

Short Communications

Evaluation of the fragrance mix in the European standard series

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Key words: fragrance; fragrance mix; patch testing technique; oakmoss; iso-eugenol; eugenol; hydroxycitronellal; cinnamic alcohol; cinnamic aldehyde; geraniol; α -amyl cinnamic aldehyde; prevention; allergic contact dermatitis; cosmetics; ingredient labelling. © Munksgaard, 1999.

Patients and Methods

During 1994–1998, 757 of our outpatients, suspected of allergy to cosmetics, were patch-tested with the European standard series, including fragrance mix, and with its 8 separate components: oakmoss, iso-eugenol, eugenol, hydroxycitronellal, cinnamic alcohol, cinnamic aldehyde, geraniol and α -amyl-cinnamic aldehyde (2% in sorbitan sesquioleate 1%). All test substances were supplied by Hermal Trolab® (Reinbek, Germany). Test results were analysed retrospectively.

Results

Of the 757 patients (91 male, 666 female; mean age 37 years, range 4–88 years) tested with both fragrance mix and its individual components, 112 were positive to fragrance mix, but only 50 (45%) of these 112 were positive to 1 or more of its components (Table 1). In addition, 9 patients were positive to 1 or more of the components, whereas fragrance mix itself was negative.

Oakmoss ($n=22$) and iso-eugenol ($n=16$) were the

top-ranking components, whereas geraniol ($n=3$) and α -amyl cinnamic aldehyde ($n=0$) were at the bottom (Table 2).

12 patients had positive patch tests to cinnamates, of whom 6 were positive to both cinnamic aldehyde and cinnamic alcohol, 4 only to cinnamic aldehyde, and 2 only to cinnamic alcohol.

Discussion

Explanations for the big discrepancy between reactions to fragrance mix and to its components are: (i) an irritant rather than an allergic reaction to the mix, due to its high concentration of fragrance components ($8\times 1\%$); or (ii) the higher concentration of the emulsifier sorbitan sesquioleate in the mix (5%) compared to the individual components (1%); or (iii) the phenomenon of “synergy”: whereby components of the mix interact positively in some way (1, 2). In 9 patients, positive reactions to components were found despite the fragrance mix being negative. This could be explained by: (i) the difference between the concentration of the components when tested in the mix (1%) and tested separately (2%); or (ii) the phenomenon of “quenching”, whereby components of the mix interact negatively in some way (1, 3).

As so few positive reactions to α -amyl cinnamic aldehyde and geraniol were seen, these compounds are the prime candidates for omission or replacement in the current mix (1, 2). On the other hand, as oakmoss and iso-eugenol rank top of the positive reactors, we would advocate extension of the legal ingredient declaration for cosmetics in the European Union to include these 2 compounds, and request perfumiers to exclude them from their future creations.

Table 1. Fragrance mix and its components

	Fragrance mix positive $n=112$ (%)	Fragrance mix negative $n=645$ (%)
$n=757$		
components positive	50 (45)	9 (1)
components negative	62 (55)	636 (99)

Table 2. Separate components in fragrance-mix-positive/component-positive patients

	$n=50$ (%)
oakmoss	22 (44)
isoeugenol	16 (32)
hydroxycitronellal	10 (20)
cinnamic aldehyde	10 (20)
cinnamic alcohol	8 (16)
eugenol	6 (12)
geraniol	3 (6)
α -amyl cinnamic aldehyde	0 (0)

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Pentaerythritol-esterified gum rosin as a sensitizer in Granuflex[®] hydrocolloid dressing

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Key words: allergic contact dermatitis; Granuflex[®]; pentaerythritol-esterified gum rosin; colophony; medicaments; cross-sensitivity. © Munksgaard, 1999.

Of the last 17 consecutive patients between 1996 and 1999 patch tested to Granuflex[®] hydrocolloid dressing in our department, 4 (24%) have been positive to colophony, Abitol[®] and Granuflex[®], 1 (6%) to Abitol[®] and Granuflex[®] and 12 (70%) to Granuflex[®] alone. Fully hydrogenated pentaerythritol-esterified gum rosin (PEGR), manufactured by Hercules Inc., Delaware, USA, is used as the sticky agent for Granuflex[®]. When PEGR was substituted for colophony as a bow resin for colophony-sensitive violinists, they were able to tolerate regular exposure to PEGR without relapse of their contact dermatitis (1).

Modified gum rosins, however, are rarely pure and contain some unmodified rosin – up to 6.2% abietic acid in the case of fully hydrogenated PEGR (2). Reactions previously attributed to PEGR have all been accompanied by positive reactions to colophony 20% pet. and could, therefore, have been due to the unmodified colophony fraction in the commercial product (2–4): we therefore recalled 7 Granuflex[®] patients for further patch testing.

Patients, Methods and Results

The patients were patch tested to freshly-prepared 10% and 20% fully hydrogenated PEGR and 10% and 20% partially hydrogenated PEGR in pet. and coconut oil (Hercules BV, The Netherlands), colophony 20% pet., Abitol[®] 10% pet., and Granuflex[®] as is. The other ingredients of Granuflex[®] were not made available to us. 10 control subjects were patch tested to fully hydrogen-

ated PEGR 10% pet., and showed no reactions at D4. Table 1 shows the patch test results at D4. There were differences in reactivity between products prepared in coconut oil and pet. All patients had developed contact dermatitis from leg ulcer dressings. Of the colophony-positive patients, 2 had reported previous allergic reactions to adhesive plaster. Of the 2 fully-hydrogenated PEGR-positive and colophony-negative patients, only 1 had had a previous allergic reaction to adhesive plasters.

Discussion

This study confirms that PEGR is a potential sensitizer independent of unmodified colophony. Without the other ingredients of Granuflex[®], we are unable to comment as to whether this product contains other potential sensitizers. Using a fully hydrogenated gum rosin prior to pentaerythritol esterification does not appear to affect the allergenicity of the final product. Partially hydrogenated PEGR is likely to be a complex blend of chemicals, since hydrogenation of gum rosin will produce a mixture rich in dihydro-, tetrahydro-, and dehydro-abietic acids (5). These modifications of gum rosin do not appear to alter its allergenicity post-pentaerythritol esterification, since cross-reactivity with fully hydrogenated PEGR is preserved.

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Table 1. Results of patch testing at D4

	Colophony	Abitol	Granuflex [®]	Fully hydrogenated PEGR	Partially hydrogenated PEGR
patient 1	–	–	–	–	–
patient 2	++	++	++	++	++
patient 3	–	–	+	+	+
patient 4	–	–	–	–	–
patient 5	+	+	++	++	++
patient 6	–	–	++	++	++
patient 7	++	++	++	++	++

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Occupational contact dermatitis caused by polyfunctional aziridine crosslinker: duct tubing for airconditioning

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Key words: polyfunctional aziridine crosslinker; (meth)acrylates; trimethylolpropane triacrylate; airconditioning duct tubing; adhesive; occupational; allergic contact dermatitis. © Munksgaard, 1999.

Case Report

An otherwise-healthy 39-year-old machine operator presented with erythematous papules and scaling of his antecubitals, neck and fingertips of 1-year duration. He had no history of atopy. The lesions had developed after his employer switched to an adhesive containing a polyfunctional aziridine crosslinker. He operated a machine that formed duct tubing for airconditioning. In spite of modest improvement with topical corticosteroids, his dermatitis recurred, leading to transfer to another position.

Patch testing was performed, with the Finn Chamber (Epitest, Helsinki) on the upper back for 2 days with readings at D2 and D4, to an extended routine series of the NACDRG, a machinists' tray and environmentalals brought in by the patient. All were negative.

The employer provided the aziridine crosslinker, which was tested at 1%, 0.5% and 0.1% pet.; the reading at D4 was + + +, utilizing the ICDRG grading system. 20 normal controls were negative. Trimethylolpropane triacrylate (0.5% pet.) was negative.

Discussion

Polyfunctional aziridine (PFA) crosslinker is synthesized by reacting a multifunctional acrylate with an aziridine compound (propyleneimine or ethyleneimine). PFA is used to crosslink numerous products, including waterborne acrylic emulsions, paint primers, inks, lacquers, topcoats and other protective coatings, thus overcoming

the systemic toxicity problems from organic solvents (1). We were unaware of its use in fabrication of duct tubing. Several case reports of allergic contact sensitization are available (1–8). PFA crosslinker may also cause occupational asthma (2).

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Occupational allergic contact dermatitis eczema caused by obeche and teak dusts

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Key words: tropical woods; obeche; *Triplochiton scleroxylon*; teak; *Tectona grandis*; patch test; plant allergen; blepharoconjunctivitis; occupational; carpenter; allergic contact dermatitis. © Munksgaard, 1999.

Case Report

The work of a 56-year-old non-atopic carpenter was to repair sauna benches with obeche and teak wood. He had handled teak for about 40 years and obeche for about 30 years. For about 10 years, obeche dust had caused itching and for about 1 year, he had suspected that obeche or teak dust caused his eyelids to swell and made his eyes itchy and red, as well as caused rhinitis and dermatitis on his hands, arms, neck and upper chest. All these symptoms disappeared when he was away from work.

Patch tests included wood dusts (obeche, teak and oak from an importer; pine and spruce from a manufacturer) as is, moistened with water, a modified European standard series, series of medicaments and cosmetics from Chemotechnique Diagnostics AB, Sweden, and Hausen's plant allergens. Obeche and teak dusts, as well as deoxylapachol and lapachol, all gave ++ reactions. Prick tests with the same dusts and with a standard series (Allergologisk Laboratorium A/S, Denmark) were negative. Determinations of obeche specific-IgE-antibodies were negative. Total IgE was slightly elevated at 210 kU/l. Investigation by a nasorhinolaryngologist, including a nasal challenge with obeche and teak dusts, did not confirm allergic rhinitis. The patient had to stop working with both woods.

Discussion

Differentiation of an allergic from an irritant patch test reaction to teak dust may be difficult. Confirmation was obtained here by ++ patch test reactions to 2 allergens in teak, deoxylapachol and lapachol (1, 2). Allergic contact dermatitis caused by teak (*Tectona grandis*) has been reported since 1905 (3). According to a Norwegian study (1) from the 1960s in furniture factories, 12% of workers exposed to teak dust developed such dermatitis.

Asthma caused by obeche (*Triplochiton scleroxylon*) has been known since the 1930s (4). In Finland, it is a well-known cause of sauna builder's asthma (5, 6), and we used the same obeche dust for patch testing as we have long used for prick testing. Contact urticaria from obeche wood has been described since the 1960s (7–9), but not allergic contact dermatitis. Dermatitis has been mentioned as being caused by a toilet seat made of obeche, with a positive patch test to obeche dust (3). The compound responsible for Type IV allergy to obeche wood has not been isolated. Hausen could find no alkalooids or chinones in the wood (10).

The patient also had conjunctival and rhinitis symptoms, but no dyspnoea, associated with exposure to the wood dusts. Exposure to teak dust can also cause respiratory and eye symptoms. All prick tests were negative. The otorhinolaryngological examination pointed to irritant rhinitis. An ophthalmological examination was not done, but the appearance and the course of the eye symptoms suggested allergic blepharoconjunctivitis, as caused by Type IV sensitization to certain chemicals, e.g., methacrylates and gold salts (11, 12).

Our patient probably had allergic contact dermatitis caused by Type IV allergy to obeche and teak, associated with blepharoconjunctivitis from exposure at least to teak dust. Type IV sensitization to obeche has not been reported previously.

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Occupational allergic contact dermatitis from N,N-methylene-bis-5-methyl-oxazolidine in a nylon spin finish

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Key words: allergic contact dermatitis; occupational; N,N-methylene-bis-5-methyl-oxazolidine; biocide; formaldehyde-releaser; spin finish; nylon industry. © Munksgaard, 1999.

Case Report

A 40-year-old man presented with a 3-month history of vesicular eczema on the forearms, with periorbital swelling and erythema. He worked in a large nylon manufacturing plant and, 4 weeks prior to the onset of the eruption, had moved to the spinning area. During nylon spinning, the polymer is melted and extruded to transform it into fine threads. Spin finish is applied to the thread line by metered pumps. After this, the threads go to spinning reels and the bobbins of yarn are packaged and distributed. A factory visit revealed that the application of spin finish was automated. In the spinning area, however, operatives did come into contact with the spin finish during cleaning of equipment, re-stringing after yarn breakages and packaging of bobbins of yarn, as well as from airborne mist. Protective gloves were available but, due to the humidity of the spinning environment, short-sleeved shirts were worn with no forearm protection.

Patch tests to standard, and preservative and cutting oil series were all negative at D2 and D4. The patient was also patch tested to 4 spin finishes at their use concentrations. 2 of these produced positive (+) reactions at D4. Both these contained the biocide N,N-methylene-bis-5-methyl-oxazolidine at 0.2%. Patch testing with this biocide in water at 1% elicited positive reactions at D2 (++) and D4 (++) . Patch testing with it at 1% in 20 control patients was negative at D2 and D4. Avoiding contact with the spin finish by leaving the spinning area resulted in resolution of the allergic contact dermatitis.

Discussion

The application of spin finish in nylon and other synthetic fibre spinning reduces friction between the fibres

and the metal guides that they move along, thus reducing electrostatic charge and preventing the filaments from fraying. Chloroacetamide in a spin finish was suggested to have caused allergic contact dermatitis in 7 nylon workers by Savage (1). Dimethoxane has been reported as a sensitizer in a polyester spin finish (2). Burrows & Campbell (3) thought that 10 workers with dermatitis after polyester spin finish exposure had irritant rather than allergic contact dermatitis (3). 6 cases of allergic contact dermatitis from methylchloroisothiazolinone, methylisothiazolinone were reported from a nylon spin finish (3).

N,N-methylene-bis-5-methyl-oxazolidine (Grotan OX) is a formaldehyde-releasing biocide. Our patient did not react to formaldehyde in the standard series or to any other formaldehyde-releasers in the preservative and cutting oil series. To our knowledge, this formaldehyde-releasing preservative has not previously been reported as a human sensitizer. Its sensitizing potential has, however, been assessed by guinea pig maximization testing, when it was found to be a strong sensitizer (4).

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Allergic contact dermatitis from dithranol

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Key words: allergic contact dermatitis; dithranol; anthralin; medicaments; psoriasis. © Munksgaard, 1999.

Dithranol (anthralin) is a synthetic derivative of a substance originally extracted from the araroba tree and is frequently used in the treatment of psoriasis (and alopecia areata). It is a known irritant and stains the skin.

Case Report

A 60-year-old man, with psoriasis vulgaris for the last 12 years, presented with an exacerbation. He was on methotrexate 2.5 mg, 3× weekly and to date had received 1210 mg of the drug. Bath water PUVA was commenced. For a few resistant plaques on the thighs, dithranol 0.01% cream was prescribed. 2 days later, erythema with vesiculation and exudation developed at the

sites treated. There was a past history of dithranol intolerance. Patch testing with various strengths of dithranol was done (Table 1). Patch testing with the same concentrations in 5 healthy volunteers was negative.

Discussion

Few cases of allergic contact dermatitis from dithranol have been reported (1–3). There is disagreement over its irritant threshold. Burden et al. (3) proposed 0.001% as the appropriate patch test concentration, while De Groot et al. (1) stated that 0.05% pet. gave sufficiently reliable results.

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Table 1. Results of patch testing with dithranol

	0.01% pet.	0.005% pet.	0.0025% pet.
D2	++	+	+
D3	++	+	+

Active sensitization to sodium metabisulfite in hydrocortisone cream

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Key words: active sensitization; sodium metabisulfite; topical corticosteroids; medicaments; preservatives; patch testing technique; allergic contact dermatitis. © Munksgaard, 1999.

In performing assays for cumulative irritancy of topical corticosteroid formulations, we have actively sensitized 2 out of a panel of 50 to sodium metabisulfite. The formulations were 1% hydrocortisone (for over-the-counter distribution) in which metabisulfite was included at an unstated concentration. An edematous patch test response led to component testing: 2 subjects had a ++ response to sodium metabisulfite 1% pet., utilizing Finn Chambers (Epitest, Helsinki), the upper back and readings at D2 and D4.

Numerous adverse reactions have been attributed to sulfiting agents, including GI symptoms, urticaria, pruritus, angioedema, headache, asthma, and non-specific cutaneous lesions. Metabisulfites, along with other sulfiting agents, are used in the food and beverage industries as antioxidants and preservatives. They are also used in topical pharmaceuticals. The bisulfite of commerce consists chiefly of sodium metabisulfite, and for

all practical purposes, possesses the same properties as the true bisulfite (9). Intolerance reactions, of both immediate and delayed type, to sulfiting agents are increasingly being reported. Results of patch testing with various formulations containing sodium metabisulfite are given in Table 1.

Giorgini et al. (1) recently reported induction of contact dermatitis to sodium metabisulfite and Melcloderm cream. Doooms-Goosens et al. (2) found a strong positive reaction to sodium metabisulfite in 2 patients sensitive to ketoconazole cream, and concluded that there probably existed a reaction with features of both the immediate and delayed-type allergy to sodium metabisulfite. Vissers-Crouchs et al. (8) patch tested a man with recurrent facial seborrhoeic dermatitis, who had developed an itchy papulovesicular dermatitis on treatment with ketoconazole cream. Patch tests with the control cream base, as well as sodium sulfite at the concentrations given in

Table 1. Reported results of patch testing with sodium-metabisulfite-containing formulations

Compound	Patch test % of sodium metabisulfite	D2	D4	Controls		Refs.
				no.	(%)	
Meclocloderm cream (pet.)	1%	++	++	NS	NS	(1)
sodium metabisulfite (pet.)	1%	++	++	NS	NS	(1)
Neo-lidocaton (aq.)	0.2%	+	+	NS	NS	(2)
sodium metabisulfite (pet.)	5%	++	++	NS	NS	(2)
potassium metabisulfite (aq.)	1% and 5%	++	++	NS	NS	(3)
Veg-white (aq.)	10%	+++	+++	NS	NS	(4)
sodium metabisulfite (aq.)	10% and 20%	+++	+++	NS	NS	(4)
sodium metabisulfite (aq.)	2%, 5%, 10%	+	+	5	10%	(5)
sodium metabisulfite (aq.)	5%	+	—	20	5%	(6)
topical hydrocortisone (aq.)	0.2%	+	+	20	5%	(6)
clobetasol cream	NNG	++	++	NS	NS	(7)
sodium metabisulfite	NNG	++	++	NS	NS	(7)
ketoconazole cream	NNG	+++	+++	NS	NS	(8)
ketoconazole cream base	NNG	+++	++	NS	NS	(8)
sodium sulfite (aq.)	0.2%, 2%	+++	+++	NS	NS	(8)
sodium sulfite (pet.)	0.2%, 2%, 5%	+++	+++	NS	NS	(8)

NS: not stated ; NNG: no number given.

Table 1, were strongly positive. They concluded that this was a Type IV sensitivity to sodium sulfite.

Nater (3) reported a woman with severe allergic contact dermatitis on the hands due to occupational contact with metabisulfites in her job at a pharmaceutical company. Patch testing with potassium metabisulfite 1% and 5% aq. was positive. Avoidance of contact with the causative agent by wearing protective gloves cleared her dermatitis; however, a subsequent injection of lidocaine (presumably containing metabisulfite) for minor surgery caused a relapse. Similarly, Epstein (4) observed hand dermatitis in a salad maker. He reported a strong positive reaction to an antioxidant (Veg-white) containing metabisulfite. Strong positive patch tests to metabisulfite 10% and 20% aq. were also reported. These concentrations may be too high and might produce false-positive results. Apetato & Marques (5) studied a pastry factory worker who had had dermatitis on the backs of his hands for the past 5 months. The dough that he handled contained sodium metabisulfite at 0.04%. Patch tests with sodium metabisulfite 2, 5 and 10% aq. were all positive. Irritancy controls at 10% in 5 subjects were all negative.

We tested 20 volunteers with 5% pet. as a control group. Slight erythema but no edema was seen at D2 but not at D4. We suspect that the ideal test concentration has yet to be determined. Repeated open application testing (ROAT) might help to confirm the aller-

genicity of metabisulfite. Additional irritancy controls would also be welcome. A cooperative research group might consider adding metabisulfite to their standard series, as a test of its frequency as an allergen.

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Contact allergy to clotrimazole: an unusual allergen

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Key words: allergic contact dermatitis; clotrimazole; antifungals; medicaments. © Munksgaard, 1999.

Case Report

A 71-year-old woman had a long history of seborrhoeic dermatitis affecting the scalp, face, flexures, and the vulva. She had used a wide variety of antifungal creams, corticosteroid creams and haemorrhoidal preparations over many years. She developed a severe exacerbation of her vulval dermatitis after 6 weeks application of Canesten[®] cream.

She was patch tested to the European standard series, an anogenital series, a hand and face series, and Canesten[®] cream 1%. Positive results were observed for neomycin 20% pet. (D2-/D4+), cinchocaine 2.5% pet. (D2-/D4++), tixocortol pivalate 1% pet. (D2++/D4++), hydrocortisone 2% alc. (D2-/D4+) and Canesten cream as is (D2++/D4+).

She was subsequently tested with all the individual ingredients of Canesten[®] 1% cream (sorbitan monostearate 5% aq., polysorbate 60 5% aq., cetearyl alcohol 20% pet., octyldodecanol 30% pet., benzyl alcohol 5% pet., and clotrimazole 1% pet.). A positive result for clotrimazole 1% pet. was observed alone (D2+/D4-), confirming clotrimazole to be responsible for the reaction to Canesten[®] cream.

Comment

Clotrimazole is an imidazole antifungal agent (1) that is able to penetrate the skin but is poorly absorbed into the systemic circulation. It is widely used in treatments for vaginal candidiasis and in several combined corticosteroid/antifungal preparations. Contact dermatitis from clotrimazole has been reported, but surprisingly infrequently (2-6).

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Prevalence of natural rubber latex allergy in hairdressers

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Key words: prevalence; epidemiology; natural rubber latex; allergy; contact urticaria; skin symptoms; hairdressers; protective gloves; questionnaire study; occupational. © Munksgaard, 1999.

Hand eczema is common among hairdressers (1, 2) and Van der Walle & Brunsveld (3) found natural rubber latex (NRL) to be a common cause.

Materials and Methods

The details of the study design have been reported earlier (4). Of a random sample of 500 hairdressers, 355 were available for a computer-aided telephone interview. 189 hairdressers reported work-related skin or respiratory symptoms, and 130 came for an occupational medical interview. On the basis of the interview, 109 met the criteria for suspected occupational skin or respiratory disease.

Prick testing was performed in 107 hairdressers. 3 NRL prick test substances were used: 2 made ourselves

from a household glove or a disposable latex examination glove, according to the recommendations of Turjanmaa (5); and 1 commercial prick test substance from Allergologisk Laboratorium (ALK, Copenhagen; NRL 1:100).

Results

313 hairdressers answered the question, "Do you use NRL gloves at work": 255 (81%) did not use NRL gloves at all; 20 (6.4%) used NRL gloves daily; 23 (7.3%) only 1× a week, and 15 (4.8%) less often than 1× a week.

3 hairdressers had an allergic prick test reaction to NRL. The ALK preparation was positive in all 3 patients, the household glove in 2 and the latex glove in 1.

In 1 case, NRL allergy was considered occupational (past relevance).

Case Report

A 40-year-old atopic hairdresser had had flexural dermatitis in childhood, and had worked in hairdressing since she was 17-years-old. She did not have respiratory symptoms. She had had hand dermatitis for 19 years. Initially, patch tests with a standard series and a hairdressing series had been negative. She was under dermatological follow-up when recruited for our study. Occasionally, she had had more extensive dermatitis, but in the past few years, only on her hands, both palmar and dorsal. She had previously used NRL gloves, but for the past 6 years, only vinyl gloves.

Patch testing with a modified European standard series and an extensive hairdressing series (4) was negative. Prick testing with environmental allergens and NRL was positive to cat and dog epithelium (diameter 5 mm), 3 NRL allergens (all 5 mm), and *Pityrosporum ovale* (6 mm). Histamine hydrochloride, 10 mg/ml, provoked a 7-mm reaction. A provocation test with an NRL glove produced whealing in 30 min, whereas a vinyl glove was negative. A RAST to NRL was negative (<0.3 kU/l).

It was concluded that the patient had been sensitized to NRL, but that the main cause of her hand eczema was irritation from chemicals and wet work. She has continued to work in her own hairdressing salon.

Discussion

The incidence of NRL allergy is highest in health-care workers (6), though industrial occupations may also be

at risk (7). The prevalence in our hairdressers was much lower than in those of Van der Walle & Brunsveld (3) in The Netherlands: 1.1% rather than 11%. Finnish hairdressers may use NRL gloves less than Dutch, or the quality of NRL gloves used by hairdressers may be better in Finland, though the latter seems unlikely (8). Vinyl gloves should probably be recommended for hairdressers.

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Allergic contact dermatitis from dithio-2,2-bis(benzmethylamide)

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Key words: occupational; allergic contact dermatitis; dithio-2,2-bis(benzmethylamide); 1,2-benzisothiazolin-3-one; preservatives; biocides; chemical industry; maintenance mechanic. © Munksgaard, 1999.

Dithio-2,2-bis(benzmethylamide) has been marketed for the last 20 years, with no reports of dermatitis.

Case Report

A 51-year-old engineering support technician presented with exposure-pattern dermatitis. He had been dismantling a mill last used in the manufacture of 1,2-benzisothiazolin-3-one (BIT) and previously of dithio-2,2-bis(benzmethylamide). He wore overalls, a facemask and alternated between vinyl and leather-palmed gloves. His overalls sleeves had become soaked with water previously used to swirl down the mill, some of which ran

into his gloves. He finished work at 01:30, having noticed no obvious symptoms. He had a shower and went home. He awoke 9 h later with itchy swollen hands and a rash on the forearms and face. That evening, he saw his occupational health nurse and was treated with a potent topical corticosteroid on the arms and with a mild topical corticosteroid on the face, with improvement. He had a history of hay fever and was on treatment for hypertension. When seen 5 days later, the dermatitis was settling, though he did still have papular eczema on the lateral wrists and between some fingers.

Patch tests were performed with BIT (Chemotechnique) and serial dilutions of manufactured product

Table 1. Results of patch testing to 1,2-benzisothiazolin-3-one and manufactured product (active ingredient %s)

	Chemical		D2	D4
Chemotechnique	1,2-benzisothiazolin-3-one	0.05% pet.	++	++
manufactured product	1,2-benzisothiazolin-3-one	0.33% aq.	++	++
		0.18% aq.	++	++
		0.03% aq.	+	+
	dithio-2,2-bis(benzmethylamide)	1.25% aq.	–	+
		0.25% aq.	–	+
		0.125% aq.	–	–
		0.025% aq.	–	–

containing either BIT or dithio-2,2-bis(benzmethylamide) as active ingredients. Positive reactions are shown in Table 1. A + response was seen at D4 to dithio-2,2-bis(benzmethylamide) at 1.25% and 0.25%. Dithio-2,2-bis(benzmethylamide) in 10 controls at 0.25%, and subsequently in 20 controls at 1.25%, was negative.

Discussion

BIT is a popular preservative and its rôle as a potential skin sensitizer is confirmed (1). Dithio-2,2-bis(benzmethylamide) is used primarily as a paint-film preservative, typically at 0.25%, and has also been used as an in-can paint preservative, typically at 0.05%. The sensitization potential of dithio-2,2-bis(benzmethylamide) has been experimentally assessed using the guinea pig maximization test (2) and the murine local lymph node assay (3), demonstrating that it had the potential to be a sensitizer at 3% w/v and above.

This employee was exposed to potentially high con-

centrations of dithio-2,2-bis(benzmethylamide), which may account for sensitization and subsequent allergic contact dermatitis. However, this is considered an isolated case, since there has been no previously reported human sensitization at in-use concentrations. The lack of other reports of allergic contact dermatitis from this chemical would suggest that it remains safe under usual working conditions.

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Contact urticaria and systemic anaphylaxis from codfish

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Key words: allergic; anaphylaxis; contact urticaria; fish; food; open test; urticaria; cod; sardine. © Munksgaard, 1999.

Case Report

A 19-year-old gas station employee developed generalized urticaria, angioedema of the face and lips, and dry cough, 20 min after his cousin, a fisherman, walked out of his store and greeted him by placing his hands firmly on his bare upper arms. The patient had a history of fish allergy from the age of 3 years and, since that time, had strictly avoided eating all seafood. Food allergy had been diagnosed by his paediatrician after 2 episodes of generalized urticaria, with diarrhoea and vomiting, following fish soup. At age 15 years, he had had an episode of localized urticaria and angioedema of the right side of the face and the lips within 30 min of his mother having kissed him on the

right cheek after having just eaten codfish. At age 18, he had had a generalized anaphylactic reaction after eating a hamburger at a fast-food restaurant: he had later been told that the hamburger had been fried in the same oil used to fry codfish.

6 months after resolution of his latest episode, the patient was investigated at our hospital for fish allergy. Open tests on intact skin with raw codfish (right forearm) and sardine (left forearm) gave large wheal-and-flare reactions at both sites after 10 min, and the tests were removed. At 20 min, the patient complained of dysphoria, generalised pruritus, including the palms and soles, nasal irritation, tachycardia and dry cough. He was treated with subcutaneous epinephrine (0.5 ml, 1:1000), parenteral antihistamines and corticosteroids,

and nebulized salbutamol (Aerolin). He responded to treatment and felt well after a further 20 min; however, at the site of the tests, intense wheal-and-flare reactions were still evident. 50 min after treatment, the patient again developed generalized urticaria, dyspnoea and dry cough. This recurrence was treated with a 2nd dose of epinephrine, Solumedrol, and Aerolin. He responded rapidly and was observed for 24 h, before discharge from the hospital.

Total IgE was elevated at 940 U/ml (normal range: 0–200 U/ml). RASTs to various fish species were positive to codfish (class 3), eel (class 3), carp (class 2), but negative to sole and halibut. Sardine was not available. RASTs were also negative to crab and lobster. A P-K transfer test on the patient's sister was positive.

Discussion

Raw fish is known to be a cause of protein contact dermatitis and occupational contact dermatitis in the fish industry (1, 2). The presence of IgE antibodies to fish was established in our patient by positive RAST and transfer test, making the diagnosis immunologic contact urticaria associated with anaphylaxis (stage 4) (3).

Foods producing contact urticaria include seafood, chicken, egg, peanut, flour, fruits and vegetables (2–7). Anaphylaxis has previously been reported from skin contact with spices (paprika) (3). 2 patients with sys-

temic allergic reactions to cooked eggs were shown to have contact urticaria from raw egg (6, 7). Fish allergens are usually destroyed by cooking (2), though the previous history in this case suggests that cooked fish may also have been causal.

In the presence of a history of severe hypersensitivity, even open testing should be performed with caution and with the appropriate medication and equipment to hand, for immediate response to systemic allergic reactions.

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Occupational protein contact dermatitis from glucoamylase

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Key words: occupational; protein contact dermatitis; industrial enzymes; glucoamylase; process operator; prick testing; allergy; lack of cross-sensitivity. © Munksgaard, 1999.

Case Report

A 28-year-old non-atopic process operator in a chemical enzyme factory developed an itchy, work-related dermatitis on the backs of her fingers and fingerwebs. The itching started within 0.5–1 h after being exposed to industrial enzymes. She had done the same work tasks for 7 years before the dermatitis started. During the summer vacation, her eczema healed, but relapsed upon return to work.

She was prick tested with common environmental allergens, a series of 17 molds and an extended industrial enzyme series, prepared for testing and tested as previously described (1–3). Glucoamylase (GA) was the only substance that provoked a reaction (diameter 3 mm; histamine 10 mg/ml, 6 mm). The glucoamylase prick test material also contained sodium benzoate, methyl- and propylparaben, and sodium disulfide as preservatives. These were all negative on prick testing. She was then prick tested with GA in a dilution series: 10%

caused a histamine-sized reaction plus pseudopodia; 1% GA, 5 mm plus pseudopodia; 0.1% 3 mm; 0.01% was negative. 20 controls were negative when prick tested with 1% GA.

Patch testing was performed and scored according to the recommendations of the ICDRG. To a modified European standard series, she had several reactions: nickel sulfate (+++), colophony (++), wool wax alcohols (++), balsam of Peru (++), and fragrance mix (++). These patch test reactions were not considered relevant to her work-related dermatitis. Patch testing with a series of industrial enzymes, including GA, and a series of antimicrobials was negative.

Discussion

The industrial enzymes currently used are strong sensitizers (1–6). Sensitization may follow minute exposure; even office personnel in factories may become sensitized (3, 5). Proper control of exposure is mandatory. Our pa-

Table 1. Industrial enzymes, their major applications, and reports of allergic skin reactions (3)

Enzyme	Major applications	Allergic skin reactions
α -amylase	alcohol production, animal feeds, baking, brewing, detergents, pulp and paper, starch and sugar production, textile industry, wine and fruit juice	(1, 11, 12, 15, 16)
cellulase (cellobiohydrolases, endoglucans, β -glucosidases)	alcohol production, animal feeds, baking, brewing, composting, detergents, protein industry, pulp and paper industry, starch and sugar production, textile industry	(2, 16, 17)
glucoamylase	alcohol production, baking, brewing	(this report)
papain	brewing, contact lens detergent, cosmetology, pharmaceuticals	(18–21)
xylanase (hemicellulase)	pulp and paper industry	(16, 17)

tient was exposed only to liquid GA, apparently mainly through the skin. Accordingly, her route of sensitization was probably via the skin, as with other proteins, e.g., natural rubber latex.

Amylases are used in the baking industry to provide fermentable sugars for yeast and to improve loaf volume and texture (7). In addition to baking, glucoamylase is used, e.g., in brewing and alcohol production. Allergies due to amylases have been reported since the late 1970s (9), since when several reports have confirmed the rôle of α -amylase as a respiratory allergen (7, 9, 10). Baur et al. (7) reported prick test reactions to α -amylase and glucoamylase in bakery workers. α -amylase has also caused contact urticaria and protein contact dermatitis in bakers (11–13).

The symptoms of our patient were mild. To prevent respiratory allergy, exposure to enzyme powder or aerosols should be minimized, as at our patient's work site where only liquid GA was used. Careful monitoring of skin and respiratory symptoms is important. Our patient was negative on prick testing to 4 other amylases (1, 2), demonstrating that industrial enzymes can induce specific sensitization. Therefore, all industrial enzymes from the work site need to be tested if sensitization is suspected.

The patient had immediate skin symptoms but no whealing. Patch testing to the chemicals used at work, and to industrial chemicals was negative. Accordingly, her diagnosis of protein contact dermatitis is in accordance with the original criteria of Hjorth & Roed-Petersen (14). The industrial enzymes that have caused allergic skin reactions have been summarized in Table 1 (15–21). Industrial enzymes may also cause irritant contact dermatitis (3).

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Protein contact dermatitis from midge larvae (*Chironomus thummi thummi*)

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Key words: protein contact dermatitis; midge larvae; hands; *Chironomus thummi thummi*; prick test; RAST. © Munksgaard, 1999.

A 28-year-old man, an industrial painter whose hobby was fishing, had had an itchy dermatitis on the palms for 2 years. He reported no personal or family history of psoriasis or atopy. He was in good health, had no other complaints, and was taking no medications. Clinical examination revealed a sharply-bordered rhagadi-form eczema with vesicles on both palms. Mycological examination was negative.

Patch tests were conducted with the standard, plastics, and glues series, as well as his own materials from work: paints and soaps (semi-open) and gloves. Results were all negative at D2 and D4. As we did not then consider the dermatitis to be related to his occupation, he was asked to bring in some midge larvae, which he would scatter on the water with his bare hands when fishing. A prick test with larvae was strongly positive, and a RAST for *Chironomus thummi thummi* was also positive: 6.89 UA/LM(+) (total IgE: 686 KU/l). The lesions healed when he stopped handling the larvae.

Protein contact dermatitis is a combined (Type I) and delayed (Type IV) allergy expressed as a chronic eczema, with acute outbreaks a few minutes after contact with a protein-containing allergen. The diagnosis is made by

means of a scratch or prick test with the allergen, and specific IgE antibodies can sometimes be demonstrated in the blood. The hemoglobin of midge larvae with a low molecular weight, mainly the χ t 1–9, is a potent Type I allergen (1–4). Our patient had no urticaria, flushing, Quincke's edema, asthma, or rhinitis. He reported that itching on the palms started immediately after handling midge larvae.

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Exposure-pattern dermatitis due to 2-aminothiophenol and 2-aminophenyldisulfide

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Key words: occupational; airborne contact dermatitis; aminothiophenol; potassium salt of aminothiophenol; aminophenyldisulfide; allergic contact dermatitis; chemical industry; cross-sensitivity. © Munksgaard, 1999.

A 50-year-old development technician, working in a chemical factory, presented with a 1-month history of 3 episodes of hand and facial eczema. He was not atopic and had no past medical history of note. The 1st episode

occurred after exposure to 2-aminothiophenol used in the chemical process, the 2nd when emptying the final product into trays to be dried, and the last after walking onto the plant to inspect a reaction vessel. The patient

was patch tested to our standard series and samples of chemicals used in the reaction process (Table 1). 15 controls were negative.

Discussion

There have been 2 previous reports of 2-aminothiophenol causing dermatitis (1, 2). This chemical intermediate may cause airborne contact dermatitis despite being oxidized in air. Petrolatum has been recommended as a diluent for patch testing (2), the chemical being degraded by acetone but not by ethanol. We used an

aqueous solution of the potassium salt, as 2-aminothiophenol also has a potent odour. A 2nd report describes systemic contact dermatitis following inhalation of 2-aminothiophenol, though no patch testing was performed (1).

2-aminophenyldisulfide is a condensation product of 2-aminothiophenol and was present in the final product. A cross-reaction between the 2 chemicals may account for the reactions in our patient to both an ingredient and the final product. A further possibility is that 2-aminophenyldisulfide is the true allergen, formed from condensation of 2-aminothiophenol. The latter seems unlikely because 2-aminophenyldisulfide has a higher melting point of 91°C than 2-aminothiophenol with a melting point of 26°C and boiling point of 234°C. On the 1st occasion, our patient was exposed to the volatile 2-aminothiophenol but not to the non-volatile condensate, and yet dermatitis still developed.

Table 1. Patch test results

		D2	D4
standard series		–	–
aminothiophenol (potassium salt)	0.01% aq.	+	++
	0.005% aq.	+	++
	0.001% aq.	+	++
other ingredients		–	–
final product	10% pet.	+	NT
	5% pet.	+	NT
	≤1% pet.	–	–
aminophenyldisulfide	0.01% aq.	++	++
	0.005% aq.	+	++
	0.001% aq.	+	++

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Exposure-pattern dermatitis caused by N-(2-amino-4,6-dichloro-5-pyrimidinyl) formamide

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Key words: occupational; airborne contact dermatitis; N-(2-amino-4,6-dichloro-5-pyrimidinyl) formamide; chemical industry; allergic contact dermatitis. © Munksgaard, 1999.

A 45-year-old chemical process technician presented with a 3-week history of facial eczema, which settled after a week off work. There was no past medical history of skin disease or atopy. He was patch tested to a standard and facial series, together with dilution series of his work materials. He reacted (+) on D4 to N-(2-amino-4,6-dichloro-5-pyrimidinyl) formamide (FADCP) 0.5 and 0.1% pet. and 0.5, 0.1 and 0.05% eth. 20 controls were negative to FADCP 0.5% pet.

Comment

A diagnosis of an airborne contact allergy to the chemical intermediate FADCP was made. The data sheet stated that there was a potential risk of skin sensitization but not of irritancy. To our knowledge, this is the 1st report of human contact allergy to this substance.