ear in the past, but not during the last 4 months. The other 4 (5.1%) had never used topical aural preparations. 13 patients (16.5%) showed reactions to substances not relevant to treatment of the auditory canal, such as nickel sulfate and fragrance mix.

Table 1 presents the different allergens in our series of topical medicaments, the no. and % of positive reactions and the no. of positive reactions after 7 days. Positive reactions to agents tested in the European standard series, additional series or as own materials are presented in Table 2.

27 patients (34.2%), 9 men and 18 women, had a history of atopic dermatitis, allergic rhinitis or asthma. 70 patients were subjected to intracutaneous tests, which were positive in 32 (40.5%). Psoriasis in the past or currently was present in 9 patients (11.4%). Irritant contact dermatitis was found in 2 patients (2.5%), atopic dermatitis in 8 (10.1%) and seborrheic dermatitis in 20 (25.3%). 1 patient had a dermatitis on the hands with an accompanying allergy to nickel.

12 patients (15.2%) used a hearing aid. In 1 patient, patch tests showed a relevant allergy to the plastic of the device. Additional patch testing showed ++ and +++

Table 1. Series of topical medicaments

Test compound	# ⊕	% ⊕	# ⊕ at D7
propylene glycol 5.0% pet. or 10% aq.	0	0	0
polyethylene glycol 8000 4.0% aq.	1	1.3	0
benzalkonium chloride 0.1% pet.	2	2.5	0
sodium pyrosulfite 2.0% pet.	3	3.8	0
Kenalog tincture ¹	3	3.8	0
Synalar biotic eardrops ²	4	5.1	2
Locacorten-Vioform eardrops ³	1	1.3	0
Otosporin eardrops ⁴	5	6.3	2
Panotile eardrops ⁵	4	5.1	2
Sofradex eardrops ⁶	5	6.3	4
Terracortril eardrops ⁷	0	0	0
Clioquinol eardrops ⁸	1	1.3	0
Bacicoline-B ⁹	3	3.8	1

¹ Per g: triamcinolone acetonide 2 mg; acid salicylicum 20 mg;

benzalkonium chloride 5 mg in alcohol 70%.

² Per ml: fluocinolone acetonide 0.25 mg; polymyxin B 10,000 IU; neomycin 3.5 mg; propylene glycol 400 mg.

³ Per ml: flumetasone 0.2 mg; clioquinol 10 mg; in polyethylene glycol.

⁴ Per ml: neomycin 5 mg; polymyxin B 10,000 IU; hydrocortisone 10 mg; methylhydroxybenzoate 1 mg.

⁵ Per ml: fludrocortisone 1 mg; neomycin 10 mg; polymyxin B 10,000 IU; lidocaine 40 mg.

⁶ Per ml: dexamethasone 0.5 mg; framycetin 5 mg; gramicidin 0.05 mg; phenylethyl alcohol 5 mg.

⁷ Per ml: oxytetracycline 5 mg; polymyxin B 10,000 IU; hydrocortisone acetate 15 mg.

⁸ Per ml: clioquinol 10 mg in macrogol.

⁹ Per ml: colistin 250,000 IU; bacitracin 500 IU; hydrocortisone acetate 10 mg.

reactions to phenyl salicylate (1.0% pet.), benzoyl peroxide (1.0% pet.), tricresyl phosphate (5.0% pet.), triphenyl phosphate (5.0% pet.) and resorcinol monobenzoate (1.0% pet.). Another patient had developed an allergic contact dermatitis due to the gold plating of his hearing aid. Patch testing showed a + reaction to gold sodium thiosulfate.

In the group of 22 patients with positive patch test reactions to ingredients of topical medicaments, only in 4 patients (5.1%) did discontinuation of the topical aural preparations result in marked improvement in the otitis externa. We considered this a relevance of 18.2% (4 out of 22).

Discussion

35 patients (44.3%) showed positive reactions, 22 (27.8%) to topical medication or its ingredients. If the skin reacted to topical medication (17 patients), 1 or more ingredients also proved to be positive, mostly aminoglycoside antibiotics or steroids. Consequently, the rate of false-positive reactions to topical ear medication was probably minimal.

In the group of 22 patients reacting to ingredients of topical medication, only in 4 patients (18.2%) were the results relevant to the actual disease at the time of testing. Van Ginkel et al. (4) found 56% relevant positive

Table 2. Positive allergens in the other test series

Test compound	# ⊕	(%)
neomycin sulfate	20.0% pet.	12 15.2
nickel sulfate	5.0% pet.	9 11.4
fragrance mix	8.0% pet.	8 10.1
carba mix	3.0% pet.	5 6.3
caine mix II	10.0% pet.	4 5.1
jodium	1.0% alc. 96%	4 5.1
acid salicylicum	5.0% pet.	3 3.8
balsam of Peru	25.0% pet.	2 2.5
budesonide	0.1% pet.	2 2.5
triamcinolone acetonide	0.1% pet.	2 2.5
thiuram mix	1.0% pet.	2 2.5
cobalt chloride	1.0% pet.	2 2.5
ethylenediamine dihydrochloride	1.0% pet.	1 1.3
hydrocortisone	1.0% pet.	1 1.3
hydrocortisone acetate	1% alc.abs./DMSO	1 1.3
betamethasone dipropionate	1% alc.abs.	1 1.3
chloracetamide	0.2% pet.	1 1.3
clioquinol	5.0% pet.	1 1.3
mercapto mix	1.0% pet.	1 1.3
2-mercaptobenzothiazole	2.0% pet.	1 1.3
epoxy resin	1.0% pet.	1 1.3
wool alcohols	30.0% pet.	1 1.3
benzocaine	5.0% pet.	1 1.3
mercuric chloride	0.1% pet.	1 1.3
chlorhexidine digluconate	0.5% aq.	1 1.3
Daktarin cream		1 1.3
Pantene pro V shampoo		1 1.3
acetic eardrops ¹		1 1.3
miconazole eardrops ²		1 1.3

¹ Dutch Pharmacopoeia.

² Miconazole 2% in propylene glycol.

reactions on patch testing in chronic otorrhoea, the difference being due either to geographical variation in medicament use, or to other criteria of relevance being used.

As in previous studies (3–7), the most important allergen was neomycin, which cross-reacted with other aminoglycoside antibiotics tested.

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Allergic contact dermatitis caused by mehindi

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Key words: mehindi; temporary tattoo; henna; allergic contact dermatitis; para-phenylenediamine; cosmetics; public health. © Munksgaard, 2000.

Mehindi is the traditional art of adorning the extremities with a paste made from leaves of the henna plant, a small shrub (*Lawsonia inermis*), also known as henne, al-khanna and al-henna. The most likely cause of contact dermatitis due to mehindi is the presence of para-phenylenediamine (PPD) in the temporary tattoo, which is added to strengthen the colour (1–3).

Case Reports

Case no. 1

A 30-year-old woman presented with an itchy dermatitis on the dorsum of her right wrist, the shape of which corresponded exactly to a temporary tattoo applied 2 weeks before in a local beauty salon. Patch testing with the GIRDCA standard series (Trolab-Hermal), using Finn Chambers on Scanpor, was positive to PPD 1% pet. (D2 ++/D3 ++). The labelled ingredients on the tube of henna paste, used to make the temporary tattoo, were natural henna powder, PPD, mehindi oil (a blend of eucalyptus and clove oils) and water. The patient's dermatitis cleared after a short course of topical corticosteroid.

Case no. 2

A 36-year-old woman presented with acute contact dermatitis on her right arm, which had developed 1 month after application of a tribal mehindi, a temporary tattoo made with "black henna", in a discotheque on the Adriatic coast. Patch testing to the GIRDCA standard series was positive to PPD 1% pet. The ingredients of "black henna" were not labelled.

Case no. 3

During a holiday in Egypt, a 48-year-old woman had a lotus flower painted on her left hand. After a few hours, an itchy erythematous vesiculobullous reaction developed exactly where the "henna" design had been traced, which healed in a week with topical and systemic corticosteroids, leaving post-inflammatory hyperpigmentation. A patch test with pure henna powder 10% aq. was negative, and the patient was already known to be allergic to PPD on patch testing some years before,

following a hair dye reaction (PPD 1% pet. +++D2/+++D3).

Discussion

In recent popular culture, the ancient art of Arabic, Asian and African mehindi has enjoyed a Western renewal. Musicians and filmstars have adopted the tradition, such that mehindi, as a temporary, pain-free body-decoration alternative to tattooing is now fashionable among both women and men, temporary tattoos frequently being featured in popular magazines. Mehindi is cheap and prices start as low as 5–6 Euro for small designs, increasing according to size, intricacy and placement.

Several cases of contact dermatitis from mehindi tattoos have already been reported in the literature, including 2 due to henna and 5 due to PPD (1–7), sensitization, as in 2 of our cases, being a primary consequence of PPD in the tattoo. We wish to stress that the number of stores and beauty salons applying such temporary tattoos is currently increasing in Italy and the rest of the EU, making the mehindi tattoo no longer an exotic art and possibly raising the spectre of an increase in PPD sensitization among the general population of Europe and North America.

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Allergic contact dermatitis from ninhydrin in a forensic scientist

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Key words: allergic contact dermatitis; ninhydrin; forensic laboratory; occupational. © Munksgaard, 2000.

Ninhydrin is a commonly used reagent for the colorimetric determination of amino acids and amino sugars, and is often used in forensic laboratories.

Case Report

A 25-year-old forensic laboratory technician had had skin problems for 1 year. Redness and itching of the eyelids had spread to the cheeks and forearms. 1% hydrocortisone cream had improved but not cleared the symptoms. There was no past history of atopy or allergies. Her job involved testing paper for fingerprints, using superglue and fluorescent dye or ninhydrin solution. On examination, she had eczema on the cheeks, eyelids and forearms.

She was patch tested to standard, preservative, vehicle, emulsifier, plasticizer and glue series and, in addition, to substances commonly used in her workplace: silicone grease (as is), methylated spirit (as is), ninhydrin (1% aq.), absolute alcohol (10% aq.), acetic acid (2% aq.), Basic Yellow (1% pet.), cyanoacrylate (1% pet.), and a piece of rubber glove. At D2 and D4, she had a + reaction to nickel sulfate (5% pet.). At D4, she had a + reaction to ninhydrin (1% aq.). RAST and prick test to latex were negative.

Discussion

There are only 2 previous reports of contact reactions to ninhydrin (1, 2), 1 in which 3 workers developed allergy to a surgical marker pen (2), and 1 in which a scientist working on the analysis of amino acids with 2–50% solutions of ninhydrin, without gloves, developed inflammation on the hands and was prick-test-positive to 0.25% ninhydrin solution (10 controls negative). Forensic laboratory workers may therefore require patch and prick testing to ninhydrin.

Acknowledgement

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Occupational allergic contact dermatitis from benzalkonium chloride

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Key words: catering; cleaning; occupational; airborne; allergic contact dermatitis; detergent; disinfectant; epidemiology; benzalkonium chloride; N-alkyl-N,N-dimethyl-benzylammonium chloride, N-alkyl-N,N-dimethyl-ethylbenzylammonium; patch testing technique. © Munksgaard, 2000.

Detergents and wet work are the commonest causes of occupational skin disease (1), but occupational allergic contact dermatitis from soaps and detergents is rare (2). During 1991–1998, we patch tested a total of 948 patients with benzalkonium chloride: in most cases at 0.1% aq. but in some cases at 0.1% pet., or at 0.01% pet. or aq. 3 patients had an allergic patch test reaction (0.3%); 87 patients an irritant reaction (9.2%). The occupational allergic contact dermatitis of 9 out of 2642 patients (0.3%) was caused by benzalkonium chloride, according to the Finnish Register of Occupational Diseases (3) during 1990–1996.

Case Reports

Case no. 1. A 32-year-old non-atopic cook was referred for investigation of a papular eruption on the backs of her hands and lower arms and a facial dermatitis, after cleaning the oven at work with a disinfecting detergent for sanitary and foodstuff areas. She had worked in the same occupation for 10 years and had 2× earlier had symptoms from a similar product for cleaning ovens. On each occasion, the symptoms started 1 day after exposure and continued for 2 weeks, despite topical corticosteroids.

She was patch tested with a modified European standard series, an antimicrobial series and a rubber chemical series. Neomycin sulfate, nickel sulfate and benzalkonium chloride (Epikon, 0.1% aq.) provoked +++ reactions (Table 1), all other test sites being negative, except for a ?+ reaction to cetylpyridinium chloride (0.01% aq.). Prick test series with both standard environmental allergens and spices were negative.

The disinfecting detergent contained, according to the material safety data sheet and the product declaration, <2.5% N-alkyl-dimethyl-benzylammonium chloride and <2.5% N-alkyl-dimethyl-ethylbenzylammonium chloride. The patient was then patch tested with a dilution series of this detergent, which provoked reactions down to 0.2%, corresponding to less than 0.005% active ingredients (Table 1). Follow-up 3 months later confirmed that she had not used similar detergents and had remained symptomless.

Case no. 2. The 2nd patient was a 42-year-old cleaner with hand dermatitis who had a ++ patch test reaction to benzalkonium chloride (0.1% aq.) and a +++ reaction to formaldehyde (Chemotechnique, 1% aq.). Both reactions were considered relevant and caused by detergents she had used at work.

Discussion

The antimicrobials triclocarbon, triclosan, chlorhexidine, formaldehyde, formaldehyde releasers, glutaraldehyde, isothiazolinones, p-tert-butylphenol, amylphenol, o-benzyl parachlorophenol, chloroxyleneol, chloroacetamide, methylidibromoglutaronitrile and dodecyl-di-(aminoethyl)glycine (2, 4, 5) have all been reported as causing occupational allergic contact dermatitis from detergents or disinfecting detergents. Benzalkonium chloride is a quaternary ammonium amphoteric detergent consisting of a mixture of alkyl dimethyl benzyl ammonium chlorides, the length of their alkyl chain being 8–18 carbon atoms. Quaternary ammonium compounds can be irritant under closed patch tests (6). Benzalkonium chloride is widely used as a disinfectant, e.g., preoperatively (7), and for surgical instruments, etc. (6), and as a preservative in, e.g., eyedrops. Allergic contact dermatitis from benzalkonium chloride has been reported to be relatively frequent (8), and it was one of the most common causes of allergic patch test reactions in a preservative series in a German multicentre study (9).

Benzalkonium chloride has been recommended for testing at 0.1–0.01%. Our study showed that benzalkonium chloride was often irritant on patch testing at 0.1%, and a rare cause of occupational allergic contact dermatitis in Finland. Benzalkonium chloride may also cause delayed irritation (10), patch test reactions increasing in intensity with time. A dilution series should always be used to confirm the allergic nature of a positive patch test reaction to this chemical.

Airborne dermatitis from benzalkonium chloride has previously been reported (11). Our patient no. 1 had respiratory symptoms, as well as facial dermatitis, indicating airborne exposure, but the former were considered to be irritant. Immediate allergy (12) and asthma (13) from benzalkonium chloride has been reported. Our patient no. 1 had earlier used a corticosteroid containing benzalkonium chloride to treat external otitis, and it cannot be excluded that sensitization had occurred from that product.

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Table 1. Positive patch test reactions of patient no. 1

Patch tests	% vehicle	D2	D3	D5
1st session				
nickel sulfate	5% pet.	+++		+++
neomycin sulfate	5% pet.	+++		+++
benzalkonium chloride	0.1% aq.	+++		+++
2nd session				
own oven detergent	2% aq.	++	++	+++
own oven detergent	0.67% aq.	+	++	++
own oven detergent	0.2% aq.	–	+	+

Contact sensitivity to budesonide in a child

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Key words: allergic contact dermatitis; budesonide; corticosteroids; medicaments; children; lack of cross-sensitivity. © Munksgaard, 2000.

The frequency of allergic contact dermatitis from corticosteroids in selected patients (1–4) is around 2%, sensitization occurring mainly in adults with chronic skin diseases.

Case Report

A 6-year-old child presented with blanching in the pubic area surrounded by an erythematous halo and massive edema of the prepuce, 1–2 days after application of topical budesonide 0.025%. The parents denied any previous prolonged use of topical medicaments and the personal and family history was negative for atopy. Treatment with topical betamethasone valerate 0.05% and oral cetirizine (1 mg/day) resulted in improvement in just a few days.

A few months later, the parents allowed patch testing with a paediatric series, 5 topical corticosteroids and the commercial product. Patch testing with the paediatric series was negative, while the corticosteroid series and commercial product showed the results in Table 1.

Discussion

This case seems worthy of note because of:

- (i) the patient's young age;
- (ii) no cross-reactivity among topical corticosteroids indicated by the Coopman classification (5);
- (iii) the presence of a so-called "edge effect" to the budesonide reaction.

Table 1. Corticosteroid patch test results

Allergen	%	Vehicle	D2	D4
hydrocortisone 17-butyrate	1	eth.	—	—
tixocortol 21-pivalate	1	pet.	—	—
triamcinolone acetonide	1	pet.	—	—
betamethasone 17-valerate	1	pet.	—	—
budesonide	0.1	pet.	++	+++
Bidien®	as is		+++	+++

An in-depth study of patients with allergic contact dermatitis from budesonide demonstrated (6) an individual threshold of patch test reactivity. This case illustrates the usefulness of patch testing with a corticosteroid series, and is a reminder of the importance of avoiding systemic administration of corticosteroids in such patients because of the risk of flare-up (7–8).

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Allergic contact dermatitis from hydrolyzed wheat protein in cosmetic cream

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Key words: hydrolyzed wheat protein; cosmetics; allergic contact dermatitis. © Munksgaard, 2000.

Case Report

A 64-year-old non-atopic housewife consulted us about itchy erythematous, oedematous lesions on the eyelids, face and neck, that had been appearing for 2 months. A moisturizing cosmetic cream (Yves Rocher®) had been applied on her face and neck every day for the last 2 years. The cutaneous lesions improved within 2 weeks of discontinuation of the cream and treatment with topical corticosteroids.

Patch tests with the GEIDC standard and cosmetics series, her own cosmetic cream, and its components were performed. Positive reactions (++) were obtained to nickel sulfate at D4, cosmetic cream as is, and 1 of its ingredients, hydrolyzed wheat protein 10% aq. at D2 and D4. Open testing with hydrolyzed wheat protein 10% aq. on the volar side of the forearm was negative at 30 min. Patch tests with hydrolyzed wheat protein 10% aq. were negative in 34 controls at D2 and D4.

Discussion

Protein hydrolysates are added to skin care and hairdressing products, such as creams, soaps, bath gels and hair

conditioners, for their moisturizing properties and to give volume to hair. Protein hydrolysates in hair conditioners have been reported to cause contact urticaria and conjunctivitis in women with atopic dermatitis, who all reacted on prick testing to hydroxypropyl trimonium hydrolyzed collagen (Crotein QR) (1). Pigatto et al. (2) have reported an occupational dermatitis in 2 bakers with positive patch test reactions to wheat, oats and barley.

We are not aware of contact sensitization having been reported to such protein in cosmetic creams, the moisturizing cream in this case containing 0.06% hydrolyzed wheat protein. The wide use of hydrolyzed wheat protein in cosmetics and hairdressing products and the increase in topical use of such products may cause further contact sensitization.

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Contact urticaria from *Matricaria chamomilla*

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Key words: *Matricaria chamomilla*; chamomile tea; Compositae; plant extracts; herbal remedies; eyelids; contact urticaria. © Munksgaard, 2000.

The term “chamomiles” refers to various species of plants belonging to the Compositae family. The most important of them are *Anthemis nobilis* (Roman chamomile), and *Matricaria chamomilla*, also named *Chamomilla recutita* or German chamomile. Chamomile tea, which is obtained from the dried flower heads, is a popular remedy for a wide variety of complaints. Chamomile has mild anti-inflammatory and bacteriostatic effects and so is also used topically (compresses or ointments).

Case Report

A 23-year-old woman, with a history of seasonal rhinitis, conjunctivitis and exercise-induced asthma, developed eyelid angioedema after applying compresses of chamomile tea to her eyelids in the hope of gaining relief from runny eyes. Prick tests showed a strong positive reaction (++++) to *Artemisia vulgaris* and *Artemisia absinthium* (Bayer, Milan, Italy) and an immediate posi-

tive skin response (++) to German chamomile tea extract and to celery. IgE antibodies to chamomile were 3.37 kUA/l. She had also high IgE levels to *Artemisia vulgaris* (4.23 kUA/l). Afterwards, an oral challenge test was also performed with diluted chamomile tea. The only symptom that the patient developed was a generalized pruritus of the face.

Discussion

Reports of anaphylactic and urticarial reactions to chamomile tea are rare (1). In our case, an immune-mediated contact urticaria was diagnosed. Subiza et al. (2) described a similar reaction in 2 patients who developed lid angioedema after eye washing with chamomile tea. The patient was atopic and had a positive prick test to celery, a vegetable of the Compositae family. It is well-known that fruits and vegetables belonging to this botanic group can cross-react and provoke oral, gastrointestinal or anaphylactic symptoms, especially in atopic subjects (3). Patients sensitized to Compositae pollens

may cross-react to the topical application (or ingestion) of chamomile tea (4). Rodríguez-Serna et al. (5) have reported allergic and systemic contact dermatitis from chamomile tea.

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Ewe milker's hand dermatitis

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Key words: hand eczema; protein contact dermatitis; ewe wool; ewe milker; occupational. © Munksgaard, 2000.

Case Report

A 25-year-old shepherd from Sardinia presented with a 4-year history of recurrent hand eczema. He had no family or personal history of atopy. He had worked for several years as a mason, a mechanic and a woodworker without any skin problems. In July 1995, he had changed his job to sheep breeding. 3 months later, he developed an itchy, fissured hand dermatitis that lasted for the whole lambing and milking season (December to July). The eczema partially cleared in summer, only to recur at the beginning of the new milking season. It was exacerbated by the activity of milking the ewes, which the patient did with bare hands, morning and evening, for a total of 3 h a day. The dermatitis worsened year after year, and eventually, in spite of topical corticosteroid treatment, he would develop intense itch, oedema and fissures within minutes of starting to milk. He also attended to lambing and to curd making. The latter activity involved dipping his bare hands into warm (40°) milk for long periods, and exacerbated his skin symptoms.

Patch testing with the GIRDCA standard series, including wool wax alcohols and Amerchol L-101, was negative. Scratch-chamber tests with ewe wool, dander and milk, supplied by the patient, were performed on the volar surface of the forearm, with readings at 20 min, D2 and D4. All were negative. An open application test on involved skin (dry eczema, no fissures) was per-

formed as follows: a lock of wet ewe wool and a piece of gauze soaked in ewe milk were lightly rubbed on the patient's right and left palm, respectively, then left in place for 20 min. After removal, whealing was clearly visible at the site where the lock of ewe wool had been applied (Fig. 1), while the milk elicited no reaction. The wheal cleared in 40 min. 2 weeks later, an open application test with curd provided by the patient was performed in the same way and was negative. Total IgE was



Fig. 1. Whealing of the hypothenar eminence elicited by a 20-min application of ewe wool.

28 KU/l. RASTs to sheep wool and dander and to sheep milk were negative, as were RASTs to common pollen and food allergens.

Comment

Protein contact dermatitis is a chronic recurrent dermatitis, usually presenting as hand eczema, caused by contact with a proteinaceous substance. Acute urticarial or vesicular exacerbations may occur shortly after contact with the causative protein. Though the exact pathogenetic mechanism remains unclear, it is thought to be some combination of Types I and IV allergies (1). The diagnosis relies on the positivity of immediate-type allergy tests, mainly prick or scratch tests, but also application tests on normal or involved skin, performed with the suspected material. Specific IgE may sometimes be detected in the serum. Patch tests are usually negative (2). Protein contact dermatitis is generally occupational, food handlers, such as kitchen workers and caterers, bakers, slaughterhouse workers, butchers and veterinarians, being among the occupations at risk. In Finland, it is particularly frequent in dairy farmers, due to contact with cow hair and dander (3). A milker with protein contact dermatitis from cow milk has also been reported (4).

To the best of our knowledge, this entity has never been described before in ewe milkers, though there are 3 cases reported of ewe milkers' hand eczema with positive patch-test reactions to ewe wool (5, 6). 2 of these also showed weak reactivity to wool wax alcohols at D2 (5). Patch test readings at 20 min were negative. In only 1 case was specific IgE to sheep epithelium looked for and found to be negative. No other tests for immediate reactivity to ewe wool were performed. Contact allergy to wool grease present in ewe wool was thus advocated as the likely cause of hand eczema in ewe milkers. The previous cases show striking clinical resemblance to our patient, in whom, however, we were not able to demonstrate any delayed reactivity to ewe wool: both patch tests and scratch-chamber tests to ewe wool as is and to wool wax alcohols were negative at D2 and D4.

Though it is immediate-type reactivity that supports the diagnosis of protein contact dermatitis, cases are reported where both immediate contact allergy and delayed contact allergy to the causative substance have been demonstrated (1). Because in the previous cases of ewe milkers' hand eczema, evidence of immediate allergy was not thoroughly looked for, we suggest that this entity might be the same as we observed in our patient, and that it could possibly be due to some proteinaceous substance present in ewe wool rather than to wool grease. In our patient, wet work (curd making) may have compromised the skin barrier, enhancing absorption of the allergen(s) during repeated handling of the ewes in the lambing and milking season. As for the reason why an immediate urticarial reaction could be elicited only when ewe wool was applied on involved skin, and not when it was scratch-chamber tested on normal skin, we can only postulate the presence of higher concentrations of inflammatory mediators and specific IgE in involved skin.

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Contact dermatitis from nickel in mobile phones

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Key words: nickel; allergic contact dermatitis; mobile phone; new sources of nickel exposure. © Munksgaard, 2000.

Case Reports

Case no. 1

1 of the authors, a 36-year-old dermatologist with a history of jewellery intolerance, developed a dermatitis of the right side of the chin with itching and red papules. She had noticed that the dermatitis worsened after the prolonged use of her mobile phone (Ericsson). Patch

tests with the GIRDCA standard series (Trolab-Hermal) gave a positive reaction to nickel sulfate 5% pet. at D2 and D3. This patient solved the problem by covering the mobile phone with a plastic case.

Case no. 2

A 32-year-old woman presented with an 8-month history of dermatitis on her left cheek. The skin lesions

persisted despite avoidance of cosmetics, and treatment with topical corticosteroids produced only temporary improvement. The patient suggested that the dermatitis might be caused or worsened by her mobile phone (Ericsson). Patch tests with the GIRDCA standard series (Trolab-Hermal) and a preservatives series showed only a positive reaction to nickel sulfate 5% pet. at D2 and D3 (++/+++). The dimethylglyoxime test for nickel on the side of the patient's phone was positive. The skin lesions rapidly resolved after covering the mobile phone with a plastic case.

Discussion

The mobile-phone culture is spreading so rapidly that possible effects connected with its use are still underestimated. Nowadays, Italy holds the highest ratio between the number of mobile phones and population. Sales of mobile phones put Italy in 1st place in Europe and 3rd place in the world after the USA and Japan

Some mobile phones may contain nickel and should be included among possible sources of nickel exposure.

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Delayed-type hypersensitivity reaction to kava-kava extract

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Key words: kava-kava; cutaneous adverse drug reaction; systemic contact dermatitis; herbal remedies; positive patch test. © Munksgaard, 2000.

A beverage made from the dried root of the kava plant (*Piper methysticum*) is used widely in the South Pacific for its intoxicating effects. During the last decade, kava-kava root extracts also became increasingly popular in Europe for their tranquillizing properties; these are ascribed to several α -pyrones contained in these preparations (1).

Case Report

A 36-year-old woman consumed 120 mg of the kava-kava root extract Antares® daily over a period of 3 weeks for anxiety. 4 days after termination of this treatment, she presented in our outpatient clinic with a generalized rash and complained of severe itching. A generalized erythema and papules were observed, along with several wheals on the trunk. There were no signs of angioedema, nor did the patient suffer from dyspnoea. With short-term systemic treatment with corticosteroids and antihistamines, the rash cleared rapidly, but the itching persisted for several weeks.

6 weeks after clearance, Antares® was tested by prick and patch tests along with the European standard series. The prick test was negative after 20 min. The European standard series also yielded negative results on patch testing but Antares® was strongly positive as early as 1 day (D) at 1:1 as well as 1:100 dilution in pet., showing a crescendo reaction by D2 (Table 1). At that time, eczematous skin changes could also be seen at the prick

test site. Patch tests with Antares® 1:1 in 10 control patients were negative.

Discussion

Heavy kava users commonly develop a pellagrous rash that cannot be effectively treated by supplementing nicotinamide (2). Cessation or reduction of kava intake results in resolution of these skin changes. In Germany, about 60 adverse reactions to kava-containing drugs have been reported since their introduction, most of them affecting the skin or central nervous system. These reactions cannot be explained by the mechanisms postulated for the kava-induced dermopathy observed in the South Pacific, since the drugs in question were taken in small quantities over relatively short periods of time. Allergic contact dermatitis seems to be among the less frequent side-effects, since the 1st description dates back only to 1996 (3) and rashes are often caused by non-allergic pathways (4).

Given the increasing promotion of herbal drugs, more

Table 1. Patch test results with kava

	20 min	D1	D2	D3
petrolatum (pet.)	–	–	–	–
Antares® 1:1 pet.	–	++	+++	++
Antares® 1:100 pet.	–	+	+	(+)

allergic reactions to such preparations can be expected. It is therefore important to document this problem to increase public awareness that herbal drugs also carry this risk.

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Allergic contact dermatitis due to avena extract

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Key words: *Avena sativa*; allergic contact dermatitis; cosmetics; atopic dermatitis; medicaments; herbal remedies; plant extracts. © Munksgaard, 2000.

Case Report

A 3-year-old girl with atopic dermatitis developed a flare-up after application of a moisturizer, which was apparent on the right arm and on the hands. She had a family and personal history of other atopic diseases (hay fever and rhinitis). IgE levels were elevated (700 u/ml) and prick tests were positive to *Dermatophagoides farinae* and *Dermatophagoides pteronyssinus*.

Patch testing was performed with the GIRDCA standard series (Trolab Hermal), using Finn Chambers on Scanpor, and the suspected cream as is (Dermalibour with Rhealba® Oat Milk; Ducray Pierre Fabre, France). She was positive to the cream at D2 and D3 (++/+++). Enquiry of the manufacturers of the cream revealed that it contained *Avena sativa* (Avena Rhealba® oat extract), Vaseline oil and zinc oxide. Further patch tests with the individual ingredients, kindly supplied by the manufacturers, showed positive reactions to Avena Rhealba® as is at D2 and D3 (++/+++) (Table 1). Patch tests with Avena Rhealba® on 20 volunteers were negative. A prick test with Avena was also positive.

The patient had complete regression of her dermatitis after avoiding further contact with the cosmetic cream.

Discussion

Oat, also known as wild oat (*Avena sativa*), is an annual grass widely cultivated for its edible grain. The common name of this herb is avena or oat, belonging to the Poaceae (Gramineae) family. In alternative medicine, oat is considered to be of particular benefit in dyspepsia, and a stimulant for the nervous system; a tea made from oat straw has been recommended for chest problems. *Avena sativa* is frequently used for various purposes in cosmetics. Oat is commonly used as oat extract in moisturizers. Oat colloidal grain suspensions have been used for decades in the treatment of atopic dermatitis.

To our knowledge, there are no previous reports of allergic contact dermatitis due to avena caused by cosmetics. In 1981, Dempster (1) described an occupational allergic contact dermatitis from oats and bran. Riboldi et al. (2) noted a worsening of atopic dermatitis in 3 children after oatmeal extract baths. Pigatto et al. (3) reported no evidence of sensitization to topical oat in a group of children under 2 years of age with mild atopic dermatitis.

Table 1. Patch test results

Tests	Results	
	D2	D3
Dermalibour with Rhealba® Oat Milk cream	++	++
Vaseline oil	–	–
Oat extract Rhealba® aq.	+	++
Oat extract Rhealba®, diluted	+	++
Oat extract Rhealba® as is	+	++
zinc oxide, diluted	–	–
zinc oxide, pure	–	–

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Simultaneous allergic reactions to quaternium-15 and methenamine

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Key words: quaternium-15; methenamine; quaternary ammonium compounds; formaldehyde; allergic contact dermatitis; preservatives; cosmetics; occupational; cross-sensitivity. © Munksgaard, 2000.

Quaternium-15 (chloroallyl methenamine chloride, N-(3-chloroallyl) hexaminum chloride, 1-(3-chloroallyl)-3,5,7 triaza-1-azolniaadamantane chloride, Dowicil 200, Dowicil 100, Dowicil 75) (1) and methenamine (hexamethylenetetramine, hexamine, aminoform) (2) are chemically-related quaternary ammonium compounds with formaldehyde-releasing capacity. Quaternium-15 is a chloroallyl derivative of methenamine. Despite their close chemical structure, I have found no data on cross-sensitivity between them.

Quaternium-15 is a potent formaldehyde donor and widely used as a preservative in cosmetic products such as shampoos, conditioners, eye cosmetics, moisturizing lotions and creams. Occupational sensitization is rare, but quaternium-15 may be incorporated in cutting oils, detergents and soaps, floor waxes and polishes, latex-based paints, laundry starch, paper and pulp products, textile finishing solutions, spinning solutions, printing pastes and joint cements (1).

Methenamine salts are used as urinary antiseptics (2). Methenamine was formerly a frequent sensitizer in the rubber industry, but nowadays only rarely used except for textile adhesives (3). Methenamine is also a catalyst for phenolic resins (3).

Patients, Methods and Results

Between 1985 and 1998, a total of 20,567 patients were tested with the standard patch test series in the Department of Dermatology at Helsinki University Central Hospital. Allergy to quaternium-15 (1% pet.) occurred

in 109 (0.5%) patients. 77 (71%) of these were simultaneously positive to formaldehyde (1% aq.).

Methenamine (1% pet.) was tested in 32 of these 109 quaternium-15 sensitive patients. Simultaneous methenamine allergy occurred in 21 patients (Table 1). 20 of these 32 patients were positive to formaldehyde. 7 (35%) of the 20 formaldehyde-sensitive patients were simultaneously positive to methenamine. 4 (33%) of the 12 formaldehyde-negative patients were positive to methenamine.

In addition, between 1995 and 1998, we had 4 patients positive to methenamine but negative to quaternium-15 and formaldehyde. Similar cases tested before 1995 were not traced, because the methenamine data were not in computer files.

Discussion

Simultaneous allergic reactions to quaternium-15 and methenamine could be explained by their formaldehyde-releasing capacity. Most of the quaternium-15 allergic patients also reacted to formaldehyde. Their proportion, 71%, was in accordance with previous studies, all reporting greater than 50% cross-reactivity (1). Approximately the same proportion, 1/3, of both formaldehyde-positive and formaldehyde-negative quaternium-15 sensitive patients also reacted to methenamine. The result implies that the simultaneous reactions to quaternium-15 and methenamine might more probably be related to their close chemical structure than to their common formaldehyde-releasing capacity.

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Table 1. Results of methenamine and formaldehyde patch tests in 32 quaternium-15 sensitive patients

	Methenamine +	Methenamine –	
formaldehyde +	7 (35%)	13 (65%)	20 (63%)
formaldehyde –	4 (33%)	8 (67%)	12 (37%)
	11 (34%)	21 (65%)	32

Reproducibility of titre of contact hypersensitivity to *Parthenium hysterophorus*

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Key words: Asteraceae; patch tests; reproducibility of results; Compositae; *Parthenium hysterophorus*; plants; plant extracts; contact allergy. © Munksgaard, 2000.

Previous studies from our department (1, 2) described the use of serial dilutions of plant antigens as a measure of the degree of contact hypersensitivity. 10-fold dilutions of the standard antigen were applied to the back and the greatest dilution of the antigen that produced a positive patch test was recorded as the titre of contact hypersensitivity (TCH). We have evaluated the reliability of the procedure by determining the titre of contact hypersensitivity in duplicate on both sides of the back.

Patients and Methods

25 patients, 17 male and 8 female, of age varying from 30 to 75 years (mean 43.88 years), and with airborne contact dermatitis for 6 months to 20 years (mean 6.9 years), were recruited for this study. Diagnosis in each case was confirmed by patch test. Subsequently, each patient was concomitantly tested on the left and right sides of the back with serial dilutions of standardized *Parthenium* extract.

Preparation of the standard plant extract

The *Parthenium* extract was prepared using the method described by Pasricha & Singh (3). A large quantity of mature, healthy-looking leaves of *Parthenium hysterophorus* was cleaned, air-dried at room temperature over 7–10 days and powdered in a blender. 50 g of the dried leaf powder was thoroughly mixed with 300 ml of water and filtered through Whatman no. 1 filter paper to obtain a clear filtrate. 10-fold dilutions varying from 1:10 to 1:100000 were prepared by adding distilled water. These were then stored in an airtight glass bottle in a refrigerator at 4°C.

Preparation of antigen-impregnated discs (3)

For preparing antigen-impregnated discs, Whatman no. 3 filter paper was allowed to soak up the standard plant extract for 30 min, after which the sheet was dried in air for 24 h. The central part of the sheet was then cut into 1 cm² pieces and stored in a dry container at room temperature until used for patch tests.

Patch test procedure

At the time of patch testing, the antigen-impregnated discs were wetted with a drop of water and applied on the upper back of patients symmetrically on both sides.

Each disc was pressed onto the skin firmly to obtain good occlusion. The patches were removed after 48 h, reading being recorded 30 min later.

None of the patients had used systemic or topical corticosteroids within 24 h prior to the testing. The back in all patients was free of any dermatitis. All the test allergens were applied simultaneously. The patches were removed after 48 h and the TCH and intensity of the patch test recorded on each side.

Results

The TCH to *Parthenium* ranged from 1:10 to 1:1000. In 19 (76%) patients, the TCH was identical on both sides. In 6 (24%) patients, the TCH was different on the 2 sides. 4 patients had greater TCH values on the left side and 2 patients had greater values on the right. The difference in the TCH was of 1 (10-fold) dilution in all 6 patients.

Of the 19 patients who had an identical TCH on both sides, the intensity of the patch test reaction was also identical in 4 patients. In 15 patients, the reaction was slightly more intense on the left side in 11 patients and on the right in 4 patients.

Discussion

Our study demonstrates that the TCH is a reliable measure. Our findings indicate that when TCH is used to compare the degree of hypersensitivity between patients or to monitor the response to treatment by serial measurements, it should be recorded without regard to the intensity of the patch reaction, and differences of 1 dilution may be ignored.

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Positive patch test to diclofenac in Stevens-Johnson syndrome

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Key words: erythema multiforme; diclofenac; positive patch test; cutaneous adverse drug reactions; non-steroidal anti-inflammatory drugs. © Munksgaard, 2000.

Diclofenac sodium is a non-steroidal anti-inflammatory derivative (NSAID) of phenylacetic acid, with analgesic and antipyretic effects. Adverse reactions to this drug are usually pseudoallergic, but some cases with immunologic mechanisms have been reported (1–3).

Case Report

A 70-year-old man with diffuse arthrosis was admitted with a widespread, pruriginous, erythematous, maculopapular rash that had appeared 10 days after he had started oral therapy with diclofenac 100 mg/day. The eruption was particularly evident on the backs of the hands and insteps of the feet and was accompanied by fever and mouth ulcers. Treatment with antihistamines and systemic corticosteroids was prescribed, and the lesions disappeared after 7 days via exfoliation.

Prick and intradermal tests with diclofenac were negative. A patch test was positive at D2 and D4 to Voltaren® ampoules (diclofenac 25 mg/ml), as is, though negative to diclofenac 0.61% pet., diclofenac 1.12% pet., and to the European standard series. 5 control patch tests with the same preparations proved negative. Biopsy of the positively patch-tested skin showed epidermal spongiosis with lymphocytes. Oedema and a lymphocytic perivascular infiltrate were observed in the dermis.

Discussion

Erythema multiforme and related syndromes produce mucocutaneous reactions to certain antigenic stimuli, usually infections or drugs; thus, a common pathogenesis appears unlikely (3). In our patient, the positive patch test suggested a cell-mediated immune response (Type IV) associated with a delayed-onset cutaneous eruption. Some authors have suggested a rôle for patch testing in drug-induced maculopapular rashes, including those observed in Stevens-Johnson syndrome (4). Our findings suggest that patch tests with Voltaren® ampoules, as is, may constitute a safe and reliable tool in the diagnosis of this type of rash.

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Airbag dermatitis

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Key words: air-bag dermatitis; irritant contact dermatitis; chemical burn; air-bag adverse effects; road traffic accidents; accidental injury prevention. © Munksgaard, 2000.

Air bags are lifesaving restraining devices installed in cars, activated by sudden deceleration due to an impact. Sudden deceleration leads to the ignition of a sodium azide cartridge, which liberates nitrogen and other gases and immediately inflates a rubber safety bag. With the wider use of these safety devices, new unexpected

cutaneous and traumatic injuries have increasingly been reported.

Case Report

A 35-year-old man presented with an acute dermatitis involving his left arm. He said that, while slowly driving

his car, he had accidentally run into the pavement; as a consequence, the air bag deployed. Inspection revealed an erythematous edematous dermatitis mostly involving the volar side of his left arm and an ecchymotic lesion of his left wrist. The anti-poison centre was consulted and sodium azide was recognized as the chemical present in the air bag. A diagnosis of chemical first-degree burn having been made, the patient denied any respiratory problem and refused a period of admission under observation. No systemic signs developed and the dermatitis healed in a week with topical corticosteroid treatment, leaving only slight post-inflammatory pigmentation.

Discussion

Azide is the propellant in air bags and aircraft escape chutes. When an air bag deploys, sodium azide may form sodium hydroxide and nitrogen gas, which may induce alkaline chemical irritation and chemical burns. Talcum powder used in the packaging of air bags may contribute to irritate the skin. A further thermal injury may sometimes complicate the damage, as the gases are ignitable when they come into contact with overheated items of the car engine (1). Cutaneous injuries have been reported to be about 7–8% of all injuries caused by air-bag deployment. They are erythematous and desquamative irritant contact dermatitis or true burns of varying degree, especially involving the face, upper arms and chest (2, 3).

Ocular and systemic damage are also reported. Ocular damage (varying from abrasions and contusions of the globe to retinal detachment) can be caused by mechanical injuries due to the sudden deployment. Chemical alkali keratitis may also leave permanent visual impairment (4, 5). Inhalation of the air-bag contents may produce airway inflammation, particularly dangerous in

asthmatic patients (6). Fractures in patients with osteoporosis, and even fatal injuries in children improperly restrained in the front passenger seat, have also been reported (7, 8).

However, as an American retrospective review concluded, an overwhelming majority (96%) of the injuries related to air-bag deployment are of only minor importance, and the potential life-saving capacity of air bags is unquestionable (9).

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Lymphedema of the hand following recurrent erysipelas secondary to fissured irritant contact dermatitis

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Key words: lymphedema; irritant contact dermatitis; occupational hand dermatitis, recurrent erysipelas. © Munksgaard, 2000.

We report a patient with secondary lymphedema (1, 2) of one hand after recurrent erysipelas which complicated occupational irritant contact dermatitis of the hands (3–5).

Case Report

A 54-year-old hairdresser had suffered for 10 years from a work-related irritant contact dermatitis of both hands, which fissured mainly in her interdigital web spaces and on the fingertips. While she showed a positive patch test to glyceryl thioglycolate, there was no indication of cur-

rent clinical relevance, as she was avoiding contact with "acid" perms. During the last 2 years, recurrent episodes of redness, hyperthermia and edema of the left hand had additionally been observed, each lasting a few weeks, and initially accompanied by lymphangitis (3). In spite of short-term antibiotic therapy, edema of the left hand had since persisted, independent of the acuity of her hand dermatitis.

On examination, the dorsum and fingers of the left hand were severely and relatively firmly swollen. The interdigital spaces and the back of the left hand showed

diffuse erythema, while on the fingertips of both hands, multiple small erosions and superficial fissures were noted. The antistreptolysin titer was elevated (250 IU/l). Antithrombin III was normal. After the lymphedema of the left hand was classified as grade II (2), daily manual lymph draining massages and compression bandages were prescribed, which led to a marked reduction of lymphedema. For home use, a custom-made firm compression glove was recommended. In addition, courses of manual lymph draining massages were regularly repeated every few weeks.

Comment

Fissures occurring in the course of hand dermatitis probably served as point of entry for streptococci. Thus, both the erysipelas and the lymphedema can be regarded as a complication of the occupational skin disease. For the prevention of further relapses, we started long-term therapy with antibiotics – because of previous allergy to penicillin, oral erythromycin 1 g per day for 5 days every 4 weeks (6).

As often observed after recurrent erysipelas, obstruction of the vessel system can induce secondary lymphedema (7). Lymphedema differs from other forms of edema by its proliferation of connective tissue, sclerosis, occasional fat deposition (8) and tendency to progress. This emphasizes the need for intensive long-term treatment to avoid irreversible end-stages or the development of angiosarcoma (9), as in Stewart-Treves syndrome. Thus, erysipelas-induced secondary lymphedema of the hands following contact dermatitis is most likely a rare,

but important, complication which needs careful therapeutic attention.

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Occupational protein contact dermatitis and rhinoconjunctivitis caused by spathe (*Spathiphyllum*) flowers

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Key words: occupational; allergy; gardener; rhinitis; conjunctivitis; contact urticaria; protein contact dermatitis; generalized urticaria; RAST; *Spathiphyllum*; (Araceae); yucca; plants. © Munksgaard, 2000.

Case Report

A 33-year-old non-atopic man worked for a firm that maintained plants in clients' offices. 10 years earlier, he had done the same job for 2 years without symptoms. Within a few months of his return, he had developed work-related, dermatitis and occasional wheals on the hands and forearms, with later rhinoconjunctivitis. He related his symptoms to spathe flowers, yucca and weeping figs (*Ficus benjamina*).

Prick testing was performed as previously described (1). Of 11 common inhalation allergens (Allergologisk Laboratorium A/S, ALK, Horsholm, Denmark), mug-

wort gave a 2+reaction. 5 different spathe flowers (flower, stem and leaves), *Spathiphyllum wallisii* (petite), *S. Mauna Loa*, *S. cupido*, *S. illusion* and *S. sensation*, gave 3+reactions with pseudopodia. Yucca and weeping fig 2× gave 2+allergic reactions, while natural rubber latex, and 20 other plants from the patient's workplace, were negative. 20 control persons were negative on prick testing to spathe flowers, yucca and weeping fig. Patch tests with the European standard series, 29 plant extracts (2) and 16 plant allergens (2) were negative. Patch tests with flower, stem and leaf of the 5 spathe flowers, weeping fig and yucca, caused slight irritation.

All spathe flowers also gave class 1–2 positive RASTs.

The RAST to *Ficus benjamina* was negative. Total IgE was 134 kU/l. A nasal provocation test with *S. petite* was positive, as was a conjunctival provocation test.

After diagnosis, the patient tried to return to work but within hours, he had developed local and generalized whealing and severe rhinoconjunctivitis. He is now being re-trained for a new job.

Discussion

36 species of *Spathiphyllum* exist in the Philippines, Central and tropical South America (3), belonging to the Araceae family. Araceae may contain glycosides, alkaloids, crystals of calcium oxalate, which are intensely irritating (3, 4), and proteolytic enzymes (4). The prick test reactions to yucca and *Ficus benjamina* may represent cross-reactivity to spathe flowers, though specific allergy to other plants cannot be excluded. There have been 2 earlier reports of allergy to spathe flowers, *S. wallisii* (1) and *S. floribundum* (5). In IgE immunoblotting, one heavy band was detected at about 14 kD (1). An IgE-binding protein with molecular weight 14 kD has been identified as profilin in several plant species (trees, grasses, weeds) and suggested as a plant pan-allergen (6). In addition, 14–15 kD allergens have been demonstrated in several vegetables and also in natural rubber latex (7, 8). Interestingly, our patient was the brother of a patient previously reported with occupational allergy to spathe flowers (1).

Contact dermatitis has been reported from other Araceae: irritant contact dermatitis from *Dieffenbachia* (9); allergic contact dermatitis from *Philodendron* (10–13) and *Scindapsus* (14). The Type-IV allergens in philodendrons are resorcinols, which share side-chains with allergenic catechols of Anacardiaceae (15–17). Philodendrons are also toxic, causing acute poisoning (18) and even infant death (19).

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