CONTACT POINTS

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Contact urticaria photoinduced by benzophenones

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Key words: benzophenones; cosmetics; photocontact urticaria; photosensitivity; sunscreens.

Case Report

A 31-year-old man presented with a 7-year history of recurrent facial dermatitis. Until 2 years ago this had occurred in the winter only, but now was also to be seen in the summer, involving the whole face including the lips. He likened it to a pruriginous sunburn that appeared within 6–12 h and disappeared in 48 h via desquamation. Symptoms seem to be triggered off by winter sporting in sunny conditions; the sunnier the weather, the more acute the symptoms. As sole treatment, he used a sunscreen that proved quite ineffective.

The Saidman test showed a normal MED at 1500 mJ/cm^2 with polychromatic spectrum in this phototype IV patient. Iterative phototests with the sun simulator and the UVASUN lamp caused no abnormal skin reaction. Conversely, among the photopatch tests, urticarial reactions appeared within minutes of irradiation, which took place 24 h after their application; they involved benzophenone-3 in the UVA (10 J) and polychromatic spectrum (0.75 MED) and benzophenone-10 in the UVA (Fig. 1). These reactions were fleeting and vanished within 30 min. There was no reaction among the photopatch tests that had not been irradiated. Similarly, there was no delayed reaction after 24, 48 and 96 h. The patient's own sunscreens, which contained benzophenone-3, were also tested. Irradiation taking place 2 h after they had been applied caused an erythematous reaction within 15 min, receding in less than 1 h.

We diagnosed a photoinduced urticaria to benzophenones. Since the patient stopped using sunscreens containing benzophenones no further abnormal cutaneous reaction has been reported.

Discussion

Photoinduced contact urticaria does not belong to the traditional photoallergies; yet a few publications have now and then discussed such symptomatologies. Thus, in 1975, Horio reported the case of a woman suffering from urticarial and eczematous lesions which, based on photobiological investigation, proved to be a urticarial reaction to chlorpromazine immediately following UVA irradiation (1). This was further enhanced by positive patch tests and photopatch tests after 24 h showing an eczematous reaction. A passive transfer test was positive, in accordance with the immuno-allergic nature of the immediate reaction. In 2 other instances the symptomatology was of similarly eczematous type with, as photobiological investigation highlighted, an immediate reaction only to benzophenone-3, as was the case in our patient, and also to methenamine hippurate (2, 3). Besides this, benzophenones are also known to cause contact urticaria

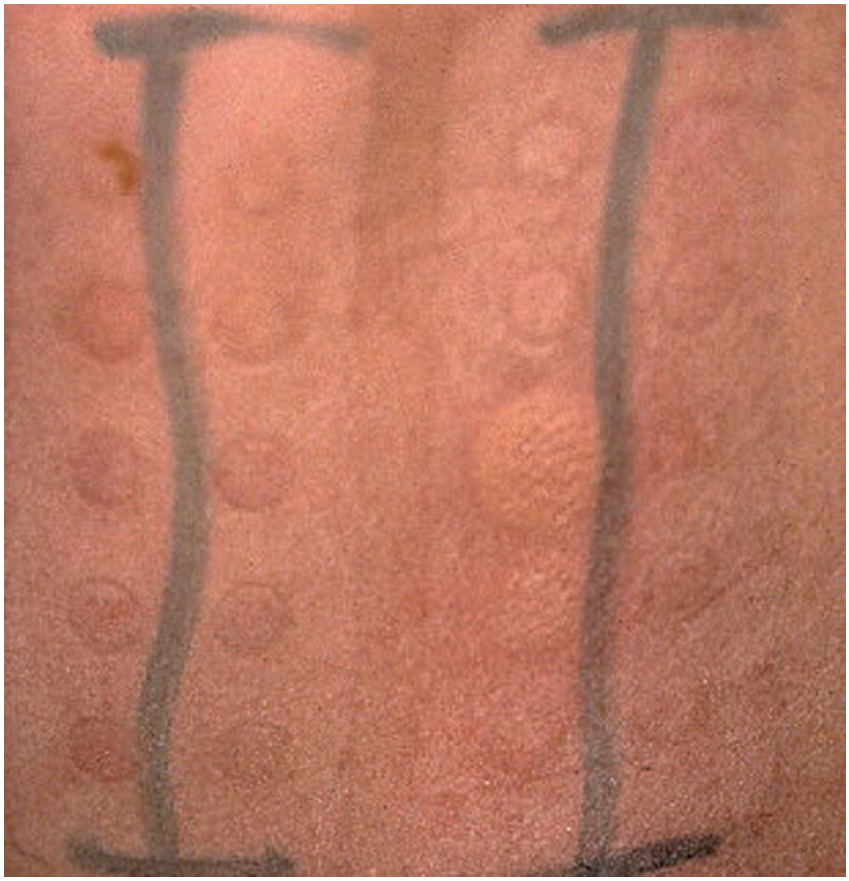

Fig. 1. Photopatch tests 15 min after UVA irradiation.

that is not photoinduced. Lastly, a publication has also discussed solar urticaria with tetracycline (4).

As far as our patient is concerned, the evolution of symptoms suggests a combination of immediate and delayed hypersensitivities. In our photobiological investigation we induced an immediate reaction only, and there was no delayed reaction, which may be explained by the fact that such an investigation does not duplicate exactly the natural conditions under which sunscreens are used or those of sunshine exposure itself, with, in particular, a higher ratio of UVA during the time of exposure, causing a different biological response. Thus, though a short UVA exposure might trigger off a contact urticaria, it might have to last longer to cause eczema. Such coexistence of immediate and delayed reactions is not exceptional, but seems to be relatively specific to certain allergens (5).

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Contact allergy to octocrylene

First 2 cases

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Key words: cosmetics; octocrylene; photoallergic contact dermatitis; sunscreens.

Patients and Methods

Photobiological testing was performed with polychromatic irradiation (1000 W Xenon light, Dermolum III, K-Müller, Moosinning, Germany) filtered with a Schott WG 305 filter 1 mm (Schott, Clichy, France) and a high-pressure metal halide UVA lamp (2000 W. Uvasun, Mutzhas, Munich, Germany). Irradiation energy measures were made with Osram UV Centra (Munich, Germany). Polychromatic phototests and UVA phototests were standardized: 2 minimal erythema dose (MED) every other day up to 7 MED and 30 J/cm^2 every other day up to 90 J/cm^2.

Patch tests and photopatch tests were performed with the French Society of Photodermatology standard series (1), Chemotechnique plants series, sunscreens used and the components of all sunscreens used, in triplicate. The patches were removed after 1 day (D). One set was irradiated with UVA (5 J/cm^2), the 2nd was irradiated with a suberythemal dose of polychromatic irradiation and the 3rd served as control. Reading was performed at D2 and D3 after irradiation.

Case no. 1

A 55-year-old man presented in June 2000 with an erythemato-vesicular eruption restricted to areas of skin where he had successively applied 3 different sunscreens a few days before. He had previously noted a cutaneous reaction after handling cypress trees. Polychromatic minimal erythema dose and UVA-MED were within the normal range: respectively, 1500 mJ/cm^2 and 30 J/cm^2. Polychromatic phototests and UVA phototests were negative. Photoallergologic studies (Table 1) showed photoallergy to octocrylene (+ + with UVA and + with UVB).

Case no. 2

A 31-year-old man presented in July 2000 with acute photodistributed eczema after application of 2 sunscreens. He had a history of cutaneous allergic reactions after topical use of ketoprofen (Ketum®, Menarini, Rungis, France) and chlorproethazine (Neuriplège®, Genevrier,

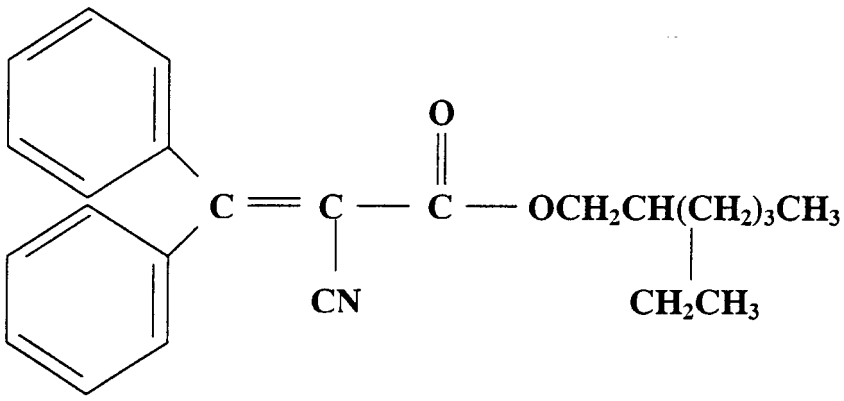

Fig. 1. Chemical structure of octocrylene.

Table 1. Photoallergologic studies: case no. 1

	Patch tests	Photopatch tests UVA	Photopatch tests UVB
triclosan	–	–	+
fentichlor	–	+ +	+ +
fragrance mix	–	+	–
promethazine	–	+	–
benzophenone-3	–	+	–
young cypress	–	+	–
Ambre Solaire® IP 7, (Garnier, Clichy, France)	–	+ +	–
Ambre Solaire® IP 12	–	+	–
Vichy Capital Soleil® IP 15/6	–	–	–
octocrylene	–	+ +	–

Sophia Antipolis, France). Polychromatic MED and UVA-MED were normal: respectively, 4000 mJ/cm^2 and 30 J/cm^2. Polychromatic and UVA phototests were negative: respectively, 5 MED and 90 J/cm^2. Photoallergologic studies (Table 2) showed photoallergy to octocrylene (+ + + with UVA).

In these cases, octocrylene was present in all 5 sunscreens used. We think that the negative results of photopatch tests for 2 of them (Vichy Capital Soleil® Lait IP 15/6 and Vichy® Capital Soleil Lait IP 60/16, Vichy, Courbevoie, France) could be explained by smaller concentrations of octocrylene.

Discussion

Due to their wider use in cosmetics, as well as in sun-protection products, sunscreens are now the most frequent photoallergens, particularly benzophenones and cinnamates (2–6). Octocrylene (Fig. 1) is an anti-UVB solar filter which has been used for less than 10 years in sunscreens and cosmetics. To the best of our knowledge, it has never previously been reported as an allergen or photoallergen.

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Table 2. Photoallergologic studies: case no. 2

	Patch tests	Photopatch tests UVA	Photopatch tests UVB
tetrachlorosalicylanilide	–	+ +	+ +
fragrance mix	+	+	+
chlorpromazine	–	+	+
chlorproethazine	+	+ +	+ +
ketoprofen 2%	–	+ +	+ +
fragrance mix	+	+	+
Ambre Solaire® IP 25	–	+ +	–
Vichy Capital Soleil® IP 60	–	–	–
octocrylene	–	+ + +	–

Allergic contact dermatitis from isopalmityl diglyceryl sebacate in lipsticks

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Key words: allergic contact cheilitis; allergic contact dermatitis; cosmetics; isopalmityl diglyceryl sebacate; lipsticks.

Case Reports

Case no. 1

A 35-year-old woman experienced worsening of lip dryness and itching 6 months before she consulted us. She had had cedar pollinosis and mild desquamating dermatitis on her perioral and periorbital areas since her teenage years. Patch tests showed a positive reaction to Lipstick A, which she had used for several years. Further patch tests with the 22 ingredients of Lipstick A showed a positive reaction to isopalmityl diglyceryl sebacate (DGS) 3% pet. (Table 1), which was the actual concentration of the substance used in the lipstick. Her lip and perioral dermatitis improved after using lipsticks without DGS.

Case no. 2

A 41-year-old woman had developed itching, erythema and scaling on her lips 2 weeks before she visited us. She had a past history of contact dermatitis from disinfectants, plasters and lipsticks in her twenties. On patch testing, she was positive to 5 lipsticks that she had used for several years (Lipsticks B, C, D, E and F), which were of the same brand as Lipstick A, but different in colour. Further patch tests with the ingredients showed a positive reaction to DGS 3% pet. (Table 1), an ingredient common to all 5 lipsticks. Her cheilitis cleared after she stopped using these lipsticks. 10 normal controls were negative to DGS 10% pet.

Comment

DGS is a relatively new base component of lipsticks that was developed in Japan in 1994. It has hygroscopic water-holding capacities and water-releasing abilities, as castor oil does, and is considered a favourable supplement to branched fatty acid esters which tend to cause lip dryness. Since then, DGS has been supplied by one producer and included, as far as we know, in at least 3 brands of Japanese lipsticks at concentrations of 3–29%.

Since the first report by Suzuki *et al*. (1) in 1999, there have been 7 cases of allergic contact cheilitis from DGS, including our 2 cases, as shown in Table 2. The period of time required for sensitization varies from 2 weeks to several years. Patch tests with DGS was performed at 3% in 3 cases and 10% in 4 cases, and all normal controls tested at 10% were negative. We suggest that optimal patch test concentration of DGS is 10% pet., and that 3% is too low, because the reaction of our case no. 2 did not become positive until the 5th day, and could have been missed if only routine D3 or D4 readings had been made.

The precise allergens in DGS are as yet unknown, but are likely to be impurities such as low molecular weight oligomers or incompletely esterified substances. 2 of the 3 brands have already withdrawn DGS base components from their lipsticks.

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Table 1. Patch test results

	D2	D3	D4	D5	D8
Case no. 1 35F					
Lipstick A as is	++	++			
Isopalmityl diglyceryl sebacate (DGS) 3% pet.	+		+		
21 other ingredients in Lipstick A	–	–			
26 Japanese standard allergens	–	–			
Case no. 2 41F					
Lipsticks B, C, D, E and F as is	–		+		
Isopalmityl diglyceryl sebacate (DGS) 3% pet.	–			+	+
21 other ingredients in Lipstick A	–	–			
26 Japanese standard allergens	–	–			

Table 2. Case reports

Reference	Year	Patient	Time required for sensitization	% DGS in lipstick	DGS patch test concentration	Result
(1)	1999	27 F	1 month	29%	10% pet.	+
(2)	2000	29 F	2 weeks	18%	18% pet.	++
(3)	2000	26 F	2 months	24%	24–2.4% pet.	++
(4)	2001	26 F	Several months	17%	10% pet.	++
		31 F	Several months	3%	3% pet.	+
Present case	2001	35 F	Several years	3%	3% pet.	+
	2001	41 F	Several years	3%	3% pet.	+

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Metal allergy resurfaces in failed hip endoprostheses

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Key words: metal allergy; surface metal-to-metal hip endoprostheses.

In the 1970s, an unexpectedly high frequency of metal allergy was found in patients with metal-to-metal hip prostheses. This was not the case in those with metal-to-plastic prostheses adopted in the 1980s (1). Surface metal-to-metal hip replacements in the 1990s have caused such concern to resurface, particularly in more active, younger patients

In patients with metal-to-metal hip prostheses, both cobalt and chromium can be detected in the blood, urine and hair (2). *In vivo* studies have found metallic particles in the surrounding tissues. This has been suggested to cause a cell-mediated immune response leading to loosening at the prosthesis–bone interface (3). However, Burrows concluded that there was insufficient evidence to recommend non-metallic prostheses in nickel-allergic patients (4).

In our orthopaedic department, 200 surface metal-to-metal (containing nickel, cobalt and chromium) hip replacements have been performed since 1995. The aim of our study was to evaluate the incidence of hypersensitivity to metals in patients with failed and asymptomatic hip endoprostheses.

Patients and Methods

The study encompassed 5 patients with endoprosthesis failure due to joint loosening (EPFG) and 18 randomly selected patients from the above-mentioned series of 200 patients, matched for age and sexTable 2. The patients in the control group had no joint loosening. At initial consultation, patients were asked about prior nickel sensitivity, current and previous dermatological disease and atopy. None had been patch tested prior to operation. Patch tests were carried out to the TRUE TEst nickel, potassium dichromate and cobalt. Readings were carried out at 2 and 4 days after application of the tests. The skin reactions were classified as follows: 0, negative reaction; +, erythema and oedema; ++, erythema and oedema with papules and vesicles confined within the chamber; +++, erythema with vesicles and papules extending beyond the chamber; and IR, irritant reaction.

Results

There were 5 patients in the EPFG: 3 females, 2 males, mean age 50. There were 18 patients in the control group: 10 females, 8 males, mean age 53.6. The mean time interval from metal implantation to patch testing was 17 months in the EPFG and 19 months in the control group. Table 1 shows the proportion of patients with a history of metal sensitivity and patch test results in both groups.

None of the patients in either group who reported symptoms of nickel sensitivity were patch test positive. 3 patients in the EPFG were found to be nickel sensitive on patch testing. 2 were female and 1 was male. None of these had a prior history of atopy. 3 patients in the control group who had no prior skin disease were found to be positive at 4 days: 1 to dichromate (+), 1 to nickel and cobalt (+) and 1 to nickel only (++). Table 2 shows the relationship between the complications of hip replacement and patch test results in the EPFG. 2 patients were diagnosed as failed prosthesis because of infection, but with 3 patients the loosening could not be explained. The former group were not metal allergic whereas all the latter group were.

2 patients in the control group had skin symptoms. 1 male patient noted eczema over the replaced joint and 1 female patient gave a history of prior sensitivity to earrings. Both these patients had negative patch tests. None of the patients had occupational exposure to metals.

Table 1. Proportion of patients with a history of metal sensitivity and patch test results in both groups

	Control	EPFG
Number with history of metal sensitivity	2	0
Number positive on patch testing	3	3

Table 2. Relation between complications of hip replacement and patch test result in EPFG

	Failed prosthesis	
	Infection	Loosening
Number patch test positive	0	3
Number patch test negative	2	0

Discussion

The development of metal hypersensitivity to metals in 3 of 5 patients with a loosened hip prosthesis in our study is higher than that reported in other studies. Milavec-Puretiæ et al. found metal allergy in $> 20\%$ patients with a failed hip prosthesis (5). Cancilleri et al. found metal allergy in 15% of their patients with total hip replacements (6). Our results also suggest a relationship between loosening and metal sensitivity in patients with metal-to-metal prostheses. This concurs with the results observed in the 1970s.

The debate in the literature continues as to whether metal sensitivity leads to the instability of a prosthesis (7, 8) or the reverse. Our study has suggested a resurgence of metal allergy with the increased use of surface metal-on-metal hip replacements.

Prospective studies are now required to decide whether metal allergy leads to loosening, because these prostheses are being increasingly performed and with much younger patients than in the 1970s. The prospect of patch testing all patients who have surface metal-to-metal problems raises large workload problems for dermatology departments. However, *in vitro* techniques (9) are not yet as reliable.

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Failure to induce sensitization to budesonide in the guinea pig

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Key words: budesonide; corticosteroids, guinea pig maximization test; sensitization.

In humans, contact allergy to the corticosteroid budesonide is quite common (1, 2). It belongs to group B (3) and cross-reacts with some of group D2 (4), being recommended therefore as a marker in the European standard series. The purpose of this study was to investigate potential cross-reactivity. A recent guinea pig maximization test (GPMT) performed traditionally (5) had failed to show the sensitizing capacity of budesonide, but we attempted 2 modified GPMTs, having regard for the anti-inflammatory effect and the need for late readings (6, 7), by varying the dose and extending readings beyond day (D)2.

Materials and Methods

Substances

Induction was performed with budesonide (Yamanouchi Pharma, Glostrup, Denmark) and 2-methylol phenol (2-MP) (Merck, Darmstadt, Germany). Challenge was performed with budesonide.

Guinea pig maximization test (GPMT) no. I

The GPMT was performed with some modifications to increase its standardization and objectification, including statistical calculations from the patch test reactions and the inclusion of a positive control group (8).

Animals

54 albino female guinea pigs of the Dunkin–Hartley strain (J. A. Sahlin, Malmö, Sweden), weighing 300–400 g, were used. 48 animals participated in the actual sensitization study, 6 in the control group, and 42 in the test group, comprising 7 groups with 6 animals in each group, while the remaining 6 animals comprised an additional control group, sensitized to and challenged with the known sensitizer 2-MP. None of the animals were engaged in tests for topical irritancy, since the former GPMT did not show budesonide to be irritant (5).

Induction procedure

Budesonide was used for sensitization. For intradermal sensitization, 3 injections were given in a row on each side of the shoulder according to the procedure detailed elsewhere (8, 9) and with the concentrations given in Table 1. Pretreatment with sodium lauryl sulphate (SLS) and patch testing also followed the normal procedures (8, 9) with the budesonide concentrations given in Table 1.

Challenge procedure

Two weeks after the 2nd stage of sensitization, 25 μL of the test solution or vehicle was tested on the right flank according to earlier studies (9). 22 test animals received the suspected sensitizer on both patches, 10 animals received the suspected sensitizer only on the cranially located patch, while the vehicle alone was applied to the other patch and 10 animals in the reverse way. The test solution and the vehicle were patch tested in the same way in the 6 (2 + 2 + 2) control animals (Table 1). The positive controls were tested with 2-MP (8).

Rechallenge with budesonide at the concentrations and in the vehicles given in Table 1 was performed at the same time as challenge I in 42 test animals and 6 controls on the left, non-tested flank. The distribution of the positions of budesonide was based on a Latin square table.

Evaluation

The evaluation procedure is described in detail elsewhere (8). The same statistical comparisons as used earlier were used and the readings were blind, i.e. the left flanks were

Table 1. Data on ethanol solutions of budesonide used for sensitization, challenge, and rechallenge in GPMT I

Group no.	Sensitization		Challenge conc. w/v	Rechallenge conc. w/v
	Intracutaneous conc. w/v	Epicutaneous conc. w/v		
1	0.3	3.0	0.1	0.032, 0.01, 0.0032, 0.001
2	0.1	1.0	0.1	0.032, 0.01, 0.0032, 0.001
3	0.03	0.3	0.1	0.032, 0.01, 0.0032, 0.001
4	0.01	0.1	0.1	0.032, 0.01, 0.0032, 0.001
5	0.003	0.03	0.1	0.032, 0.01, 0.0032, 0.001
6	0.001	0.01	0.1	0.032, 0.01, 0.0032, 0.001
7	0.0003	0.003	0.1	0.032, 0.01, 0.0032, 0.001

Table 2. Data on budesonide used for sensitization, challenge, and rechallenge in GPMT II

Group no.	Sensitization			vehicle	Challenge		Rechallenge	
	Intracutaneous conc. w/v	vehicle	Epicutaneous conc. w/v		conc. w/v	vehicle	conc. w/v	vehicle
1	3.0	Acetone	3.0	Acetone	0.1	Acetone	0.032, 0.01, 0.0032, 0.001	Ethanol
2	3.0	Ethanol	3.0	Ethanol	0.1	Ethanol	0.032, 0.01, 0.0032, 0.001	Ethanol
3	2.0	Acetone	2.0	Acetone	0.1	Acetone	0.032, 0.01, 0.0032, 0.001	Ethanol
4	2.0	Ethanol	2.0	Ethanol	0.1	Ethanol	0.032, 0.01, 0.0032, 0.001	Ethanol
5	1.0	Ethanol	1.0	Ethanol	0.1	Ethanol	0.032, 0.01, 0.0032, 0.001	Ethanol

Table 3. Test reactions after sensitization to and challenge with budesonide in GPMT I

Sensitization substance *n*	Number of positive animals*		
	C	T	V
	6	42	20
Budesonide			
Group 1	0	1	0
Group 2	0	2	0
Group 3	0	0	0
Group 4	0	1	0
Group 5	0	0	1
Group 6	0	1	4
Group 7	0	0	2

*C, test reactions to the suspected sensitizer in control animals; T, test reactions to the suspected sensitizer in test animals; V, test reactions to the vehicle in test animals; *n*, number of tested animals in the 3 groups C, T, V.

Table 4. Challenge with budesonide in guinea pigs sensitized to budesonide in GPMT I

Sensitization substance	No. animals	No. positive animals after rechallenge with			
		Budesonide 0.032%	Budesonide 0.01%	Budesonide 0.0032%	Budesonide 0.001%
Budesonide					
Test group 1	6	2	2	0	3
Test group 2	6	0	1	0	2
Test group 3	6	0	1	1	1
Test group 4	6	1	0	2	1
Test group 5	6	1	1	2	2
Test group 6	6	0	1	1	0
Test group 7	6	1	2	3	0
Control group	6	2	1	1	1

read without knowledge of the readings on the right flanks.

Statistical calculation

The Fisher's exact test was used.

GPMT no. II

The GPMT was performed in the same way as no. I but only with 10 test animals, comprising 5 groups with 2 animals in each group, and 2 controls. A positive control group was not used. The concentrations and vehicles used at sensitization, challenge and rechallenge are shown in Table 2.

Evaluation

The reactions were evaluated blind 3 h after removal of the patches on D1 and then on D2, D3, D4 and D6.

Results

Tables 3 and 4 show the results of the first GPMT with sensitization to and challenge with budesonide. Budesonide could not be demonstrated to be a sensitizer in the study.

In GPMT no. II no test animals reacted to budesonide at any of the readings (data not shown).

Discussion

When using different non-irritating concentrations for induction and challenge for a suspected sensitizer with the GPMT, a non-monotonous dose–response relationship for challenge is usually obtained (10). However, this may not hold for corticosteroids, since they have anti-inflammatory and anti-allergic effects as well as possible sensitizing capacity. These 2 properties may not have the same biological basis in man or the guinea pig, and hence the dose–response curves may have different slopes (6). Therefore, higher concentrations of corticosteroids for induction and challenge may not result in more reactions (11). Furthermore, the vehicle may be decisive for the outcome of patch testing with corticosteroids (12). It is also known that patch test reactions to corticosteroids in humans may appear later than D3 or D4 (7, 13), probably due to different time courses for the anti-allergic effect and the sensitizing capacity. However, in spite of experiments designed to overcome all the above difficulties, virtually the same negative results were still obtained.

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Photoaggravated allergic contact dermatitis due to *Rosmarinus officinalis* cross-reactive with *Thymus vulgaris*

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Key words: *Thymus vulgaris*; Rosmarinus officinalis; photoaggravated allergic contact dermatitis; cross-reactivity; photodermatitis; plants.

Rosmarinus officinalis (rosemary) is a plant of the Labiatae family, which also includes *Thymus vulgaris* (thyme), *Mentha piperita* (mint), and *Origanum vulgare* (origanum). All these plants are commonly used both as preservatives in cosmetics due to their antioxidant and antimicrobial effects (1), and as spices in meat casseroles due to their flavouring properties.

Case Report

A 62-year-old nonatopic woman presented with several episodes of itchy hand, forearm and face dermatitis after picking rosemary on sunny days. Lesions appeared hours after handling rosemary leaves and resolved within 7 days on topical corticosteroids. Prick-by-prick testing with rosemary leaves was carried out with negative results at 15 min. At day (D) 2 a ++ reaction was detected. Patch testing with the European standard series (TRUE-Test™, Pharmacia & Upjohn Hillerod AS, Denmark), rosemary (as is), mint (as is), origanum (as is), and thyme (as is) gave positive reactions to paraphenylenediamine (++), rosemary (++), and thyme (+) at D2 and D4. Photopatch tests (10 J/cm) with rosemary and thyme showed stronger reactions (+++ and + +, respectively) at D4. 5 control subjects were negative.

Discussion

Since 1958, when Klarman published the first case of allergic contact dermatitis from *Rosmarinus officinalis* (2), 3 cases have been reported, 1 of occupational origin (1), and the other 2 due to its therapeutic use (3,4). Although some authors have looked for possible cross-reaction with other plants of the Labiatae family, they have failed to demonstrate such a relationship (3). The case presented here is the first in which a positive reaction to another plant of the same family has been obtained. Moreover, the influence of sun exposure was also investigated, because the distribution of lesions over exposed areas (the face, the backs of the hands, and the dorsal forearms) suggested photodermatitis. From the results obtained, exposure to light seems to aggravate lesions due to both rosemary and thyme contact sensitization.

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Patch test sensitization to methylchloroisothiazolinone + methylisothiazolinone and 4,4′-diaminodiphenylmethane

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Key words: 4, 4′-diaminodiphenylmethane; MDA, methylchloroisothiazolinone + methylisothiazolinone; patch test sensitization.

Case Report

A 50-year-old woman was referred with suspected contact allergy to inhaled corticosteroids. She was patch tested on the upper back to the Swedish standard series and some additional allergens, our corticosteroid series, and an asthma/rhinitis series. Readings were performed on day (D)3 and D7 without any positive reactions being found. Prick testing with the ingredients of the corticosteroid spray was also negative. However, the patient returned on D26 because on D25 she had noticed 2 itchy eczematous lesions, each the size and shape of a positive patch test reaction, on the back. From the previous charts one could localize the reactions to panels 3 and 5, which were again patch tested, this time on the lower back. She returned on D3 and a + + + reaction was noted to methylchloroisothiazolinone + methylisothiazolinone (MCI + MI) 200 p.p.m. active ingredients (a.i.) and a + + reaction to 4,4′-diaminodiphenylmethane, synonymous with methylenedianiline (MDA) 0.5% (w/w). On D7 the reaction to the former was + + and to the latter + +.

Discussion

Methylchloroisothiazolinone + methylisothiazolinone, in the ratio 3:1, was shown to be a sensitizer in the mid 1980s (1, 2). Patch testing with 300 p.p.m. and 250 p.p.m. a.i., respectively, sensitized approximately 1% of tested patients (3). Some years later, an aqueous test preparation of 100 p.p.m. a.i. was recommended internationally (4), and is still the test concentration used in the European standard series. However, when reducing the patch test concentration from 300 p.p.m. a.i. to 100 p.p.m. a.i., 50% of sensitized individuals may be missed (3). In Sweden, aqueous 200 p.p.m. a.i. has been recommended for routine patch testing since the late 1980s, and this is the preparation that Chemotechnique Diagnostics, Tygelsjö, Sweden, has distributed since 1990 in the Swedish standard series. No active patch test sensitization to 200 p.p.m. a.i. has previously been reported (5). The patient had not experienced any dermatitis between the 2 test sessions and did not work in an environment where one would expect MDA exposure. Thus, we consider this to be a case of active sensitization to both MCI + MI and MDA, chemically unrelated compounds. De Groot has previously reported 1 patient actively sensitized to MCI + MI 150 p.p.m. a.i. (2).

One reason for the active sensitization to MCI + MI seen here could be that the concentration was higher than declared. Thus we analysed the test preparation with respect to the a.i. using an HPLC system (6) and found the concentration to be accurate. Furthermore, to obtain an accurate volume when testing MCI + MI, one should always use a micropipette when applying the 15 μL used in the Finn Chambers (Ø 8 mm) (Epitest Ltd, Tuusula, Finland) test system, and this had also been done.

Flare-up reactions to MDA have been reported before (7, '8). In 1 case (8), 4 chemically unrelated compounds were implicated in active sensitization and MDA tested at 0.5% (w/w) was 1 of them. Also in that patient, there were no positive patch test reactions to any of the tested substances at D3 or D7.

It has been argued that a contact allergy acquired at patch testing seldom if ever becomes clinically relevant, because the patient is advised what to avoid before any significant exposure has been possible (9). In this case, though, with a high patch test reactivity to MCI + MI, undeclared and/or erroneously declared products containing the sensitizer may elicit allergic contact dermatitis, especially if present in products of

leave-on type or in rinse-off products used on damaged skin (3, 5).

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Textile dyes sensitization: a study of 49 patients allergic to disperse dye alone

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Key words: allergic contact dermatitis; clinical relevance; clothing; disperse dyes.

Cases of contact dermatitis caused by disperse dyes may remain undiagnosed and underreported for many reasons(1–4). In Modena, they have therefore been included in the standard patch test series since 1988. Since then, we have patch tested with disperse dyes in around 15 000 patients, and noted sensitization rates of 5.2% (1988–90), 3.8% (1990–1995) and 6.7% (1996–2000) (1, 5, 6). We describe a subgroup of dye-sensitive patients who showed no concomitant sensitizations to other allergens in our standard patch test series.

Patients and Methods

From January 1996 to December 2000, a total of 6478 patients with suspected allergic contact dermatitis were patch tested with a series of 46 allergens including 7 disperse dyes: Disperse Blue 124 (DB124), Disperse Blue 106 (DB106), Disperse Red 1 (DR1), Disperse Yellow 3 (DY3), Disperse Orange 3 (DO3), para-aminoazobenzene (PAAB), and para-dimethylaminoazobenzene (PDAAB). In children under 10 years of age, we used a reduced series without DB106 and PAAB. The dyes, provided in a preparation suitable for patch testing by FIRMA (Firenze, Italy), were applied with Finn Chambers on Scanpor tape (Epitest, Tuusula, Finland) for 3 days. Patch test reactions were evaluated 30 min−3 h after removal, according to international guidelines.

Table 2. Skin site involvement in 49 subjects reacting to disperse dyes alone

Site	No. (%) of cases
Hands	16 (32.7%)
Skin folds*	16 (32.7%)
Upper limbs	10 (20.4%)
Lower limbs	10 (20.4%)
Face	8 (16.3%)
Axillae	7 (14.3%)
Neck	7 (14.3%)
Trunk	5 (10.2%)
Widespread	5 (10.2%)
Feet	4 (8.2%)
Buttocks	4 (8.2%)
Thighs	4 (8.2%)
Genitalia	3 (6.1%)
Wrists	3 (6.1%)
Abdomen	2 (4.1%)

*Neck, axillae, and flexural areas of the limbs included.

Results

Of the 6478 patients tested, 437 (6.7%) showed positive reactions to 1 or more of the dyes listed above. Among these, 49 (11.2%) patients reacted to disperse dyes alone, comprising 25 males and 24 females, aged from 4 to 77 years. 8 patients had atopic eczema, and 3 were occupationally exposed to textiles. 35 reacted to DB124, 26 to DB106, 13 to DO3, 11 to DR1, 10 to DY3, 7 to PAAB, and 4 to PDAAB(Table 1). The group included 3 children who were not patch tested with DB106 and PAAB. Sensitization to 1 dye alone was observed in 12 (25%) patients, 7 of whom reacted to DB124. In this patient group the sensitization rate to

Table 1. Patch test results in 49 patients sensitized to textile dyes alone

Allergen	No. of positive patients	% of positive patients
DB124	35	71.4%
DB106*	26	56.5%
DO3	13	26.5%
DR1	11	22.4%
DY3	10	20.4%
PAAB*	7	15.2%
PDAAB	4	8.2%

*Not tested in 3 children.

DB124 (73%) was significantly higher than that observed in the group of 437 dye-sensitive patients also reacting to other substances (44%). Moreover, a high degree of cross-reactivity between blue disperse dyes, explained by their similar chemical structure (7), was detected. In fact, almost all the subjects sensitive to DB106 (92%) reacted to DB124, showing positive reactions of the same degree of intensity.Table 2 shows the most frequently involved skin sites in our study population. In about 85% of our study population, patch test reactions were considered relevant, as judged by the history and clinical pattern of the dermatitis, and the response to avoidance of synthetic fibres.

Comment

This clinical characterization of patients allergic to disperse dyes alone awaits confirmation by others, as well as further analysis and explanation.

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