

Short Communications

Recommendation to include ester gum resin when patch testing patients with leg ulcers

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Key words: allergic contact dermatitis; leg ulcers; ester gum resin; colophonium; Granuflex; Lestreflex; medicaments.
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Colophonium (rosin) is a complex mixture of over 100 compounds derived from pine trees of the Pinaceae family (1). There are 3 major types, gum, wood and tall oil, distinguished by their different methods of recovery (2). Gum rosin, the most common form, is tapped from the sap of living trees, wood rosin is extracted from pine stumps and tall oil is obtained as a by-product from paper pulp production.

Colophonium has numerous applications both at home and in the workplace. In medicine, derivatives of colophonium are found in plasters, bandages, and medicated creams and ointments. Patients with leg ulcers may come into contact with a modified form of colophony, ester gum resin, in Granuflex® hydrocolloid dressing (3, 4) and Lestreflex bandages.

Patients with leg ulcers are usually patch tested to colophonium in the European standard series but are not routinely tested to ester gum resin. At Amersham Hospital, we have been patch testing leg ulcer patients to both colophonium and ester gum resin since 1972. Some patients have had positive patch test reactions to ester gum resin but not to colophony. If this test had not been included, an important relevant allergen would have been missed.

Patients and Methods

Using a computerized database, all the patients patch tested in the Dermatology Department at Amersham Hospital between 1 January 1982 (when the results were first put on a database) and 14 June 2000 were identified. The patch test results of all patients found to be allergic to colophonium, tested at 20% pet. from Trolab, and ester gum resin, tested at 25% pet. and made up by the hospital pharmacy from the manufacturer's sample, were analysed.

Results

9110 patients were patch tested during the study period. Of these, 33% (3006) were male, 12% (1087) had an oc-

cupational dermatitis, 41% (3706) were atopic and 24% (2202) had hand eczema.

1270 (14% of the total 9110) patients with leg ulcers were patch tested to both colophonium and ester gum resin during this period. 106 patients were patch test positive to either gum resin or colophonium. 75 (71%) of these patients were patch-test positive to ester gum resin and 64 (60%) patients were positive to colophonium. 33 (31%) patients were positive to both ester gum resin and colophonium. 42 (40%) were positive to ester gum resin alone and 31 (29%) patients were positive to colophonium alone.

Discussion

Screening for an allergy, using unmodified gum rosin such as colophonium, may not detect an allergy to modified rosin such as ester gum resin. If "aimed" testing to ester gum resin had not been performed, 42 patients (40%) with leg ulcers with a relevant contact allergy would have been missed.

We recommend that all leg ulcer patients should be tested to both colophonium and ester gum resin when referred for patch testing.

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Erythema multiforme-like eruption: an unusual presentation of primula contact allergy

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Key words: allergic contact dermatitis; erythema multiforme; *Primula obconica*; primin; standard series; plants; occupational; horticulture; active sensitization. © Munksgaard, 2001.

The main pattern of primula allergic contact dermatitis is acute or chronic eczema of the hands and/or face (1). Photodermatitis (2), herpes simplex (3) or vitiligo presentations (4) can also be observed.

Case Report

A 30-year-old horticulturist was patch tested with the European standard series, including synthetic primin (Trolab) 0.01% pet., and relevant plants because of chronic hand eczema. The patch tests, using Finn Chambers (Epitest, Helsinki, Finland), were + to colophonium, nickel and *Pelargonium peltatum*, but – to primin.

After maternity leave, she started working again without allergic symptoms. 5 months later, she worked for the 1st time in a greenhouse where primulas (*P. obconica*) were grown. Within hours of handling the plants, a pruriginous erythema appeared on the backs of hands. The next day, an itchy burning rash with swelling of the hands brought her work to a halt.

Erythematous urticarial papules were disseminated over the backs of the hands and forearms. Some lesions had a target appearance, resembling erythema multiforme morphologically. The lesions became purpuric on the backs of the fingers. 2 days later, the eruption spread to the face, with erythematous urticarial papular and plaque lesions, sharply delineated, on the cheeks and chin. Pustulation of perioral lesions, with lip oedema but no mucosal lesions, was observed.

No topical non-steroidal anti-inflammatory drug had been used. Thus, a diagnosis of erythema multiforme-like eruption due to primula was made and the patient hospitalized. Investigations, including blood count, liver function and collagen disease markers, were normal. The dermatitis improved within 1 week with the administration of oral prednisone (0.5 mg/kg per day), anti-H1 antihistamines, topical corticosteroid and emollient.

Patch tests (as recommended by the ICDRG) with the European standard series and pieces of the plant were positive (++ D2/ ++ D3), with an eczematous reaction to primin 0.01% pet., the leaf and the flower of *P. obconica*. The reaction was +++ (bullous) to the stem. The remainder of the patch tests were ++ for colophonium, nickel and MCI/MI. No recurrence was noted during patch testing. The patient was advised to avoid contact with this plant and an occupational disease notification was made.

Discussion

Several contact allergens (e.g., metals, topical drugs, tropical woods, and industrial chemicals) have been reported to cause erythema multiforme-like eruptions (5). Goh (5) prefers the term urticarial papular and plaque eruption.

Most allergic contact dermatitis from *Primula* spp is due to *P. obconica*. The main sensitizer is primin (2-methoxy-6-pentyl-1,4-benzoquinone), contained in the terminal cells of the microscopic hairs on the surface of the leaves, stems and flowers (6). Erythema multiforme-like eruption is an unusual presentation of allergic contact dermatitis from *P. obconica* (7, 8).

In Europe, the prevalence of positive patch tests to primin has varied between 1% (9) and 1.8% (10), justifying its inclusion in the European standard series. The rapidity of the eruption after 1st primula contact could only be explained by active sensitization during initial patch testing. While safer in this respect than primula extracts or pieces of the plant (9, 10), synthetic primin therefore still carries this risk.

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Fixed-drug eruption due to metronidazole with positive topical provocation

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Key words: adverse drug reactions; fixed drug eruption; metronidazole; antibiotics; lack of cross-sensitivity; positive lesional patch test. © Munksgaard, 2001.

Case Report

A 25-year-old woman, after treatment 2× with Rhodogil® (spiramycin 750,000 u and metronidazole 125 mg) for a dental infection, showed 3 itchy erythematous lesions. These were on the back of the right wrist, the right forearm and the left thorax, where there remained a hyperpigmented lesion 3×4 cm. A fixed-drug eruption (FDE) was diagnosed.

Prick and intradermal tests with metronidazole and spiramycin were negative. Subsequently, topical provocation was carried out, the results of which are detailed in Table 1. Each topical provocation was carried out with a month in between. The tablets, crushed and dispersed at 50% pet. were used; tioconazole was tested at 1% (Trosid® cream as is). Test preparations were applied closed, and removed after 2 days. Readings were carried out at 2 and 4 days.

Topical provocation with Rhodogil® and metronidazole reproduced the symptoms of itchiness and erythema in the residual lesion, which lasted for 4 to 5 days. Subsequently, oral provocation with 750,000 u of spiramycin, the same dose as in a tablet of Rhodogil®, was carried out and tolerated well.

Discussion

FDE due to metronidazole has not often been reported. Shelley & Shelley (1) report a 37-year-old woman with

positive oral provocation to 250 mg metronidazole. There are 2 cases (2, 3) of positive oral provocation to metronidazole and tinidazole, both nitroimidazoles with similar structure. 1 of these patients also underwent provocations with albendazole, ketoconazole and mebendazole, which were all negative.

In our patient, topical provocation was positive to metronidazole, but despite its pharmacological similarity, tinidazole was negative on topical provocation. Izu et al. (4) described cross-reactivity between metronidazole (a nitroimidazole) and tioconazole (a phenethyl imidazole), in a patient with contact dermatitis due to tioconazole. In our patient, topical provocation with tioconazole was negative.

In our experience, and in agreement with published data (5–7), in the diagnosis of FDE, the use of topical provocation on a residual lesion is very useful, and in many cases avoids the need for oral provocation.

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Table 1. Results of topical provocation tests

Drug	Normal skin	Residual lesion
Rhodogil® (50% pet.)	–	+
metronidazole (Flagyl® 50% pet.)	–	+
tinidazole (Tricolam® 50% pet.)	–	–
tioconazole 1% (Trosid® cream as is)	–	–

Evaluation of eugenol allergy in a patch-test population

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Key words: allergic contact dermatitis; fragrance; eugenol; clinical relevance; cosmetics. © Munksgaard, 2001.

Fragrance mix is accepted as a screening tool and is reported to detect 50–80% of patients with fragrance allergy (1, 2).

Patients and Methods

1754 patients with suspected allergic contact dermatitis were patch tested with the Italian standard series, plus eugenol (1% pet.), from September 1998 to January 2000. The test substances, provided by Hermal-Trolab (Germany) and FIRMA (Italy), were applied to healthy skin of the back with Finn Chambers (Norgesplaster, Norway) on Scanpor tape (Epitest, Finland) for 3 days. Reactions were evaluated 30 min after removal, according to ICDRG guidelines.

Data were collected for each patient with a positive patch test to eugenol, including site and type of the dermatitis, personal history of atopic dermatitis, test results and their relevance. All those reacting to eugenol, fragrance mix or fragrance mix + sorbitan sesquioleate were considered.

Results

Of the 1754 patients tested, 240 (13.6%) were positive to 1 of the preparations above. Of these, 37 reacted to

fragrance mix, 119 to fragrance mix + sorbitan sesquioleate and 75 to both. 21 patients (1.2%), 13 female and 8 male, were positive to eugenol. Their mean age ($\pm$ SD) was 34 ± 10.5 years. 1 patient alone had a history of atopic eczema. The site of dermatitis was the hands (24%), face or neck (19%), legs (14%), genital area (9%). The arms, trunk and feet were more rarely involved. In 14%, the eruption was widespread.

Of 21 patients reacting to eugenol, 1 was also positive to fragrance mix, 5 to fragrance mix + sorbitan sesquioleate and 6 to both, whereas in 9, eugenol was the only indicator of fragrance allergy (Table 1). All patients but 1 were positive to other substances in the Italian standard series, in particular to preservatives: 57%, nickel sulfate: 48%, disperse dyes: 24%, Myroxylon Pereirae: 19%, Propolis Cera: 19%, lanolin (wool wax alcohols): 19%, and para-phenylenediamine: 9%.

Discussion

Eugenol is 1 of the 8 components of the fragrance mix, and a moderately strong sensitizer. It is a constituent of essential oils and obtained from spices, such as cloves, cinnamon leaves, sassafras, bay, pimento and patchouli. It is used in colognes, toilet waters, tonics, dressings, hair cosmetics, toothpaste, impression materials and

Table 1. Patient population and patch test results

No.	Sex	Age (year)	Occupation	Site/symptoms	E ^{a)} /intensity	FM ^{b)} /intensity	FMS ^{c)} /intensity	PR ^{d)}	CR ^{e)}	DR ^{f)}	NR ^{g)}
1	f	25	student	wrist	+++						×
2	f	53	maid	hands	++						×
3	f	37	trader	diffuse itch	+						×
4	m	21	student	penis	+						×
5	f	25	trader	hands, vulva	+++			×			
6	f	37	hairdresser	face	+++					×	
7	m	41	employee	legs, feet	+			×			
8	f	41	store-keeper	diffuse	+					×	
9	f	22	student	urticaria	+++					×	
10	m	31	chemist	legs	+++	+++			×		
11	f	48	shop assistant	neck	+		++		×		
12	f	16	student	limbs	++		++	×			
13	f	41	trader	angioedema	++		++				×
14	f	30	employee	diffuse itch	+++		++			×	
15	f	41	nurse	hands	++		+++	×			
16	m	30	butcher	legs	++	+++	+++		×		
17	m	43	metal worker	hands	+++	+++	+++		×		
18	m	15	student	face, trunk	+++	+++	+++			×	
19	m	35	unemployed	limbs	++	+++	+++		×		
20	f	47	worker	back, arms	+++	+++	+++		×		
21	m	36	ceramist	hands, lips	+	+	+			×	

a) Eugenol; b) fragrance mix; c) fragrance mix + sorbitan sesquioleate; d) past relevance; e) current relevance; f) doubtful or not known relevance; g) no relevance.

periodontal packings. Eugenol cross-reacts with Myroxylon Pereira, benzoin and isoeugenol.

Approximately 10% (range 6 to 11%) of patients with dermatitis have a positive patch test to fragrance mix, but only 1/2 of these react to 1 or more of its constituents. Conversely, fragrance mix can be negative, with a positive patch test to 1 or more of its ingredients.

The response rate to fragrance mix (13.6%) and to eugenol (1.2%) in our patients was slightly higher than that reported (1, 2). In Italy, 0.6% of patients were sensitized to eugenol in 1984–1985 (3). The median age, female predominance and sites of predilection, observed in our study, were similar to those seen previously (2–4), though positive reactions (not, however, with relevance) were seen in 2 patients with urticaria/angioedema.

Positive reactions to eugenol and fragrance mix were considered currently relevant in 6 patients out of 12 (5). The addition of eugenol established fragrance allergy in a further 8 subjects (0.5%). However, many such patients could tolerate fragrance and only in 2 cases was past

relevance suspected. In none such patients was current relevance established.

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Allergic contact dermatitis due to both chlorpheniramine maleate and dibucaine hydrochloride in an over-the-counter medicament

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Key words: allergic contact dermatitis; chlorpheniramine; dibucaine; medicaments; over-the-counter; lack of cross-sensitivity; amide local anesthetics. © Munksgaard, 2001.

Case Report

A 71-year-old Japanese man presented with an itchy erythematous lesion, with seropapules and erosions, on his right lower leg following an injury. He had applied Actosin® (bucladesine sodium) ointment to the site for the past 10 days and the lesion had worsened. He had a past history of an erosive lesion on his finger 2 months before, when Actosin® had been applied along with several other topical agents. He had also applied Makiron® (0.2% *dl*-chlorpheniramine maleate, 0.1% dibucaine hydrochloride, 0.1% naphazoline hydrochloride, 0.1% benzethonium chloride) to the wound on his leg, as well as to his finger. Application of Actosin® and Makiron® was stopped and treatment with topical corticosteroid started, with rapid improvement in the lesion.

Patch tests (as is) were positive (D2+/D3++) to Makiron® and negative to Actosin®. Further patch testing with the ingredients of Makiron® was positive (D2+/D3+/D6+) to *dl*-chlorpheniramine maleate (1% pet.) and positive (D2+/D3++) to dibucaine hydrochloride (1% pet.). Patch testing with lidocaine hydrochloride (1% pet.) and mepivacaine hydrochloride (1% pet.) was negative.

Discussion

Makiron®, an over-the-counter (OTC) medicament for skin wounds, now widely used in Japan, contains both *dl*-chlorpheniramine maleate and dibucaine hydrochloride. The patient had repeatedly used Makiron® for minor wounds. He had also taken oral drugs containing chlorpheniramine maleate for the common cold. Patch tests suggested that both drugs caused allergic contact dermatitis on his leg.

There are recent reports of allergic contact dermatitis due to (chlor)pheniramine maleate (1–3) and dibucaine (4–6) used topically, but no instance due to both drugs at once. Many other OTC medicaments for wounds sold in Japan contain both these drugs, which must surely increase the risk of sensitization.

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Allergic contact dermatitis due to methyldibromo glutaronitrile in Euxyl K 400 in an ultrasonic gel

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Key words: allergic contact dermatitis; preservatives; Euxyl K 400; methyldibromo glutaronitrile; CAS 35691-65-7; phenoxyethanol; CAS 122-99-6; cosmetics; ultrasonic gel. © Munksgaard, 2001.

Euxyl K 400 contains 2 active ingredients: phenoxyethanol (80%) and methyldibromo glutaronitrile (20%). Considered to have a low sensitizing potential, it has gradually been replacing MCI/MI in cosmetics over the past 15 years.

Case Report

A 62-year-old man developed dermatitis 24 h after an ultrasonic gel had been applied on his abdomen. He had no previous history of dermatitis. Patch testing with our standard series, ointment bases, preservatives, and the ultrasonic gel was positive to MCI/MI, Euxyl K 400 1.0% pet., methyldibromo glutaronitrile 0.3% pet. and the ultrasonic gel as is, which the manufacturer confirmed as containing Euxyl K 400. Patch testing with all the constituents of the ultrasonic gel showed a positive reaction only to methyldibromo glutaronitrile 0.3% pet., and not to any other components or to phenoxyethanol 1.0% pet. Readings were performed on days 2, 3 and 7 using the ICDRG grading scale.

Discussion

Since the 1st use of methyldibromo glutaronitrile as a single preservative, namely Tektamer 38, in 1982, and the introduction of the combination of methyldibromo glutaronitrile with phenoxyethanol, Euxyl K 400, 3 years later, there have been a number of reports of contact dermatitis due to these preservatives (1–13). Euxyl K 400 is mainly used as a preservative in cosmetics and toiletries. However, methyldibromo glutaronitrile is also used in coating systems, such as latex emulsions, cutting fluids, adhesives, wood preservatives, color photographic processing solutions, seed disinfectants and paper and paperboard, into which it may be incorporated as a slimicide during manufacture (14). In almost all cases, contact dermatitis from Euxyl K 400 has been induced by methyldibromo glutaronitrile, positive reactions to phenoxyethanol having been described only rarely (3, 15).

To our knowledge, 2 previous case reports of allergic

contact dermatitis due to Euxyl K 400 in ultrasonic gels have been published. 1 patient (7) was sensitized to methyldibromo glutaronitrile, but not to phenoxyethanol, 1 (4) was patch tested only to Euxyl K 400 and not to each of its constituents. In our patient, the original source of sensitization to Euxyl K 400 and MCI/MI remains unclear, though various ultrasonic gels had been applied before. With no occupational exposure to Euxyl K 400 or MCI/MI, our patient was probably sensitized by cosmetics or skin-care products.

Bruze et al. (16) could demonstrate no sensitizing capacity for Euxyl K 400 in the guinea pig maximization test and Hausen (14) demonstrated only a weak sensitizing potential for methyldibromo glutaronitrile by a modified FCAT. Despite this, several recent studies have demonstrated an increasing sensitization rate to Euxyl K 400 in the EU, attributed to its increasing use in leave-on and rinse-off cosmetic products (2, 5, 13). In 1995, up to 25–35% of all cosmetics in The Netherlands contained Euxyl K 400 (2). In The Netherlands, methyldibromo glutaronitrile in moist toilet paper seems to be a major source of sensitization (1, 2). In a German multicentre study, masseurs/masseuses were frequently positive to Euxyl K 400.

The optimal test concentration and vehicle for patch testing Euxyl K 400 remain elusive. In a German multicentre study, the following were used: Euxyl K 400 0.5% pet., methyldibromo glutaronitrile 0.1%, and phenoxyethanol 0.4% pet. (3). However, De Groot et al. (2) point out that using Euxyl K 400 0.5% pet. (containing 0.1% methyldibromo glutaronitrile) and methyldibromo glutaronitrile 0.1% pet., might result in false-negatives, and suggest 0.3–0.5% as the optimal test concentration for methyldibromo glutaronitrile. Tosti et al. (13) tested Euxyl K 400 at 2.5% pet., containing 0.5% methyldibromo glutaronitrile.

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Fixed drug eruption from ticlopidine, with positive lesional patch test

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Key words: ticlopidine; antiplatelet drugs; adverse drug reactions; fixed drug eruption; positive lesional patch test; lack of cross-sensitivity; oral provocation © Munksgaard, 2001.

Ticlopidine and clopidogrel are thienopyridine-derived agents that inhibit platelet aggregation (1). Side-effects of ticlopidine include gastrointestinal symptoms, rash, haemorrhagic disorders, hematologic effects (2), TTP (3), and erythroderma (4).

Case Report

A 54-year-old woman presented with pruritic erythematous vesicular lesions on the back. 3 months earlier, she had begun a course of oral ticlopidine (Tiklid 250 mg/day; Sanofi) for cerebrovascular disease. The drug was discontinued and the lesions resolved in 20 days, with residual hyperpigmentation.

She was patch tested with ticlopidine (5% and 1% pet. on both lesional and non-lesional skin. Oral challenge with both ticlopidine (250 mg) and clopidogrel (Iscover 75 mg; Bristol-Myers Squibb) was additionally performed. 20 controls were also patch tested with ticlopidine. The ticlopidine patch test was positive (+++) on lesional skin, and negative on non-lesional skin. All 20 controls were negative. Skin biopsy showed a predominantly chronic inflammatory infiltrate, with vacuolar degeneration of the basal layer, findings consistent with a fixed drug eruption. Oral challenge test with ticlopidine was positive, with the patient developing pruritic erythematoviolaceous lesions in the same distribution as before. Clopidogrel oral challenge was negative.

Discussion

Fixed drug eruptions are commonly caused by tetracyclines, barbiturates, oxyphenbutazone, aspirin and sulfadiazine (5). Cross-sensitivity between related drugs may occur, such as between phenylbutazone and oxyphenbutazone and between tetracyclines (6). Since the underlying pathogenic mechanism is unknown, few diagnostic tests are available (7). Patch testing has been used with variable results (8). Although the characteristic pathologic findings are helpful, they are not pathognomonic (9). Oral provocation is not without risk but remains the standard diagnostic test.

To the best of our knowledge, this is the 1st case report of fixed drug eruption to ticlopidine. We also demonstrated a lack of cross-sensitivity between clopidogrel and ticlopidine in this particular patient, who is currently taking clopidogrel without any adverse reaction. Lesional patch testing was as reliable as oral provocation in this case.

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Allergic contact dermatitis from triethanolamine in a sunscreen

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Key words: allergic contact dermatitis; patch test; triethanolamine; sunscreen; emulsifier; cosmetics. © Munksgaard, 2001.

Triethanolamine has not been included in previous reviews of contact sensitivity to sunscreens (1).

Case Report

An 8-year-old girl, with a past history of allergic rhinitis and urticaria, had a nevus of Ota over her right cheek. She received ruby laser therapy at our department, and a sunscreen application was suggested thereafter. The active ingredients of the sunscreen were benzophenone-3 and octyl methoxycinnamate. 2 weeks later, an ill-defined pruritic erythematous plaque, with many vesicles, was noted over the laser treatment area on her right cheek (Fig. 1).

Patch testing with the European standard series and the sunscreen, as well as photopatch testing with the sunscreen, were performed. She was positive to the sunscreen on day (D) 2 (++) and D4 (++) on both

patch and photopatch tests. Patch testing was subsequently carried out to all the ingredients of the sunscreen, showing a positive reaction only to triethanolamine 1.0% pet. (+) and 5.0% pet. (++) on D3 (Table 1).

Table 1. Patch test results with the ingredients of the sunscreen

	%	Vehicle	D3
benzophenone-3	5	pet.	—
stearic acid	5	pet.	—
glyceryl stearate	30	pet.	—
methylparaben	5	pet.	—
propylparaben	5	pet.	—
cetyl alcohol	30	pet.	—
allantoin	0.5	aq.	—
Aloe barbadensis	10	pet.	—
sesamum indicum	50	o.o.	—
propylene glycol	5	aq.	—
rice bran wax	30	o.o.	—
octyl methoxycinnamate	10	pet.	—
dimethicone	5	pet.	—
dimethicone	10	pet.	—
carbomer 940	5	pet.	—
carbomer 940	10	pet.	—
triethanolamine	1	pet.	+
triethanolamine	5	Pet.	++



Fig. 1. Patient's right cheek.

Discussion

Triethanolamine, a mixture of 3 alkanolamines, is used as an emulsifier in many cosmetics and topical medications (2, 3). There are only a few reports of triethanolamine-induced allergic contact dermatitis, from emollients (3, 4), eardrops (5), cutting oils (6, 7), and a fluorescent marking pen (2).

Contact allergy to emulsifiers is rare (8, 9), though triethanolamine may be commoner than most (8). Patch tests with sensitized patients' triethanolamine-containing preparations are, however, frequently negative. Therefore, it is advisable to test all the ingredients of the sunscreen, including emulsifiers, in patients with suspected sunscreen-related contact dermatitis.

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Occupational contact dermatitis from colophonium in a dental technician

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Key words: occupational; allergic contact dermatitis; colophonium; dental staff; dental prosthetic baseplate.
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Colophonium is a mixture of over 100 compounds derived from pine trees and has multiple applications at both home and work (1). Occupational allergic contact dermatitis from colophonium in a dental setting has been reported from impression materials and fluoride varnishes (2, 3). Oral lichen planus has also been reported in a dental patient due to colophonium in the sealant with which a dental prosthesis had been repaired (4).

Case Report

A 38-year-old dental technician, with a life-long history of atopy, presented with a 2-year history of work-related dermatitis of the hands and forearms. He wore latex gloves for work and handled plaster of Paris, wax, acrylic and Cavex® dental baseplate moulding materials. On examination, he had a chronic scaly fissured dermatitis on the palms of the hands, the left more so than the right. There was also involvement of the extensor right elbow.

He was patch tested to the European standard, preservative, vehicle, dental, medicament and plasticizer and glues series. He was also patch tested to the plaster of Paris, wax, acrylic and Cavex® dental baseplate moulding materials with which he worked. He had positive reactions to colophonium (+), fragrance mix (+) and the Cavex® dental baseplate (+) at both D2 and

D4. There was no reaction to latex on patch or prick testing. An allergen-specific IgE test to latex was also negative.

Discussion

Dental personnel may handle a wide range of potent irritants and sensitizers (5). Occupational allergic contact dermatitis has been reported from colophonium in impression materials (2) and fluoride varnishes (3, 6). Our patient worked with Cavex® dental baseplates, which are used as an intermediate in making dental prostheses. The baseplate can be heated and remodelled to fit the patient's mouth, before being replaced by synthetic resin for the final prosthesis. Cavex® dental baseplates come in brown, pink and mica-free forms, which contain colophonium-containing wood resins at 5%, 7.5% and 7.5%, respectively.

Acknowledgement

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Contact allergy to terephthalic acid diglycidylester in a powder coating

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Key words: terephthalic acid diglycidylester (CAS 7195–44–0); trimellitic acid triglycidylester (CAS 7237–83–4); powder coating; occupational contact allergy; airborne dermatitis; allergen replacement; prevention.   Munksgaard, 2001.

Powder coating is an ingenious method of coating metallic objects. Electrostatically-charged resin particles are sprayed onto the metal part, which acts as an anode. The thermosetting coating is fixed to the metal by heat treatment in an oven. The resins used are mainly polyester and/or epoxy systems. As the process is usually automated, exposure of workers to resin dust is low.

Case Report

A 37-year-old non-atopic woman worked in a small factory, where she had applied powder coatings to parts made of steel or aluminium, with a spray gun, since October 1991. She wore cotton gloves, a face mask, and an overall. In July 1998, itchy erythema, infiltration and papules occurred on the hands for the 1st time. Over the following months, this dermatitis worsened and spread to the wrists, forearms, neck, and periorbital region. The condition improved when she was off work and relapsed on her return. When she changed her place of work within the factory to the unloading of coated metal parts from the oven, between November 1998 and December 1999, the skin lesions cleared completely. After returning to her former workplace because of the higher salary, the dermatitis relapsed immediately and severely, with secondary spread once again.

In the factory, various powder coatings based on epoxy or polyester resins were used. The patient had contact almost exclusively with a white coating. Until 1997, this product, based on a polyester resin, contained triglycidyl isocyanurate (TGIC, CAS 2451–62–9) (Fig. 1) as a hardener. At the beginning of 1998, the manufacturer changed

the hardener to a 2-component product, consisting of terephthalic acid diglycidylester (CAS 7195–44–0) and trimellitic acid triglycidylester (CAS 7237–83–4). The product was labelled as both irritating and sensitizing (R phrases 36/38 and 43), and suitable gloves as well as face masks and safety goggles were recommended with its use.

After the patient's dermatitis had subsided with treatment and time off work, we performed patch tests according to internationally accepted guidelines with an extended standard series (excluding nickel sulfate), rubber chemicals, plastic and glue materials, including epoxy resin and amine hardeners, methacrylates, ointment bases, preservatives, nickel sulfate at a reduced concentration (because of known reactivity to costume jewellery), and the patient's own products. Among the latter were terephthalic acid diglycidylester and trimellitic acid triglycidylester, kindly supplied by the manufacturer, as well as the patient's gloves and face mask. Positive patch test reactions are listed in Table 1. All other tests were negative, including trimellitic acid triglycidylester 0.1% MEK, triglycidyl isocyanurate 0.5% pet., gloves, face mask, and epoxy resin compounds.

Comment

We diagnosed airborne allergic contact dermatitis due to terephthalic acid diglycidylester in the powder coat-

Table 1. Positive patch tests

			D2	D3	D4
terephthalic acid diglycidylester	0.1% MEK	+	+	+	+
phenol-formaldehyde resin (novolak)	5% pet.	?	+	+	+
phenol-formaldehyde resin (resol)	5% pet.	?	+	+	+
nickel sulfate	0.5% pet.	+	++	++	++

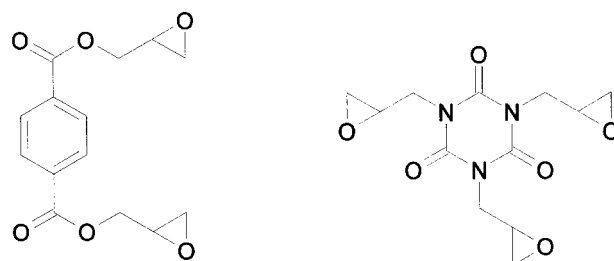


Fig. 1. Structures of terephthalic acid diglycidylester (left) and triglycidyl isocyanurate (right).

ing. As the manufacturer informed us that this substance was a known sensitizer in the guinea pig, and the product is labelled as "sensitizing", we did not perform any control tests, for ethical reasons. The patient's skin protection at work was inadequate. The powder coating penetrated her cotton gloves, and her face was not completely covered, leaving the periorbital region particularly unprotected.

The relevance of the patch test reactions to phenol-formaldehyde resins could not be elucidated. There was no clear past or present occupational exposure.

We could find no previous report of contact allergy to terephthalic acid diglycidylester. However, contact allergy to triglycidyl isocyanurate (TGIC) in polyester or epoxy resin hardeners has repeatedly been reported in recent years (1–7). Some of these patients worked as polyester powder paint sprayers and developed airborne allergic contact dermatitis (5, 6). Our patient, who had worked with powder coatings containing TGIC for several years, had no history of adverse reaction to this substance, and was negative on patch testing to it.

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Occupational allergic contact dermatitis from quaternium-15 in an electroencephalography skin preparation gel

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Key words: occupational; allergic contact dermatitis; electrode gel; quaternium-15; preservatives; antimicrobials; biocides; electroencephalography; neurophysiology technician; health-care workers. © Munksgaard, 2001.

Case Report

A 47-year-old non-atopic neurophysiology technician presented with a 5-year history of periorbital and hand dermatitis. This was exacerbated by handling Nuprep[®] skin preparation gel (D. O. Weaver & Co., Aurora, Colorado, USA) in connection with EEG examinations. The gel was applied to the electrode site on the scalp and rubbed lightly with a cotton swab. Electrode gel and the electrode plate were then positioned over the Nuprep[®], an abrasive gel containing aluminum oxide, 1,2-propanediol, sodium polyacrylate, sodium oleate, quaternium-15 (1–4), FD&C Blue 1, FD&C Red 40, FD&C Yellow 5 and water (as listed on the packaging).

She was patch tested to our standard, preservative, clothing and dyes, hairdressers, acrylate and cosmetic series, in addition to Nuprep[®] gel. She was positive at 2 and 4 days to nickel sulfate (5% pet.), cobalt chloride (1% pet.), palladium chloride (2% pet.), quaternium-15 (1% pet.) and Nuprep[®] gel (as is and 10% aq.). Type-I hypersensitivity to latex was excluded with negative use and prick tests.

The results confirmed an allergic contact dermatitis

from quaternium-15, rather than an irritant contact dermatitis from the gel. The patient's symptoms improved dramatically on her changing to a gel that was not preserved with quaternium-15.

Discussion

There have been reports of allergy to electrode gels containing propylene glycol (5, 6), parabens, FD&C Yellow 5, pine oil (6) and parachlorometaxyleneol (6, 7), in addition to allergic reactions to nickel-plated electrode plates and rubber fasteners (6). There have also been reports of allergies to similar gels used for ultrasound scanning (8) and transcutaneous electrical nerve stimulation (TENS) machines (9).

To our knowledge, this is the 1st report of occupational allergic contact dermatitis from quaternium-15 in a skin preparation gel used for EEG examinations.

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Non-eczematous pigmented interface dermatitis from para-tertiary-butylphenol-formaldehyde resin in a watchstrap adhesive

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Key words: para-tertiary-butylphenol-formaldehyde resin; pigmented allergic contact dermatitis; watchstrap adhesive; interface dermatitis; non-eczematous. © Munksgaard, 2001.

Case Report

A 51-year-old white woman presented with a 1.5-year history of a well-defined, pigmented pruritic lesion on the left wrist, confined to the contact area of her leather watchstrap (Fig. 1). There had been slight erythema, but no vesiculation, in the acute phase. On changing the watch to the right wrist, a similar reaction began to develop after 3 days (Fig. 1).

Patch tests with the European standard series showed a ++ reaction by D3 to para-tertiary-butylphenol-formaldehyde (PTBPF) resin (1% pet.), and a small piece of the watchstrap was also ++. Punch biopsies from the lesion on the wrist and from the positive patch test site of the strap revealed similar findings (Fig. 2), correlating with an interface dermatitis.

Avoidance of the watch resulted in complete healing within 1 month.

Discussion

Watchstrap dermatitis from PTBPF resin contact allergy is well-known (1-3). All reported cases of PTBPF resin contact allergy have been eczematous and histopathologically characterized by epidermal spongiosis (1-5). Pigmentation has not been reported; on the contrary, free PTBP may be a cause of depigmentation, due to its toxicity to melanocytes (6-8).

Our case differs from previous reports both clinically and histopathologically, being a non-eczematous pigmented contact reaction. Pigmentation can be explained by interface dermatitis, characterized by prominent



Fig. 1. Localized pigmented lesion on the left wrist corresponding to the contact area of the leather watch strap; note also the start of a reaction on the right wrist.

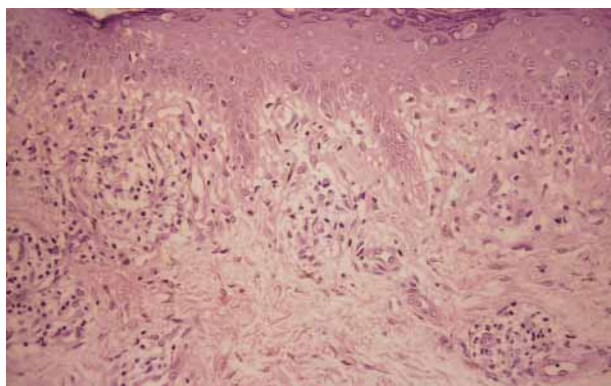


Fig. 2. Histopathology of lesion on the left wrist: sparse dyskeratotic cells, hydropic degeneration of the basal layer, pigmentary incontinence, and mononuclear perivascular inflammatory infiltration in the upper and mid-dermis (hematoxylin-eosin stain; original magnification, ×200).

damage to the epidermal basal layer. Such a pigmented interface dermatitis is unusual for allergic contact dermatitis, and mainly seen in fixed drug eruptions. Interface dermatitis from contact with color-film developers is well-known but clinically consists mainly of lichenoid papules (9).

To the best of our knowledge, this is the 1st report of pigmented interface dermatitis from PTBPF resin contact allergy.

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Natural rubber latex allergy to adhesive in chocolate bar wrappers

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Key words: contact urticaria; natural rubber latex; coldseal adhesive; chocolate bar wrappers. © Munksgaard, 2001.

Case Report

A 31-year-old atopic nurse presented with a typical history of being unable to use natural rubber latex (NRL) gloves. Her problems included urticaria on her hands. Her presumed allergy was confirmed when a RAST for NRL antibodies was found to be positive at level 2.

She also gave a history of sometimes developing tingling and swelling of her lips when the latter came into contact with the inside of the wrapper of her favourite chocolate bar. Moreover, she stated that she was able to eat the chocolate bar itself without noticing any symptoms, provided that the wrapper never came into contact with her lips.

The patient was given a wrapped chocolate bar and asked to demonstrate how she opened the wrapper. She did so by biting open the end of the wrapper with her teeth. When the smooth, inside, centre portion of the wrapper was held against her lip there was no visible reaction, although the patient complained of a little tingling at the site.

When the procedure was repeated on another occasion, this time using the inside of the glued end-section of the wrapper, a mild but definite urticarial eruption formed on the lip. The patient also complained of some tingling of her palate but was otherwise symptomless.

Discussion

The manufacturers of the chocolate bar in question provided the following information. The wrapper consists of a polypropylene film-based material, with product information printed on the outer surface and with a coldseal adhesive material printed onto the inside in a registered pattern. This would mean that only a minimal amount of the adhesive (edge contact) would come into contact with the product, but depending on how the wrapper was opened, it could come into contact with the consumer. The coldseal adhesive is based on a mixture of NRL and polyacrylate resins. The adhesive material is specially cleaned to reduce to a minimum the residual acrylate monomers, which would produce a malodour. All of the manufacturers' wrappers were stated to be similarly produced and were approved for use in food packaging.

2 studies have shown the prevalence of NRL sensitization in the general population to be around 6% (1, 2). This does not mean that such a significant minority of the population are likely to develop obvious or severe allergic reactions as a result of contact with NRL. However, lip contact might increase such a risk.

Schwartz (3) has reported 2 patients who suffered severe allergic reactions after eating food that had been

handled by staff who wore NRL gloves. To my knowledge, this is the 1st reported case of a consumer having suffered a likely allergic reaction to NRL, as a result of contact with the adhesive used in a chocolate bar wrapper, or indeed any other similar food wrapper. The ability to recognize hidden sources of NRL may well allow causality to be shown in otherwise unexplained allergic reactions.

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Allergic contact dermatitis due to lansoprazole, a proton pump inhibitor

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Key words: allergic contact dermatitis; occupational; proton pump inhibitors; lansoprazole; omeprazole; cross reaction; pharmaceutical manufacture; cutaneous adverse drug reactions. © Munksgaard, 2001.

Case Report

A 58-year-old non-atopic man had been working for a pharmaceutical company for 30 years. 4 years ago, he had started working in the section where lansoprazole was made. 6 months ago, he had developed pruritic papules on the face, neck, upper arms and forearms. At this point, he had stopped working and, on oral antihistamine and topical corticosteroid, had healed in 15 days. 5 days after returning to work, he had relapsed severely.

By the time that he was patch tested, his skin had cleared again with time off work. Initial patch tests gave the following results.

	D2	D4
TRUE Test standard series	—	—
Chemotechnique medicaments series	—	—
lansoprazole 50% pet.	++	++

2 months later, patch tests were carried out with all the excipients and with omeprazole, another proton pump inhibitor, with the following results.

	D2	D4
lansoprazole 10% pet.	++	+++
lansoprazole 50% pet.	++	++
omeprazole 10% pet.	++	+++
omeprazole 50% pet.	++	++
magnesium carbonate 10% pet.	—	—
saccharose	—	—
starch	—	—
hydroxypropylcellulose	—	—
methacrylic acid 2%	—	—
ethyl acrylate 0.1%	—	—
talcum powder	—	—

polyethylene glycol 4% pet.	—	—
titanium dioxide 10% pet	—	—
polyoxyethylenesorbitan monooleate		
5% pet.	—	—
colloidal silica TC	—	—

Patch tests with the same preparations of lansoprazole and omeprazole in 50 controls were negative.

After restriction from further work with lansoprazole, the patient experienced no further symptoms.

Discussions

The substituted benzimidazole class of protein pump inhibitors, of which lansoprazole is a member along with omeprazole, decrease parietal cell acid secretion by inhibiting the hydrogen-potassium adenosine triphosphatase enzyme system, the final step in the secretion of gastric acid.

Lansoprazole has been reported to cause lichenoid reactions (1), glottal edema (2), glossitis and stomatitis (3), acute generalized exanthematous pustulosis (4), and anaphylactic cross-reaction with imeprazole (5), but not previously allergic contact dermatitis.

Omeprazole has been described as a cause of fixed-drug eruptions (6), anaphylactic reactions (7) exfoliative dermatitis (8–10), alopecia (11), pityriasis rosea-like eruption (12), erythema nodosum (13), bullous skin reactions (14), oral candidiasis (15), dry-mouth syndrome (16), urticaria and angioedema (17–19), and acute disseminated epidermal necrosis (20). However, no case of allergic contact dermatitis has been reported before.

Because our patient had never been in contact with omeprazole, his patch-test reaction to it represented cross-sensitivity between lansoprazole and omeprazole, both drugs commonly used for gastric and duodenal ulcers.

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Allergic contact dermatitis due to both lanoconazole and neticonazole ointments

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Key words: allergic contact dermatitis; lanoconazole; neticonazole; diethyl sebacate, antifungals; medicaments.
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Case Report

A 65-year-old man presented with dermatitis on the feet in May 1999. He had been using lanoconazole ointment (Astat®, Tsumura Inc., Tokyo, Japan) to treat tinea pedis for 10 months. Patch testing with lanoconazole (10%, 1%, 0.1% pet.) was positive. Patch testing with other imidazoles (isoconazole, sulconazole, micronazole, neticonazole, ketoconazole) was negative at that time. He then started using neticonazole ointment (Atolant®, SS Pharmaceut. Inc., Tokyo, Japan). 4 months later, he again developed dermatitis on the feet. Patch testing was positive to neticonazole (1%, 0.3%, 0.1% pet.) and diethyl sebacate (5%, 1.7% pet.), an emulsifier in neticonazole ointment (Table 1). He now uses terbinafine cream.

Discussion

Neticonazole and lanoconazole are vinyl imidazoles in use in Japan since 1993 and 1994, respectively. Although there are more than 10 reports of contact dermatitis from each of them, contact dermatitis due to both has

not so far been reported. Patients sensitized to 1 of these vinyl imidazoles and 1 or 2 2,4-dichlorophenylethyl imidazoles have been reported (1–3). However, our patient was probably freshly sensitized to neticonazole after he

Table 1. Patch test results

	D2	D3
Astat® ointment	+	+
lanoconazole (10% pet.)	+	+
(1% pet.)	+	+
(0.1% pet.)	+	+
Atlant® ointment	+	+
neticonazole (10% pet.)	+	+
(1% pet.)	?+	+
(0.1% pet.)	–	+
diethyl sebacate (5% pet.)	+	+
(1.7% pet.)	?+	+
(0.5% pet.)	–	+
other components of Atlant® ointment	–	–
pet.	–	–

stopped using lanconazole, because of the 4-month delay.

Diethyl sebacate is a rare sensitizer: 4 cases have been reported (4–6), 1 of which was due to neticonazole lotion (5), containing 30% diethyl sebacate. Neticonazole ointment also contains diethyl sebacate, albeit at a much lower concentration (5%).

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Patch testing with the European standard series and Compositae extracts in patients with airborne contact dermatitis

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Key words: airborne contact dermatitis; *Parthenium hysterophorus*; *Xanthium strumarium*; *Helianthus annuus*; patch testing technique; plant extracts; Compositae; sesquiterpene lactone mix. © Munksgaard, 2001.

In India, airborne contact dermatitis (1, 2) accounts for 40% of patients attending contact dermatitis clinics (3). The most common causes are *Parthenium hysterophorus* and *Xanthium strumarium* (3, 4). We have studied whether patch testing with the European standard series can help in addition to plant extracts in such patients.

Patients and Methods

103 patients suspected of having airborne contact dermatitis were recruited for the study. Patch testing was carried out with ethanol dilutions of ether extracts of *Parthenium hysterophorus* (1:100 and 200), *Xanthium strumarium* (1:10 and 20), *Helianthus annuus* (1:10 and 20), prepared as previously described (5). In addition, patch testing was carried out on the upper back with the European standard series from Chemotechnique, Sweden. Readings were made on day (D) 2 and 3 and only reactions persisting to D3 were considered positive.

Results and Discussion

103 patients, comprising 68 men and 35 women, were patch tested. The majority (70%) had had dermatitis for more than 2 years and only 10% for less than 6 months. 78 out of 103 were positive to 1 or more allergens and 25 were negative to both plant extracts and the standard series. Plant extracts were positive in 73 patients, includ-

ing 34 patients with 1 or more allergens in the standard series also positive. *Parthenium* along with xanthium and sunflower were positive in 38 patients; *parthenium* along with xanthium, and *parthenium* alone, in 14 patients each; *parthenium* along with sunflower in 6 patients; and xanthium alone in 1 patient. The standard series allergens positive are shown in Table 1. They included sesquiterpene lactone (SL) mix in 17 (23.3%), nickel in 7 (9.6%); and chromate, colophonium, cobalt,

Table 1. Frequency of positivity to European standard series in Indian patients with airborne contact dermatitis

Allergens	Plant extracts positive (n=73)	Plant extracts negative (n=5)
SL mix	17	0
nickel sulfate	7	1
colophonium	4	2
potassium dichromate	4	0
cobalt chloride	4	0
formaldehyde	4	0
neomycin sulfate	3	1
mercapto mix	3	0
fragrance mix	3	1
benzocaine	2	1
primin	1	0
lanolin (wool wax alcohols)	1	0
epoxy resin	1	0
Myroxylon Pereirae (balsam of Peru)	1	0
quaternium-15	1	0

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and formaldehyde in 4 (5.5%) each. SL mix was relevant in all patients, as it was accompanied in all cases by positive reactions to plant extracts. 4 patients were positive to chromate and cobalt, and 3 to mercapto mix, 2 of whom had a history of footwear dermatitis. 7 patients, including 5 women, were positive to nickel, and 3 women had a history of jewellery allergy. The relevance of fragrance mix, colophonium and formaldehyde positivity was not evident.

In 5 cases negative to plants and positive to the standard series, 1 woman was positive to nickel (past relevance), and 2 patients to colophonium, 1 of whose dermatitis cleared after avoiding exposure to freshly painted rooms. 2 men were positive to chromate, 1 with photo-sensitivity of current relevance. The other had a history of footwear dermatitis and was also positive to black rubber mix.

It may be concluded that the European standard series is a poor instrument for identifying plant allergens, at least in India, though it may help by identifying other allergens of current or past relevance.

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Non-occupational protein contact dermatitis due to crayfish

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Key words: protein contact dermatitis; non-occupational; crayfish; fish allergy. © Munksgaard, 2001.

Case Report

A 23-year-old housewife, with no personal or family history of atopy, presented with an itchy erythematous reaction with papules, vesicles and edema around the lips, 45 min after preparing and eating crayfish, on several occasions during the last 6 months. The reaction developed desquamation and persisted for several days, despite treatment with topical corticosteroids. She had no systemic symptoms or lesions.

Patch tests with the GEIDC standard series were positive to formaldehyde. Prick testing performed with a commercially available shrimp allergen (Leti Laboratory, Madrid, Spain) was negative. Total serum IgE was 89 IU/ml, and CAP serum specific-IgE to shrimp and lobster (Pharmacia Laboratory, Uppsala, Sweden) was also negative. Prick-by-prick tests with raw and cooked crayfish showed wheal reactions of 5 mm and 6 mm, respectively, 15 min later. Patch tests with the same allergens on normal skin were positive, with papules and erythema, at D2. 10 subjects tested with the same preparations as controls were negative. An open oral challenge test with cooked crayfish (1/2 unit) was followed by a

popular, erythematous and oedematous reaction on the upper lip, 30 min later.

Discussion

The patient reported represents an example of non-occupational protein contact dermatitis (1) with lesions in an unusual location. Commonly, lesions are confined to the hands and the forearms, because occupational allergens are by far the most relevant etiologic agents and affect food handlers (2, 3). This was not the case in our patient, who usually used a fork to convey the crayfish to her mouth.

A combined Type I and IV hypersensitivity seemed to be present in our patient, because of the positive results of both immediate prick-by-prick and delayed patch tests with raw and cooked crayfish. The causative relationship between the crayfish and the lesions was further confirmed by a positive oral challenge test.

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Contact dermatitis from soybean extract in a cosmetic cream

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Key words: contact sensitivity; soybean extract; ceramide 3; Type I (immediate) hypersensitivity; soy; soya; cosmetics. © Munksgaard, 2001.

Case Report

A 55-year-old housewife presented in 1999 with a 5-month history of reacting to a facial cosmetic cream. Within a few hours, she developed erythema and, by the next day, swelling of the face. She was using Boots No. 7 Time Defying Night Cream (batch 2S).

She had previously been seen in 1992, with another apparent cosmetic reaction. Patch testing at that time to standard, preservative, fragrance, facial, medicament and metal series, plus her own cosmetics, had been positive to fragrance mix (8% pet.) and to a proprietary makeup. She gave a history of reacting to an anti-tetanus toxoid injection and to other facial creams. Some members of her family were said to react to washing powder and her son had reacted to a cream.

She was patch tested to standard, preservative, perfume and flavours, vehicle/emulsifier, cosmetic and facial series, along with some extras which included the facial cream Boots No. 7 Time Defying Night Cream, as is. She was positive on day 4 (D) to para-phenylenediamine (+) and cocamidopropyl betaine (+), and on D2 and D4 to fragrance mix (++) and Boots No. 7 Time Defying Night Cream (++/++) (Table 1).

After discussion with the patient and correspondence with Boots, the patient was patch tested to the components of Boots No. 7 Time Defying Night Cream (Positive Action Original). She was once again positive on D2 and D4 to the cream, and also to its components

soybean extract and ceramide 3 together (2% pet.), but not to ceramide 3 alone (5% pet.) (Table 1).

She attended for further patch testing to the potentially reactive components, i.e., ceramide 3 and soybean extract (dilutions 20%, 10% and 1% eth.). Soybean extract dilutions (20%, 10% and 1%) were also applied on Finn Chambers to the forearm and read at 30 min, when there was slight erythema with the 20% dilution. There was subsequently a palpable erythema at the 20% and 10% dilution sites when read at 36 h.

Conventional patch tests were negative once again to ceramide 3 (2% pet.) at both D2 and D7. Soybean extract 20% and 10% reacted at both D2 and D7 (+/+), while soybean extract 1% was also positive (?+/+) (Table 1). Despite the rapid reaction at 30 min to soybean extract, the patient had eaten soybean previously without adverse reactions, and an allergen-specific IgE test (Pharmacia CAP method; fluorometric assay) to soybean was negative.

Discussion

Soybean is used extensively as an inexpensive filler in many food products. Its nutty flavour improves taste, its high protein content increases nutritional value, and it serves to prolong shelf life. Indirect exposure to soy, because of its many commercial uses, including cosmetics, is almost inevitable (1).

Type I hypersensitivity reactions have been well docu-

Table 1. Positive patch tests to standard, cosmetic and facial series, allergens in the cosmetic, and dilutions of soybean extract

Series tested	Allergen	D2	D4	D7
standard	para-phenylenediamine 1% pet.	–	+	NT
standard	fragrance mix 8% pet.	+	+	NT
cosmetic/facial	cocamidopropyl betaine 1% pet.	–	+	NT
extras	No. 7 Time Defying Night Cream (as is)	++	++	NT
components of Boots No. 7 Time Defying Night Cream	ceramide 3 and soybean extract 2% pet.	++	++	NT
	ceramide 3 5% pet.	–	–	NT
	ceramide 3 2% pet.	–	–	NT
dilutions of soybean extract	soybean extract 20%	+	NT	+
	soybean extract 10%	+	NT	+
	soybean extract 1%	?+	NT	+

mented in a study of 22 exposed workers in a soybean mill, 8 of whom had a Type I reaction, of whom 4 had increased levels of soy-specific IgE (2). Our patient showed contact allergy when tested to all dilutions of pure soybean extract, as well as an immediate response to the 20% dilution, suggesting a possible Type I hypersensitivity reaction. However, her allergen-specific IgE for soybean was negative and she had previously eaten soybean without adverse reactions. The usefulness of radioallergosorbent tests in diagnosing food allergy has been assessed in a group of children with atopic dermatitis and shown to yield a false-negative result in 27% of cases (3). Therefore, a negative IgE for soybean does not preclude a diagnosis of Type I hypersensitivity.

Contact dermatitis has not previously been reported from soybean extract.

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Type I allergic reaction to hyaluronidase during ophthalmic surgery

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Key words: hyaluronidase; enzymes; ophthalmic surgery; adverse drug reactions; systemic; Type I allergy; positive prick test. © Munksgaard, 2001.

Case Report

A 67-year-old woman developed gross chemosis and periorbital oedema within minutes of administration of local anaesthetic consisting of prilocaine 3% with octapressin and Hyalase® (hyaluronidase) 15,000 units in 2 ml, for a cataract operation. The operation was abandoned and subsequently she became hypertensive, sweaty, nauseated and incontinent. Her condition responded to supportive measures within a few hours. The clinical diagnosis was an allergic reaction to local anaesthetic. 2 weeks later, the operation was carried out uneventfully under general anaesthesia. She had developed a swelling around her eye during a previous operation.

She was patch tested to the European standard series, an eye series and the materials used at the operation. She had a + reaction to phenylmercuric acetate, a preservative in eyedrops, but no relevance was found. Prick testing was performed with the materials used at the operation. A 2-cm wheal to Hyalase® was observed 20 min later. 10 controls were negative.

Discussion

Most ophthalmic surgery is now performed under local anaesthetic (1), during which it is vital that both anaesthesia and akinesia of the eye are obtained (1–3). Hyaluronidase is an enzyme that depolymerizes the polysaccharide hyaluronic acid in the extracellular matrix of

connective tissue (4). It increases the spread of locally injected anaesthetic and improves the efficacy and speed of nerve blocks (1–3).

As far as we are aware, there are no previous reports of immediate allergic reactions to hyaluronidase during ophthalmic surgery. There is 1 report of IgE-mediated allergic reactions to hyaluronidase in paediatric oncological patients (5). In our case, the systemic reaction was not clinically anaphylactic, and might have been due to the additional presence of octapressin allowing for rapid absorption into the circulation.

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A child with "occupational" allergic contact dermatitis due to MCI/MI

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Key words: allergic contact dermatitis; Kathon® CG; children; beeswax; preservatives; antimicrobials; biocides; furniture polish; restoration antique furniture. © Munksgaard, 2001.

Kathon® CG is a trade name for a mixture of methylchloroisothiazolinone and methylisothiazolinone (MCI/MI). Occupational allergic contact dermatitis from MCI/MI occurs not only in hairdressers and perfumers, but also in metalworkers, painters and bricklayers, the biocide being present in paints, lacquers, polishes, cleaning agents and construction materials (1–5).

Case Report

An 8-year-old non-atopic boy presented with exudative eczema of his hands. Patch tests with the GIRDCA standard series showed only a + D2/+ + D3 reaction to Kathon® CG. The dermatitis cleared in a few days using topical corticosteroids and avoiding the use of toiletries preserved with Kathon®. 3 years later, he presented with an itchy erythematous vesicular eruption mainly of his right hand. The onset of the dermatitis coincided with the use of a beeswax for polishing furniture, the boy helping his father in his passion for restoring old wooden furniture. The manufacturer of the wax was asked about its composition; he denied the presence of Kathon® CG in it.

Mass-spectrometry of both the wax and the pure standardized allergen Kathon® CG 0.01% aq. was performed; unfortunately, it was impossible to distinguish the molecular peaks of the 2 substances as they fell in the same area of the matrix of the spectrometer. HPLC was therefore carried out with the pure allergen: 2 peaks, corresponding to the 2 components of Kathon®, were observed. HPLC was successively performed with an aqueous extract of the wax: the same peaks were represented. The presence of Kathon® in the wax was therefore confirmed.

Discussion

Over the last 20 years, Kathon® CG has become a common allergen, even in pediatric patch-tested populations (6–11). Its wide use in skin-care products and creams and its strong sensitizing power, deriving from the chlorination of 1 of the 2 isothiazolinones, are responsible for sensitization, especially in early childhood (8). A problem with occupational sensitization in children emerges clearly from the literature; the sensitization rate at pediatric age was found to range from 7% to 18% (9–12). As would be expected, the risk of occupational allergic contact dermatitis increases with age. Hairdressing and catering are the activities most often involved in girls, metalworking and construction in boys (9).

In our case, this was not a true "occupational" dermatitis; the child helped in his father's hobby and he had

already been diagnosed as sensitized to Kathon® CG, due to exposure to toiletries, earlier in childhood. As stressed in the literature, positive reactions to Kathon® CG are frequently relevant (11); in our case, only analysis by HPLC allowed us to confirm such relevance. It might be hypothesized that preservatives had been added by bee-keepers before the beeswax was processed.

The child was deeply disappointed at our advice to stop using furniture wax, as he was extremely proud of being his father's workmate.

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Allergic contact dermatitis from gentamicin in eyedrops, with cross-reactivity to kanamycin but not neomycin

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Key words: gentamicin; kanamycin; eyelid dermatitis; aminoglycoside antibiotics; medicaments; ophthalmics; cross-sensitivity. © Munksgaard, 2001.

There is some structural similarity, in the form of 2-deoxystreptamine, between the 2 aminoglycoside antibiotics gentamicin and kanamycin, both of which are complexes of closely related components (1, 2).

Case Report

A 55-year-old housewife, with no personal history of atopy, presented with a 3-week history of pruritic, erythematous, scaly plaques on the eyelids, spreading in a few days periorbitally. The condition had developed 24 h after starting treatment with Colircusi Gentamicina® eyedrops. The patient had been unsuccessfully treated by her ophthalmologist with topical tobramycin. However, her lesions improved in 2 weeks with avoidance of all ophthalmic preparations, and oral and topical corticosteroids.

Patch tests were carried out with the GEIDC standard series, a medicaments series (Chemotechnique), tobramycin, Colircusi Gentamicina® eyedrops and their components. Positive reactions at D2 (+) and D4 (++) were obtained to Colircusi Gentamicina® eyedrops as is and to gentamicin 20% pet. A positive reaction at D4 (++) was obtained to kanamycin 10% pet. Neomycin was negative at D2, D4 and D7. Patch tests at D2 and D4 with gentamicin 20% pet. in 20 controls were negative.

Discussion

Allergic contact dermatitis due to gentamicin is rare in patients with eyelid dermatitis (3–5). The positive patch

test reaction to kanamycin, to which the patient had not apparently been previously exposed, suggests cross-reactivity. Although gentamicin frequently shows cross-reactivity with neomycin (6), in our case, the latter did not react on patch testing. Dermatitis after systemic kanamycin or streptomycin has been reported (7).

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Female predominance of gold allergy

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Key words: gold allergy; patch testing; female predominance; pierced earrings; dental alloys; clinical relevance. © Munksgaard, 2001.

Gold allergy has recently been increasingly reported (1-15).

Patients and Methods

Between January 1996 and December 1997, 398 consecutive unselected patients were patch tested with gold sodium thiosulfate (GST) 0.5% pet. 289 were female and 109 male. 177 had contact dermatitis, 29 pustulosis palmaris et plantaris, 98 atopic dermatitis and 94 other disorders. They were analysed by age, sex, reason for patch testing, clinical symptoms of contact dermatitis or stomatitis, and use of gold dental alloys, gold-pierced earrings or other gold jewelry.

Patch testing was performed on the upper back for 2 days (D), GST being provided by the Japanese Society for Contact Dermatitis, using Finn Chambers® (Epitest, Tuusula, Finland) on Scanpor® tape (Norgesplaster, Oslo, Norway). Readings were made at D3 and D7 according to the recommendations of the ICDRG (16).

We analyzed our data with the χ^2 test and the Fisher exact test. Statistical significance was set at $p=0.05$.

Results

A total of 54 (13.6%) among the 398 cases showed a positive reaction to GST. Their ages ranged from 19 to 78 years with a mean age of 44.8 years. Of the 54 cases, 50 were female and 4 were male. The positive ratios of GST were 17.3% (50/289) in females and 3.7% (4/109) in males, which showed a significant female predominance ($p<0.05$).

The presumptive sources of gold sensitization were dental alloys in 29 cases (53.7%), pierced earrings in 11 cases (20.3%), dental alloys and pierced earrings in 6 cases (11.1%), dental alloys and necklaces in 3 cases (5.6%) and unknown in 5 cases (9.3%) (Table 1).

Discussion

We have previously reported that gold allergy is predominant in females (2). In this study, we demonstrate such female predominance in subjects with gold dental alloys ($p<0.01$). Table 2 shows the data of previous reports compared with ours, with statistical analysis by the Fisher exact test. 3 such reports show a female pre-

Table 1. Sex difference in positive ratios of gold sodium thiosulfate according to exposure history

Exposure history	Positive ratios				Statistical analysis between males and females
	female	(%)	male	(%)	
dental alloys	26/161	16.1	3/78	3.8	$p<0.01$
pierced earrings	11/16	68.8	0	0	NS
dental alloys and pierced earrings	6/24	25.0	0	0	NS
dental alloys and necklaces	2/22	9.1	1/9	11.1	NS
others	0/28	0	0	0	NS
unknown	5/38	13.2	0	0	NS

NS: not significant.

Table 2. Sex difference in gold allergy in previous reports compared with ours

Reported year	Reported country	Ref.	Positive ratios				total	(%)	Statistical analysis between males and females
			female	(%)	male	(%)			
1994	Sweden	Björkner et al. (5)	56/544	10.3	15/279	5.4	71/823	8.6	$p<0.01$
1995	UK	McKenna et al. (7)	13/179	7.3	0/99	0	13/278	4.6	$p<0.01$
1996	UK	Sabroe et al. (8)	11/65	16.9	2/35	5.7	13/100	13	NS
1997	Portugal	Silva et al. (13)	23/2114	1.1	0/739	0	23/2853	0.81	$p<0.01$
1999	Japan	this report	50/289	17.3	4/109	3.7	54/398	13.6	$p<0.001$

NS: not significant.

dominance similar to ours (5, 7, 13). In the remaining one, the number tested may be too small to show any female predominance (8). Our study also suggests that the 2 main presumptive sources of gold allergy may be gold-pierced earrings and dental alloys.

Only 3 (7.9%) of our 38 cases with gold dental alloys had symptoms of the mucous membranes and tongue. Dental alloys appear to be a source of gold sensitization, though they elicit very few (7.9%) clinical symptoms compared to pierced earrings (76.5%). Only 16 (29.6%) cases showed clinical relevance.

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Contact sensitivity to quinazoline oxide

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In previous publications (1, 2), we reported quinazoline oxide as a strong contact allergen in Poland for pharmaceutical workers producing chlordiazepoxide (Elenium: Polfa). Recently, we have observed that sensitivity to this compound persists and can be worsened by airborne contact.

A 35-year-old woman had had atopic dermatitis in childhood. She had worked in the pharmaceutical industry in various capacities, and for some time on the production of chlordiazepoxide. After 5 years of such work, she developed dermatitis on the face and hands. A patch test with quinazoline oxide 0.5% pet. was ++. She started working in the office and the contact dermatitis regressed rapidly without recurrences. She lived at a dis-

tance of about 1 km from the pharmaceutical plant, and claimed that wind coming from that direction bore the odour of pharmaceutical production, and had caused sporadic facial erythema and itching, which no doctor had witnessed.

9 years after work change (and last occupational contact with quinazoline oxide), she was referred for reasons of compensation. 1 day after application of 0.5% quinazoline oxide as a patch test, a +++ reaction developed, requiring withdrawal of the contactant and administration of corticosteroids for several days. The reaction was much stronger than observed 9 years earlier after patch testing with the same preparation of the allergen. 3 weeks later, another patch test was made with 0.01%

quinazoline oxide and a somewhat less strong +++ reaction developed, persisting for 7 days.

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Helicobacter pylori in acquired cold urticaria

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Key words: acquired cold urticaria; *Helicobacter pylori*; penicillin; antibiotic therapy. © Munksgaard, 2001.

Urticaria is one of the commonest skin diseases, with enormous numbers of triggering factors (1). Current aetiological concepts separate physical and non-physical subgroups (2). Recent studies of otherwise unexplained chronic non-physical (idiopathic) urticaria have provided evidence that enteric infection with *Helicobacter pylori* may induce the disease (3, 4), though other investigators have found contradictory results (5–7).

Acquired cold urticaria (ACU) is one of the most frequent, and sometimes harmful, variants of physical urticaria. It may be classified as primary, of unknown etiology, or as secondary, frequently associated with infectious diseases. Besides cold desensitization, recommended regimens include antihistamines and, above all and for many years, intramuscular (i.m.) depot penicillin to eliminate undefined focal infection (8).

Patients and Methods

During the winter season, patients with the presumptive diagnosis of cold urticaria underwent precise history taking, ice-cube test and cold-water immersion test, according to the recommendations of the EAACI (2), laboratory tests (Table 1), X-ray of the chest and paranasal sinuses, and gastroscopy.

Table 1. Laboratory tests performed in patients with acquired cold urticaria (ACU)

total and differential blood cell count
erythrocyte sedimentation rate
enzyme screening
antistreptolysin titer
test for virus antibodies
test for <i>Borrelia burgdorferi</i> antibodies
RAST (CAP-FEIA, Pharmacia) for IgE-antibodies against
milk and egg proteins
acute phase proteins
cryoglobulins and cold agglutinins
urinalysis

Results

We saw 10 ACU (5 female) patients, diagnosed by case history and a positive ice-cube test or cold-water immersion test.

In 5 patients (3 females), the diagnostic program gave no pathological result. In the other 5 patients (aged 16 to 61 years; 2 female) previously undiagnosed gastric complaints were detected, and in 4 of these patients, normal laboratory tests, as well as absence of drug intake, indicated no other underlying disease. All 5 patients accepted gastroscopy, and in 4 patients, slight gastric erosions were found. Histological examination of biopsy specimens confirmed *H. pylori* infection.

The *H. pylori*-positive patients were treated daily with i.m. penicillin G (4.5 Mio.) for 5 days, since there were no reports of *H. pylori*-associated physical urticaria to date that would have justified treatment with an eradication scheme (9). The gastrointestinal, as well as cold-derived, symptoms improved rapidly. The patients were observed for 10 weeks thereafter, and in 3 patients, the whealing reaction in the cold water immersion test recurred, while 1 patient has since remained free of complaints.

Discussion

In the majority of patients with ACU, antihistamines remain the mainstay of therapy. However, i.m. penicillin has been recommended for many years by a small number of clinical studies as a possibly causal treatment without known pathogenetic evidence (8). Findings in our patients, as well as data from the literature, may point to *H. pylori* infection as at least a trigger factor in patients with ACU.

Firstly, penicillin V as well as i.m. penicillin have been shown to suppress *H. pylori* infection, though they are not able to eradicate it (10, 11). Secondly, i.m. depot penicillin is able to suppress or eliminate symptoms in a notable number of patients with primary ACU (8). However, in the majority of reported patients (8), cold exposure-associated symptoms returned some time after antibiotic treatment, as was the case in our patients. This

may indicate that the suppressive effect of penicillin on the *H. pylori* infection has lost its efficacy.

Since our study has certain limitations, (e.g., number of participants, and control persons) (1), controlled studies should be performed to elucidate the role of *H. pylori* in otherwise unexplained ACU, because this particular disease is distinct from previously-investigated variants of urticaria (1, 2).

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Allergic contact dermatitis due to deer-fat cream (*Hirschtalgreme*)

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Key words: deer-fat cream; *Hirschtalgreme*; Euxyl™ K 400; methyltribromo glutaronitrile; patch testing; natural cosmetics; preservatives. © Munksgaard, 2001.

Case Report

A 44-year-old woman presented with acute dermatitis of the left axilla, spreading to the trunk and limbs. She had used 21 different cosmetics (deodorants, perfumes, creams and lotions), many of which were 'natural'. Patch testing with the standard series and cream base series of the DKG showed a + reaction to fragrance mix and a ++ reaction to Euxyl™ K 400 on D1–D3 (1). Patch testing with the patient's own cosmetics gave a ++ reaction to *Hirschtalgreme* (deer-fat cream) on D2 and D3, the result being confirmed by a ROAT. The manufacturer was asked to supply the ingredients of the *Hirschtalgreme*: patch testing with these showed a +++ reaction only to Euxyl™ K 400.

Comment

Natural cosmetics have become increasingly popular in recent years. The manufacturers recommend *Hirschtalgreme* to hikers to prevent blisters and to cyclists to prevent soreness of the thighs, and it was used by our patient for skin care in the axilla. To our knowledge, contact dermatitis from deer-fat cream has not previously been reported. The fat itself was not the cause

of the contact dermatitis, but the well-known allergen Euxyl™ K 400. Euxyl™ K 400 consists of phenoxyethanol and methyltribromo glutaronitrile in a 4:1 ratio, the latter usually being the allergen. Increasing sensitization rates to Euxyl™ K 400 and methyltribromo glutaronitrile have recently been observed in European countries (2–4). In our case, the deer-fat cream acted as a Trojan horse, carrying the allergen to an unusual area.

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Simultaneous immediate and delayed hypersensitivity to chlorhexidine digluconate

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Key words: chlorhexidine digluconate; contact urticaria; allergic contact dermatitis; anaphylaxis; Type I allergy; Type IV allergy; antimicrobials; biocides; preservatives. © Munksgaard, 2001.

Chlorhexidine digluconate is widely used as a disinfectant, as well as a preservative in topical skin products. Considering its wide usage, contact allergy is relatively rare. Even more rare seems to be immediate hypersensitivity. However, an increasing number of reports on immediate chlorhexidine allergy have been published recently (1–4).

Case Report

A 61-year-old man went for an inguinal hernia operation. Apart from hernia and multiple arthrosis, he was otherwise healthy. The skin was washed with a chlorhexidine-containing fluid. An urticarial eruption developed during the operation on the back, arms and stomach. It was treated with intravenous glucocorticosteroid, which rendered the patient symptomless.

He was referred for allergy testing. Prick tests with natural rubber latex (NRL) remained negative. Prick, intradermal and subcutaneous tests with up to 2.0 ml Marcain (bupivacaine hydrochloride) at 2.5 mg/ml were negative. In contrast, a prick test with 1% chlorhexidine gluconate was positive (10-mm wheal and flare, histamine control 6 mm). In patch tests also performed,

chlorhexidine digluconate was positive. Additionally, patch testing with a serial dilution of chlorhexidine gluconate was positive.

Comment

Combined immediate and delayed hypersensitivity to chlorhexidine digluconate has been reported 2× before (1, 2). Immediate allergy has been reported alone more often (3), and may be severe. Reports from patients of discomfort after use of chlorhexidine-containing products should therefore be taken seriously.

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Colophonium in sanitary pads

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Key words: colophonium; rosin; abietic acid; formaldehyde; (meth)acrylates; consumer; allergic contact dermatitis; sanitary pad; diaper; hygiene product. © Munksgaard, 2001.

Karlberg & Magnusson (1) have identified rosin components in diapers, but no studies seem to have clarified allergens in sanitary pads.

Materials and Methods

Sanitary pads (Table 1) were bought from department stores in Helsinki, Finland, and Copenhagen, Denmark. Colophonium was determined as the methylesters of the main resin acids (dehydroabietic acid, abietic acid), after hydrolysis of the sample with ethanolic potassium hydroxide (2, 3). Formaldehyde was measured according to

the European standard SFS-EN ISO 14184-1:1999 (4). Acetone-soluble (meth)acrylates were determined by gas chromatography, as previously described, with a detection limit of 0.002% (5).

Results

The contents of formaldehyde, resin acids and (meth)acrylates are given in Table 1. Formaldehyde and methacrylates were not detected. The highest content of resin acids was 0.056%, corresponding to approximately 0.08% colophonium (3). 3 other products had more than

Table 1. The contents of free formaldehyde, colophonium-derived resin acids and (meth)acrylates in sanitary pads

Name of product	Easy/ultra bind-super plus	Softline/normal	Apoteks/Ultra plus normal	Always/Ultra long plus (Procter & Gamble)	Libresse/Invisible Super Clip (SCA Hygiene Products Oy)	Vuokkoset/Slim Wings Super (Delipap)	Spar Terveysside (Delipap Oy, Suomen Spar)	Softline Super (Delipap, Inex Partners Oy)	Pirkka/Ohut terveysside Long (Kesko Delipap)
bought from	Denmark	Denmark	Denmark	Finland	Finland	Finland	Finland	Finland	Finland
form-aldehyde	<10 ppm	<10 ppm	<10 ppm	<10 ppm	<10 ppm	<10 ppm	<10 ppm	<10 ppm	<10 ppm
(meth)-acrylates	<0.003%	<0.003%	<0.003%	<0.003%	<0.003%	<0.003%	<0.003%	<0.003%	<0.003%
colophonium	0.056%	0.048%	0.008%	0.006%	<0.004%	0.020%	0.006%	0.029%	0.011%
(resin acids)									

0.02% resin acids, corresponding to 0.03% colophonium, whereas the other 4 contained very low amounts of resin acids.

Discussion

The present report continues a series of studies of the safety of cosmetics and consumer products (3, 5–7). The content of colophonium in sanitary pads was similar to that in mascaras (3) and thus probably an eliciting level for allergic contact dermatitis in some sensitized individuals. Patients very allergic to colophonium should therefore choose sanitary pads containing low levels of colophonium (8, 9).

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