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Short Communications

Allergic contact dermatitis caused by a nickel-containing headband

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Key words: allergic contact dermatitis; nickel; headband; children.

Case Report

A 14-year-old girl presented with a 1-year history of a recurrent pustular eczema of the retro-auricular area and the anterior scalp, occasionally spreading to her face. Oral erythromycin, prescribed for concurrent acne, and topical hydrocortisone helped partially.

She had a history of mild childhood eczema and an atopic family history. There were no allergies and she was otherwise well. Her earlobes had been pierced in early childhood, but she had not worn earrings for some time and had never noticed any problems when she did. Patch testing to standard, medicament and facial series, together with samples of her own hair cosmetics, was positive to nickel sulfate 5% pet. (−/+).

When attending the clinic on day (D) 2, the patient wore a headband made of white metal, resulting in a flare of her scalp dermatitis by D4. On closer questioning, she was able to link exacerbations of her eczema with wearing this particular headband, which extended behind both ears. A diagnosis of allergic contact dermatitis from the nickel-containing headband was therefore made.

Discussion

Nickel continues to be the most common contact allergen (1–3). A recent UK study found a frequency of 21.3% in patch-tested patients (2). The Nickel Directive became law in the EU in 1996 (4), though doubt remains as to whether there is a threshold below which nickel is safe (5).

Most women become sensitized during ear piercing or the subsequent wearing of nickel-containing fashion jewellery (6, 7). Nickel is also among the agents most frequently responsible for occupational contact dermatitis (8). The release of nickel from metal objects by ammonium thioglycolate in permanent-wave solutions may explain the high frequency of nickel allergy in hairdressers (9, 10).

To our knowledge, nickel allergy due to wearing headbands has not been reported before, though uncommon sources of this common contact sensitizer continue to emerge (11, 12).

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Contact dermatitis from organophosphorus pesticides

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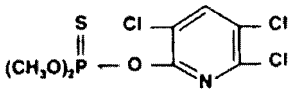
Key words: allergic contact dermatitis; organophosphorus pesticides; chlorpyriphos-methyl; fenthion; methidathion; parathion-methyl; malathion; cross-sensitivity; occupational; agriculture.

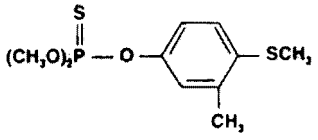
While the irritancy action of organophosphorus compounds is well-documented (1), there have been few reports of allergic contact dermatitis.

Case Report

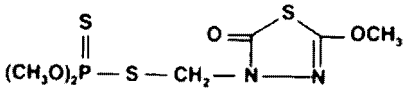
A 78-year-old man presented with eczema on the hands, forearms and face, which had appeared 2 months earlier. For the past year, he had done occasional agricultural work, often using pesticides without wearing gloves or protective clothing. He had used 5 particular pesticides, most frequently: Daskor® (with a chlorpyriphos-methyl and cypermethrin base), Lebaycid® (fenthion), Supracid® (methidathion), Seccatutto® (a combination of diquat dibromide and paraquat dichloride) and Trifrina® (dinitrocresol). The dermatitis resolved after 2 weeks ap-



Chlorpyriphos-methyl



Fenthion



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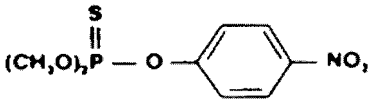
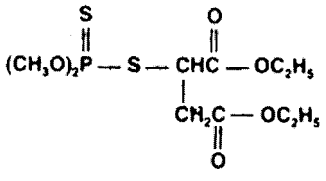
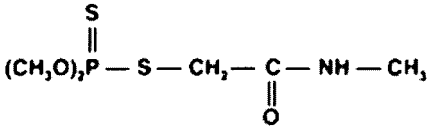


Parathion-methyl

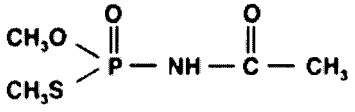


Malathion

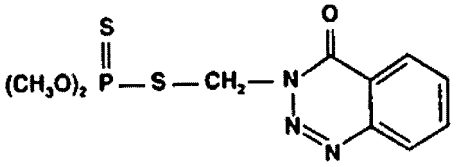
Fig. 1. Chemical structures of organophosphorus pesticides which were positive.



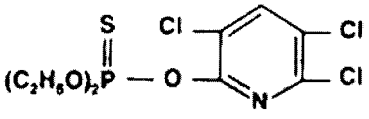
Dimethoate



Acephate



Azinphos-methyl



Chlorpyriphos-ethyl

Fig. 2. Chemical structures of the pesticides which were negative.

Table 1. Patch test results

Substance	Concentration (% pet.)	D2	D4
European standard series		−	−
Daskor®	1	++	++
Lebaycid®	1	++	++
Supracid®	1	++	++
Seccatutto®	1	−	−
Trifrina®	1	−	−
chlorpyriphos-methyl	1	++	+++
cypermethrin	0.2	−	−
fenthion	1	++	++
methidathion	1	++	++
diquat dibromide	1	−	−
paraquat dichloride	1	−	−
dinitrocresol	1	−	−
parathion-methyl	1	++	++
malathion	0.5	++	++
azinphos-methyl	1	−	−
dimethoate	1	−	−
chlorpyriphos-ethyl	1	−	−
acephate	1, aq.	−	−
diethyl fumarate	1	−	−

plication of topical corticosteroids and temporary suspension of his agricultural work.

Patch testing with the European standard series, supplemented by the above 5 pesticides at 1% pet., was positive to Daskor®, Lebaycid®, and Supracid®. The active ingredients of the pesticides that had been positive were then tested, together with a wide range of organophosphorus and other pesticides, including diethyl fumarate, a contaminant of malathion. The results are shown in Table 1. Photopatch tests were negative. 10 healthy volunteers tested with the organophosphates listed in Table 1 were negative.

Discussion

Organophosphates have been shown experimentally to be powerful sensitizers, though clinical reports of allergic contact dermatitis are rare (2). Some authors have described simultaneous sensitization to several organophosphorus insecticides, resulting in cross-reactions to dichlorvos and methidathion (3). Our patient was positive to chlorpyriphos-methyl, methidathion, fenthion, parathion-methyl, and malathion (Fig. 1), all organophosphorus pesticides, whereas he was negative to all the other pesticides tested (Fig. 2). Cross-sensitivity appears probable, since he was also positive to 2 substances that he had never used in his work.

Chlorpyriphos-methyl, commonly used as an insecticide as it has a broad spectrum, gave a strongly positive reaction. Only 1 previous case of a positive reaction to chlorpyriphos has been reported (4). The rare cases of contact allergy to malathion reported are generally due to the presence of diethyl fumarate as a contaminant (5), which was negative in our patient.

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Type I allergy to natural rubber latex and Type IV allergy to rubber chemicals in children with risk factors

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Key words: natural rubber latex; allergic contact dermatitis; rubber chemicals; Type I hypersensitivity; Type IV hypersensitivity; thiuram mix; tetramethylthiuram monosulfide; carba mix; 1,3-diphenylguanidine; hexamethylenetetramine.

Allergic contact dermatitis (ACD) from rubber chemicals is relatively common in childhood (1, 2). The aim of this study was to see whether this coexisted with Type I natural rubber latex (NRL) allergy.

Patients and Methods

We observed 19 children (8 female and 11 male), ranging from 2 to 13 years, with a history suggestive of NRL allergy. They all underwent prick testing to common aero-allergens, and foods cross-reacting with NRL. Specific serum IgE to latex and cross-reacting foods was measured with an FEIA assay (Pharmacia CAP System). A prick test for NRL with a commercially available extract was carried out in 17/19 children. The other 2 underwent a glove use test (3). All subjects were also patch tested with an extensive rubber chemicals series (Table 1), as well as 16 children undergoing spirometry and methacholine bronchial challenge.

Table 1. Rubber chemicals patch tested

4-phenylenediamine base 1% pet.
black rubber mix 0.6 % pet.
N-isopropyl-N-phenyl-4-phenylenediamine 0.1% pet.
N,N-diphenyl-4-phenylenediamine 0.25% pet.
N-cyclohexyl-N- phenyl-4-phenylenediamine 0.25% pet.
2,2,4-trimethyl-1,2-dihydroquinoline 1% pet.
4,4′-diaminodiphenylmethane 0,5% pet.
hydroquinone monobenzylether 1% pet.
mercapto mix 2% pet.
N-cyclohexylbenzothiazyl sulfenamide 0.5% pet.
dibenzothiazyl disulfide 0.5% pet.
morpholinyl mercaptobenzothiazole 0.5% pet.
mercaptobenzothiazole 0.5% pet.
mercaptobenzothiazole 2% pet.
thiuram mix 1% pet.
tetramethylthiuram monosulfide 0.25% pet.
tetramethylthiuram disulfide 0.25% pet.
tetraethylthiuram disulfide 0.25% pet.
dipentamethylenethiuram disulfide 0.25% pet.
carba mix 3% pet.
1,3-diphenylguanidine 1% pet.
bis(diethyldithiocarbamato) zinc 1% pet.
bis(dibutyldithiocarbamato) zinc 1% pet.
zinc dimethyldithiocarbamate 1% pet.
hexamethylenetetramine 1% pet.
triethylenetetramine 1% pet.
diphenylthiourea 1% pet.
dibutylthiourea 1% pet.
diethylthiourea 1% pet.
ethylene thiourea 1% pet.
dodecylmercaptan 0.1% pet.
dithiomorpholine 1% pet.

Results

All patients reported clinical reactions to NRL and previous surgical procedures ranging from 2 to 12 years before the first signs of such allergy. The results of in vivo and in vitro tests are summarized in Table 2.

Discussion

Children with spina bifida and others requiring multiple surgical procedures are known to be at increased risk of IgE-mediated NRL hypersensitivity (4). It has also been established, both in vivo and in vitro, that NRL can cause delayed-type hypersensitivity (5–7). All the subjects whom we examined presented with IgE-mediated NRL allergy. Only 3 of them, however, had positive patch tests to rubber chemicals.

The allergens responsible for Type I hypersensitivity induce production of specific IgE by B lymphocytes (8), whereas delayed hypersensitivity is instead mediated by antigen-presenting cells (macrophages and Langerhans cells) and the activation of T cells (9). These are mainly Th1 lymphocytes, whereas in patients with IgE-mediated allergy, Th2 cells are increased (10).

Although co-existence is not common (11), it is worthwhile evaluating both Type I allergy to NRL and Type IV allergy to rubber chemicals in known high-risk groups.

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Table 2. Clinical and immunological features in the 19 children examined

Pt. no.	No. of operations	Disease requring operation(s)	Time (years) between symptoms and 1st operation	Clinical symptoms°	Positivity to NRL prick test	NRL RAST (kU/l)	Prick test positivity to common inhalant allergens*	Prick test and/or RAST positivity to cross-reacting foods**	Bronchial provocation test	Positive patch test reactions to rubber chemicals
1	2	congenital urological anomaly	4	CU-RC-D	yes	37.2	neg	neg	neg	
2	0			CU	yes	8.79	DF-DP-G-O	U	neg	
3	4	spina bifida	12	CU	yes	2.39	O-G-P-DF-DP	K-C-T-N-Z-B-A	neg	
4	3	cryptorchidism	6	CU	yes	1.62	neg	neg	not done	
5	1	appendicitis	3	CU	yes	3.12	O-P	P	neg	
6	0			D	yes	10.1	A	T-C-A	neg	
7	4	spina bifida	3	CU	yes	1.93	neg	neg	neg	
8	4	congenital urological anomaly	6	RC-CU	yes	27.3	A	T-A-B	neg	
9	8	syndactyly	6	CU-GU-RC-A	yes	5.95	O	A-K-C-U-B-T	neg	
10	1	adenoid hyperthrophy	2	CU	yes	<0.35	DF-DP	N	not done	
11	1	adenoid hyperthrophy	2	CU-RC	not done	12.3	DF-DP	neg	pos	
12	0			CU	yes	1.69	DF-DP-O	K-H-U	neg	
13	0			CU	yes	1.50	G-DP	neg	neg	
14	0			CU	not done	1.75	O-G-P-C-DF-DP	K-H	not done	
15	6	spina bifida	4	GU-A	yes	16.29	DF-DP	B	pos	thiuram mix and tetramethylthiuram monosulfide
16	3	congenital urological anomaly	3	CU	yes	2.47	neg	neg	neg	
17	5	spina bifida	4	CU-RC	yes	11.73	P-G	neg		carba mix and 1,3-diphenylguanidine
18	3	spina bifida	2	CU	yes	5.33	neg	B	neg	
19	6	spina bifida	12	GU-CU	yes	>100	O	A-C-B-Z-T-P-O-H	neg	hexamethylenetetramine

° CU: contact urticaria; GU: generalized urticaria/angioedema; RC: rhinoconjunctivitis; A: asthma; D: dyspnoea.
* O: olive pollen; G: grass pollen; C: cypress pollen; A: *Alternaria tenuis*; P: *Parietaria officinalis*; DP: *Dermatophagoides pteronyssinus*; DF: *Dermatophagoides farinae.*
** A: avocado; K: kiwi; B: banana; P: peach; T: tomato; O: potato; C: chestnut; N: pineapple; U: peanut; Z: maize; H: hazelnut.

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Phytodermatitis from *Ranunculus damascenus*

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Key words: Ranunculaceae; *Ranunculus damascenus*; ranunculin; anemonin; protoanemonin; phytodermatitis; herbal remedies; toxic; vesicant; plants; irritant.

Annual or multi-annual Ranunculaceae have in common a glycoside called ranunculin. The newly damaged plant produces from ranunculin, protoanemonin, which is a strong contact irritant to the skin and mucous membranes (1), leading to medicinal use as a counter-irritant (2–4). *Ranunculus damascenus* grows in certain regions of Turkey such as Van (5).

Case Report

A 45-year-old woman was referred to an emergency clinic with open wounds on the abdomen, right knee and neck. She had previously applied overnight a plant with yellow flowers and green leaves to these sites, and also drunk its juice, because of pain. This had resulted in blisters surrounded by erythema 2 days prior to presentation. On examination, there were bullae, vesicles and pustules on an erythematous base, forming ulcers on the neck, abdomen and right lower leg (Fig. 1). Mucous membranes were unaffected.

Treatment was with 1000 mg/day ciprofloxacin, 2 mg/day clemastine, wet dressings and topical fusidic acid. Because of hyperglycemia, insulin was started. Her lesions began to recover in 3–4 days. After 10 days, complete healing was obtained and she was discharged from hospital. A plant sample was identified as *Ranunculus damascenus* by the Education Faculty Botanic Department.

Discussion

The toxicity of ranunculin is explained by its inhibition of DNA polymerase, resulting in increased free oxygen radicals (6). Protoanemonin is a volatile and highly irritant oil, which inhibits mitosis in plants. In contact with the skin, it produces subepidermal disjunction and bulla formation by disrupting sulfur bridges (7). Protoanemonin polymerizes rapidly to anemonin, its harmless crystal form. Dried and boiled plants contain no protoanemonin.

Many peoples use members of the Ranunculaceae family as traditional treatments for abscess drainage (3), blister formation (4), hemorrhoids (4, 8), burns, lacerations and abrasions as poultices (2), and as herbal remedies for myalgia, common cold and other diseases (2). *Ranunculus damascenus* (Boiss & Gaill) derives from the Damascena region of Syria (5), and is also found in northern Iraq and in the middle and southern Anatolian region of Turkey. It grows on 600–1700 m unforested plains, and flowers in April–May.

There is sparse dermatological data about Ranunculaceae phytodermatitis (9–11), and this is the 1st case report, to our knowledge, involving *Ranunculus damascenus*. This species needs to be widely recognized as highly irritant and vesicant.

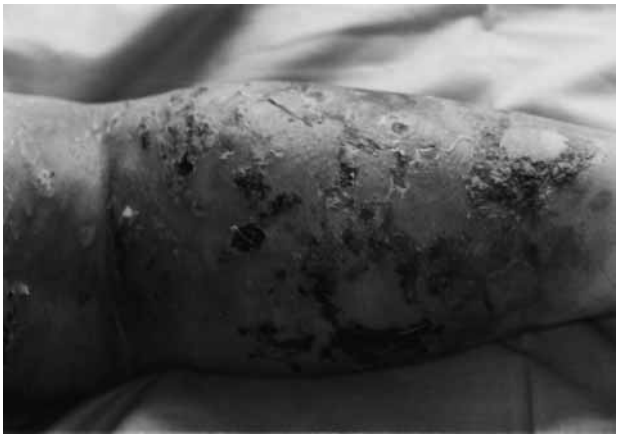

Fig. 1. Skin lesions of right lower limb.

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Occupational and systemic contact dermatitis with photosensitivity due to vitamin B_6

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Key words: pyridoxine hydrochloride; vitamin B_6; contact hypersensitivity; systemic contact dermatitis; occupational; cutaneous adverse drug reaction; photosensitivity; paramedical worker; health care workers; medicaments.

Case Report

A 45-year-old paramedical worker presented with eczema over the dorsa of the hands, dorsa and sides of the fingers (sparing little fingers), forearms and face, for the past 6 years with recurrences and remissions. He was patch tested with CODFI (Contact and Occupational Dermatoses Forum of India) allergens, supplemented with a drop each of various injectable medicaments, viz., streptomycin, benzyl penicillin, ampicillin-cloxacillin, oxytetracycline, B_1 B_2 B_{12}, gentamicin, amikacin and analgesics. Positive patch test reactions on D2 and D3 were observed to nitrofurazone and 3 different brands of B_1 B_6 B_{12} injections. Reactivation of lesions on the hands, face and neck was noted during patch testing, which subsided within a week. After he stopped injecting B_1 B_6 B_{12} into his patients, remarkable clinical improvement was observed.

6 weeks later, he was patch tested on the forearms with B_1, B_6 and B_{12} 1% each in 10% propylene glycol. The D2 reading to B_6 showed a ++ reaction. Another B_6 patch was applied and a final reading taken 5 days later. Both sites showed positive reactions. Prick testing was also carried out with B_1, B_6 and B_{12} solutions, with negative results.

2 months later, oral provocation was carried out with 2 tablets of B_6, 100 mg each (Elder Pharma), given 6 h apart. The patient started to itch before the intake of the 2nd tablet and, 18 h later, presented with itching and severe erythema over the face, V of the neck, dorsa of the hands, forearms and distal half of the upper arms (sun-exposed areas). Reactivation of previous positive patch-test sites (both on the back and forearms) and a negative B_6 prick test site were also observed.

Discussion

In India, pyridoxine hydrochloride (B_6), along with thiamine hydrochloride (B_1) and cyanocobalamin (B_{12}), is frequently injected or given orally as a "neurotonic" to large numbers of people. Pyridoxine is otherwise indicated for the prevention and treatment of sideroblastic anaemia, depression, congenital deficiency syndromes, prevention of neuritis in isoniazid treatment, etc.

Contact hypersensitivity to B_6 is rare. Only 3 cases of contact allergy to pyridoxine, in hair lotion (1), corticosteroid cream (2), and a skin cream, Iruxol (3), appear to have been reported. There have also been a few reports of photosensitivity due to pyridoxine hydrochloride in pharmacological doses (4–6). Murata et al. (6) described 2 such patients, in whom patch tests with pyridoxine hydrochloride 1% and 5% pet. were negative, while photopatch tests were positive.

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Generalized eczema due to codeine

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Key words: codeine; opioid drugs; drug allergy; generalized eczema; cutaneous adverse drug reactions; positive patch test; cross-sensitivity; morphine; lack of cross-sensitivity; tramadol; pentazocine.

Case Report

A 72-year-old man developed a pruriginous generalized maculopapular eruption 12 h after oral Cod-efferalgan® (codeine 10 mg and acetaminophen 500 mg). Lesions persisted for 7 days and disappeared via scaling. He reported similar eruptions several hours after an antitussive drug (unknown) and Dolviran® (acetylsalicylic acid, codeine and caffeine). He had high blood pressure and took daily treatment with Diovan® (valsartan) and Seguril® (furosemide). He had also had short courses of Voltaren® (sodium diclofenac) for joint pains.

Patch tests with the European standard series (TRUE Test™), Cod-efferalgan (50% aq.), codeine phosphate (5% and 1% pet.), morphine chloride (5% pet.), pentazocine (5% pet.), tramadol (5% pet.) and acetaminophen (5% pet.) were carried out. Positive results were obtained with perfume mix (+), Cod-efferalgan® (+++), codeine 5% (+++) and 1%, and with morphine chloride (++) at D2 and D4.

Codeine phosphate 5% patch tests were also done in 2 healthy controls with negative results.

Discussion

Codeine is an opioid agonist widely used as an antitussive and analgesic. Adverse reactions have rarely been reported at therapeutic doses, and mostly consist of nausea, vomiting, drowsiness and dizziness. Codeine has also been described as an unusual cause of immunological urticaria (1), fixed drug eruption (2) and generalized dermatitis (3). In our patient, the positive codeine patch test pointed to a Type IV allergic reaction. We also demonstrated cross-reactivity with morphine but not with other opioid drugs such as tramadol or pentazocine; similar findings were obtained by Rodríguez et al. (3). These observations might suggest that these latter drugs could be an alternative therapy when opioid drug treatment is essential

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Occupational allergic contact dermatitis in hairdressers due to glutaraldehyde

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Key words: glutaraldehyde; allergic contact dermatitis; hairdressers; occupational; antibacterials; preservatives; biocides; cold sterilants..

Occupational allergic dermatitis in hairdressers has been much reported (1–6), but not from glutaraldehyde.

Case Reports

Case no. 1

A non-atopic 26-year-old woman had worked for 3 years at a hairdressing salon. Erythema with papules had already appeared after 4 months of employment. Initially, lesions were on the dorsum of both hands and then spread to the face. She used Aldesan (Septoma, Poland), which contains glutaraldehyde, to disinfect scissors, combs and hairbrushes.

Patch tests were done, using the method recommended by the ICDRG (7), with allergens from Chemotechnique Diagnostics AB (Malmö, Sweden): the standard series, the hairdressers series, and additionally 0.2% glutaraldehyde. Table 1 shows the results.

Table 1. Positive patch test results

Allergens		Case no. 1	Case no. 2
potassium dichromate	0.5% pet.	++	−
nickel sulfate	5% pet.	++	−
4-phenylenediamine base	1% pet.	+++	−
2-nitro-4-phenylenediamine	1% pet.	+++	−
ammonium persulfate	2.5% pet.	++	−
glutaraldehyde	0.2% pet.	+++	++

Case no. 2

A 46-year-old woman had worked for 28 years as a hairdresser. She reported dyspnoea, cough attacks, and rhinostenosis. For 8 years, she had had episodes of erythema and papules on the dorsal hands and on the face, accompanied by pruritus. To disinfect her hairdressing equipment, she used Lysoformin 3000 (Aldoquat) (Lysform, Dr. H. Rosemann, Germany), which contains glutaraldehyde, glyoxal and quaternary ammonium compounds.

Positive prick tests were obtained to common environmental allergens (house dust, *Dermatophagoides pteronyssinus* and *Dermatophagoides farinae*, and tree pollens) (Allergopharma, Germany); prick test with latex was negative (total IgE=878.0 kU/l).

Patch tests with the standard and hairdressers allergens series (Chemotechnique Diagnostics AB (Malmö, Sweden) were negative, while 0.2% glutaraldehyde was positive (Table 1). The patient did not react to the remaining components of Lysoformin (0.1% aq. benzalkonium chloride, 1% aq. glyoxal).

Discussion

Glutaraldehyde, a component of many sterilizing preparations, has long been a source of contact dermatitis in medical staff (8–10). Current viral infection prevention practices have also made it necessary to use active disinfectants for hairdressers' equipment. Glutaraldehyde allergy should now also be looked for in hairdressers.

Acknowledgements

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Palmar contact dermatitis due to (meth)acrylates

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Key words: (meth)acrylates; bone cement; allergic contact dermatitis; occupational; nurse, health-care workers; orthopaedic surgery.

Hand dermatitis due to bone cements, although referred to in all textbooks (1–3), and in several papers in the past (4–8), has seldom been reported in recent years.

Case Report

A 64-year-old nurse, working in the operating room of an orthopaedic hospital, complained that, in the last 3 months, she had had 3 episodes of acute left palmar dermatitis, with oedema, erythema and a very pruriginous bullae. There was no evident cause, but she suspected a new brand of latex gloves she had been using for the last few months. The day before she was admitted, a further such episode had begun on the left palm, with some milder lesions in the 4th web space. She had been in the operating room, helping in 2 operations for implanting total hip prostheses, during which she had had contact, for a short period, with bone cement, without change of gloves.

Table 1. Main sensitizing (meth)acrylates (rank orders in brackets)

Allergen	Kanerva et al. (1997)	Tucker et al. (1999)
hydroxyethyl acrylate (HEA)	12% (1)	10% (1)
hydroxypropyl methacrylate (HPMA)*	12% (2)	8% (7)
hydroxyethyl methacrylate (HEMA)*	11% (3)	9% (4)
hydroxypropyl acrylate (HPA)	11% (4)	9% (3)
ethylene glycol dimethacrylate (EGDMA)*	10% (5)	8% (6)
triethylene glycol dimethacrylate (TEGDMA)	8% (6)	6% (9)
ethyl acrylate (EA)*	8% (7)	9% (4)
methyl methacrylate (MMA)*	7% (8)	5% (10)
ethyl methacrylate (EMA)	7% (8)	4.5% (12)
triethylene glycol diacrylate (TEGDA)	7% (10)	9.5% (2)
diethylene glycol diacrylate (DEGDA)	5% (11)	6% (8)

* Positive (meth)acrylates in the present case.

Patch tests were performed with the standard series and with a battery of 18 (meth)acrylates. At D4, positive reactions were seen to:

- nickel sulfate +++
- methyl methacrylate (MMA) ++
- ethylene glycol dimethacrylate (EGDMA) ++
- hydroxyethyl methacrylate (HEMA) ++
- hydroxypropyl methacrylate (HPMA) +
- ethyl acrylate (EA) ++
- tetraethylene glycol dimethacrylate (TEGDMA) ++

Comment

Bone cement is obtained by mixing 2 components – a liquid one, which contains mainly methyl methacrylate, and a powder containing polymethacrylate, which is the hardener. Due to its known sensitizing potential and capacity for penetration through rubber gloves (4), this mix is made in a bowl without any skin contact. However, before delivering the cement to the surgeon, the nurse used to knead the cement to improve homogenization of the mix. It is usually recommended to use 2 pairs of gloves and to change them immediately after handling the cement. This was not done by the nurse, thus allowing penetration of the cement, skin contact and sensitization.

This is an uncommon clinical picture; only in the case reported by Pegum (4) were the lesions localized on the left palm and fingers. In all other reports, besides the fact that the surgeon was the one who was affected, the usual appearance was of a scaly fissured dermatitis of finger pulps, sometimes accompanied by sensations like burning, tingling or numbness, which can last for several weeks after the dermatitis subsides (9).

Although methyl methacrylate is the usual sensitizer, other (meth)acrylates may cross-react. Such cross-reactions are common (10), though in some cases, mainly from other sources of sensitization like dental resins, multiple concomitant sensitization cannot be ruled out. Nevertheless, a relatively small number of (meth)acrylates are responsible for the great majority of sensitizations. In 2 recent reports (11, 12), the main sensitizers have been almost the same (Table 1), although ranked differently, and 5 out of the 6 positive (meth)acrylates in our case belong to that list. It is therefore possible that, in cases of suspected (meth)acrylate allergy, a short series could identify the sensitizer in the majority of cases.

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Occupational allergic contact dermatitis from benzophenone-4 in hair-care products

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Key words: benzophenones; CAS 4065–45–6; 2-hydroxy-4-methoxybenzophenone-5-sulfonic acid; Uvinyl MS-40; sulisobenzone; occupational; allergic contact dermatitis; hairdresser; hair-care product; cosmetics.

Case Report

A 47-year-old hairdresser had had worsening dermatitis on her fingers and palms for 2 years. On patch testing, she was positive to tixocortol-21-pivalate and budesonide, but negative to other standard allergens, antimicrobials, cosmetics and hairdressing series, as well as to 15 of her own hair care products. She had not recently used hydrocortisone or budesonide. The dermatitis continued in spite of sick leave and topical treatment.

3 months later, further patch tests with hairdressing chemicals provided by a manufacturer were performed, and benzophenone-4 gave a ++ reaction. When the patient stopped using hair-care products with sun protection, her dermatitis finally began to improve. On further patch testing, benzophenone-4 (10% pet.) showed reactions in 2 commercial sunscreen series (Chemotechnique, Trolab), though benzophenone-3 remained negative. The products used by the patient at work, such as shampoos, hairsprays and conditioners, contained both benzophenone-4 and benzophenone-3 according to their labels, and positive patch-test reactions were also obtained with such products.

Discussion

Benzophenones are chemical UVA absorbers which are used not only in sunscreens, but also in many cosmetic products, mainly facial, to prevent photoageing and carcinogenesis. More than 10 different benzophenones are thus used (1). In earlier reports, distinction has not always been made between the different benzophenones (2), although they are individual chemicals and may not necessarily cross-react. Benzophenones have caused photocontact and contact allergic dermatitis (3–5) and rarely also contact urticaria (4).

In recent studies, the most frequent sunscreen allergens have been UVA absorbers, namely benzophenone-3 (2-hydroxy-4-methoxybenzophenone, oxybenzone, Escalol 567, CAS 131-57-7), and dibenzoylmethanes, e.g., Parsol 1789 (3–5. Contact and photocontact allergy to benzophenone-4 (2-hydroxy-4-methoxybenzophenon-5-sulfonic acid, Uvinyl MS-40, sulisobenzone, CAS 4065–45–6) has been reported only rarely (6). This may indicate that benzophenone-4 is a weak allergen. On the other hand, the incidence of allergic reactions may be related to the use of the chemical: in 1996, 20–30% of sunscreens on the German market contained benzophenone-3, whereas less than 5% contained benzophenone-4 (3). As in earlier studies (3), benzophenone-4 and benzophenone-3 did not cross-react in our patient. Instead, cross-sensitivity between benzophenone-3 and ketoprofen may occur (7–9).

Cosmetic ingredient labeling helped to solve the cause of our patient's hand dermatitis, and will also help her to select appropriate products in the future. To our knowledge, allergic contact dermatitis from benzophenone-4 in hair-care products has not previously been reported.

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Fixed-drug eruption caused by allylisopropylacetylurea

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Key words: fixed drug eruption; allylisopropylacetylurea; positive lesional patch test; bromvalerylurea; cross-sensitization; cutaneous adverse drug reactions; hypnotics and sedatives.

Case Report

A 27-year-old woman was diagnosed as having labial herpes simplex and treated at another hospital, suffered from recurrence, and consulted us. 3 days prior to the initial consultation, she had taken orally EveA®, an over-the-counter analgesic, and, 1 h later, developed itchy painful purple-red eruptions on the lips and body. By the time of the consultation, well-demarcated edematous erythemas with partial erosions were seen, with 6 nearly-round edematous purple-red eruptions with a small bleb in the middle also being visible.

Patch tests and scratch-patch tests on EveA® and its components were performed on sites with and without previous eruptions. Both EveA® and 1 of its components, allylisopropylacetylurea, were positive on lesional skin. Oral provocation tests with each component proved that allylisopropylacetylurea elicited eruptions 1 h after the oral administration of 6 mg. Oral provocation tests with other components were negative.

Bromvalerylurea, similar chemically to allylisopropylacetylurea, was negative on patch testing, scratch-patch testing and oral provocation testing (Table 1).

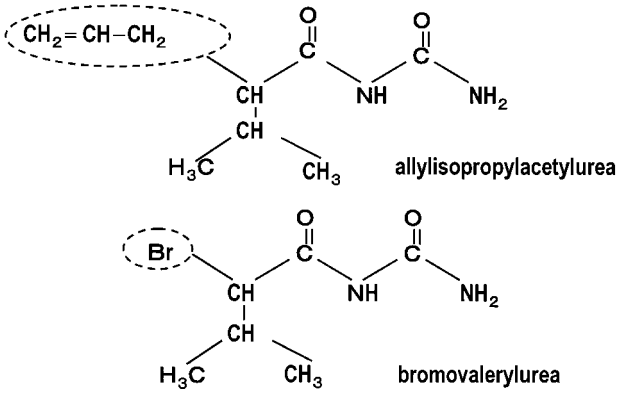

Fig. 1. Chemical structures.

Discussion

Allylisopropylacetylurea belongs to the monourenoid compounds made by binding between the carbonyl group of a fatty acid and the amino group of uric acid

Table 1. Test results in case reported

	Pigmented lesion		Non-pigmented lesion		Oral provocation test
	patch test	scratch-patch test	scratch test	scratch-patch test	
EveA®	+	+	−	−	NT
allylisopropylacetylurea	+	+	−	−	+
ibuprofen	−	−	−	−	-
anhydrous caffeine	−	−	−	−	-
bromvalerylurea	−	−	−	−	−

Table 2. Our cases of fixed drug eruption from allylisopropylacetylurea (1992–1997)

Year	Sex/age (years)	Causative drug	Oral provocation test	
			allylisopropylacetylurea	bromvalerylurea
1992	M/38	New Kaitekiz®	+	+
1993	M/30	Rinses®	+	−
1994	F/22	New Sedes®	+	NT
1995	F/24	Bufferin®	+	+
1996	F/18	EveA®	+	−
1997	F/27	EveA®	+	−
1997	F/18	EveA®	+	−

(Fig. 1). 6 out of 7 cases of fixed drug eruption from allylisopropylacetyl urea that we have seen were subjected to oral provocation tests with bromvarelylurea, 2 being positive and 4 negative (Table 2). The chemical structures of allylisopropylacetylurea and bromvalerylurea differ only in aryl group and bromo group, electronic distributions of each substitutional group being almost the same.

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Sorbitan sesquioleate as an allergen

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Key words: allergic contact dermatitis; sorbitan sesquioleate; fragrance mix; fragrance mix breakdown; patch-testing technique.

It has long been recognized that, when patch testing with mixes, great care must be taken that the individual constituents and components of the breakdown preparations are prepared identically in order to be able to draw meaningful conclusions. This is especially pertinent when testing with the fragrance mix, as a false-positive reading can result in the incorrect advice being given to the patient and unnecessary hardships in avoiding fragrances. Currently, both of the fragrance mixes supplied by Trolab® and Chemotechnique® contain sorbitan sesquioleate (SSO) as an emulsifier to allow satisfactory dispersion of their 8 constituents.

We undertook a retrospective review of our positive allergic reactions to SSO in relation to positive allergic reactions to the fragrance mix and breakdown constituents, over the period 1982–2000. The total number of patients with a positive allergic reaction to SSO (20% pet.) Trolab® was 14, and all of these had a concomitant positive reaction to the fragrance mix (8% pet.) Trolab®. In our department, all patients who show a positive reaction to the fragrance mix automatically have a 2% fragrance mix Chemotechnique® breakdown applied.

Interestingly, in those 14 patients who had concomitant positive allergic reactions to both SSO (20% pet) Trolab® and fragrance mix (8% pet.) Trolab®, and who also had the 2% fragrance mix Chemotechnique® breakdown applied, there were 2 positive reactions. Both showed a necrotic reaction to oak moss (2% pet.), and 1 also showed a positive allergic reaction to isoeugenol (2% pet.) and geraniol (2% pet.).

From the clinical history and patch test results in this subset of patients, we concluded that 12 reactions to the fragrance mix were false-positives and 2 were of relevance. In addition, 1 patient who was allergic to SSO (20% pet.) Trolab® and fragrance mix (8% pet.) Trolab® also came up positive to Compositae mix (6% pet.) Trol-

Table 1.

Current Trolab® patch test allergens containing the emulsifier sorbitan sesquioleate (SSO) (personal communication)
fragrance mix (8% pet.) with 5% SSO
α – amyl – cinnamal (1% pet.) with 1% SSO
oak moss absolute (1% pet.) with 1% SSO
eugenol (1% pet.) with 1% SSO
geraniol (1% pet.) with 1% SSO
hydroxycitronellal (1% pet.) with 1% SSO
isoeugenol (1% pet.) with 1% SSO
cinnamal (1% pet.) with 1% SSO
cinnamyl alcohol (1% pet.) with 1% SSO
Compositae mix (6% pet.) with 10% SSO
tansy extract (1% pet.) with 5% SSO
arnica extract (0.5% pet.) with 5% SSO
yarrow extract (1% pet.) with 5% SSO
chamomile extract (2.5% pet.) with 5% SSO
feverfew extract (1% pet.) with 5% SSO
Current Chemotechnique® patch test allergens containing the emulsifier sorbitan sesquioleate SSO (personal communication)
fragrance mix (8% pet.) with 5% SSO
glutaraldehyde (0.2% pet.) with 5% SSO
Myroxylon Pereirae resin (25% pet.) with 5% SSO
ethylene urea (5% pet.) with 5% SSO
melamine-formaldehyde resin (7% pet.) with 5% SSO

ab®. There was no concordant history of sensitization and we concluded that this was also a false-positive reaction.

In view of these findings, we sought confirmation from the 2 main manufacturers of patch test materials as to the presence of SSO in their allergens. The results are shown in Table 1.

From these listings, it is clear that patients may be falsely attributed as having an allergic reaction to fragrance mix and Compositae mix if they are not concomitantly patch tested with sorbitan sesquioleate. In addition, it is also clear that in order to be able to interpret results from the fragrance-mix breakdown, one must also know that SSO may be found in some individual constituents.

The prospective multicentre trial run by the European Environmental and Contact Dermatitis Research Group in 1995 recommended that SSO be included in the European standard series owing to its widespread use and its potential for sensitization. We recommend that all patients tested with the fragrance mix should have concomitant testing with SSO, even if the breakdown of the mix is not applied. Furthermore, one should interpret the breakdown results in light of the current inclusion of SSO in some individual constituents.

We reiterate that when patch testing with mixes, it is imperative to know the exact composition of the mix and of its individual components, in order to be able to draw meaningful conclusions and advise patients accordingly.

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Allergic contact dermatitis from pharmaceutical grade BHA in Timodine®, with no patch test reaction to analytical grade BHA

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Key words: allergic contact dermatitis; butyl hydroxyanisole; BHA; antioxidants; Timodine® cream; medicaments.

We report 2 cases of allergic contact dermatitis from butyl hydroxyanisole (BHA) in Timodine® cream, in which both patients were negative when tested to analytical grade BHA (2% pet.) Chemotechnique®, but positive when tested to pharmaceutical grade BHA (2% pet.), as supplied by the manufacturer Reckitt & Coleman, Huddersfield, UK.

Case Reports

Case no. 1

A 68-year-old non-atopic man gave a 2-year history of lichen simplex chronicus of the scrotal and perianal skin exacerbated by the use of Timodine® cream. Patch testing with the European standard series, the departmental anogenital series, Timodine® cream as is, and the ingredients of Timodine® obtained from the manufacturer showed the following relevant results.

	D2	D4	D7
Timodine® cream as is	–	–	+
analytical grade BHA (2% pet.) Chemotechnique®	–	–	–
pharmaceutical grade BHA (2% pet.) Reckitt & Coleman	+	++	
other ingredients of Timodine® cream	–	–	–

Case no. 2

A 58-year-old woman, with longstanding atopic eczema and recent vulval involvement, reported deterioration after using Timodine® cream. She gave a past history of eyelid eczema from certain cosmetics. Patch testing with the European standard series, the departmental face and hand series, anogenital series and steroid series, and the ingredients of Timodine® cream, showed the following relevant results.

	D2	D4
tixocortol pivalate	+	++
hydrocortisone (2% alc.)	–	–
analytical grade BHA (2% pet.) Chemotechnique®	–	–
pharmaceutical grade BHA (2% pet.) (Reckitt & Coleman)	–	+++
other ingredients of Timodine® cream	–	–

Discussion

Timodine® cream contains hydrocortisone 0.5%, nystatin 100,000 units/g, BHA at 0.4% and other excipients.

BHA consists chiefly of 3-t-butyl-4-hydroxyanisole with lesser amounts of 2-t-butyl-4-hydroxyanisole. It is used widely as an antioxidant by food, pharmaceutical and cosmetics manufacturers. To date, there have only been a few case reports of allergic contact dermatitis from BHA, principally via cosmetics, though also from medicaments, including other antifungals (1–4).

There have been 2 previous case reports of allergic contact dermatitis from Timodine® cream, involving nystatin, and dibutyl phthalate, propyl gallate and hydrocortisone (5, 6). In neither case is it clear whether

the BHA tested was of analytical or pharmaceutical grade, though in each case, it was negative.

It is not yet clear why there is a discrepancy in patch testing between the 2 sources of BHA, but we are in communication with the manufacturers and await further analysis.

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Allergic contact dermatitis from enoxolone

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Key words: allergic contact dermatitis; enoxolone; patch test; medicaments; ethyl aminobenzoate; procaine hydrochloride.

Case Report

A 43-year-old man developed a perianal eruption 2 h after applying Rec H® ointment (enoxolone 0.7%; ethyl aminobenzoate 0.25%; procaine hydrochloride 1%; allantoin 0.8%; l-menthol 0.2%; zinc oxide 20%; Wakunaga, Japan), which he had previously used for haemorrhoids for 2 years without problems. Patch testing with both Rec H® ointment (as is, and 10%) and enoxolone (10% pet.) was + at D2 and ++ at D3. Ethyl aminobenzoate (1% pet.) and procaine hydrochloride (1% pet.) were + at D2 and D3. Allantoin (10% aq.), l-menthol (10% pet.), zinc oxide (10% pet.) and pet. (as is) were all negative.

Discussion

Enoxolone (18-glycyrrhetinic acid), derived from glycyrrhizinic acid (1), is a widely used topical anti-inflammatory (2). There have been only 2 reports of sensitization to it (3, 4), 1 topical and 1 oral, the latter showing an allergic reaction to ethyl aminobenzoate as well as to enoxolone. We suspect that our patient was sensitized to the 3 constituents identified independently, since their respective chemical structures are quite different.

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Occupational allergic contact dermatitis from ethylhexylzinc dithiophosphate and fatty acid polydiethanolamide in cutting fluids

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Key words: occupational; allergic contact dermatitis; 2-ethylhexylzinc dithiophosphate; CAS 4259-15-8; fatty acid polydiethanolamide; CAS 68603-38-3; coconut diethanolamide; Amerchol L-101; lanolin; colophonium; extreme pressure additive; metalworking fluids.

Case Report

A 33-year-old non-atopic metalworker had been in his current job for 3 years before developing recalcitrant, work-related hand dermatitis. It started as paronychia, which progressed to dermatitis of the finger webs and backs of the fingers. He also had dermatitis periorally and on his neck. 3 patch test sessions were performed according to the recommendations of the ICDRG.

In a modified European standard series, colophonium (++) and lanolin alcohols (++) were positive. In a series of oils and cutting fluids, Amerchol L-101 (++) and coconut diethanolamide (cocamide DEA: ++) were positive. 2 cutting fluids, an insoluble cutting oil (ICO) and a water-emulsifiable semisynthetic cutting fluid (ESCF), used at work, gave positive patch test reactions: ICO 20%–10% pet. ++, and ESCF 10%–1%, pet. ++. A liquid soap used at work also elicited a ++ reaction (10% pet.).

No sensitizers present in the cutting fluids were declared in the material safety data sheets (MSDS). The manufacturers stated that the fluids did not contain colophonium, lanolin alcohols or cocamide DEA, but that the ESCF contained a cocamide DEA-related compound, namely Texamin PD 1 (Henkel KGaA, Düsseldorf, Germany), which, according to the MSDS, was a fatty acid polydiethanolamide (FAPDEA). Our analyses, performed as previously described (1), also confirmed that no colophonium was present in the cutting fluids. The Finnish supplier of the liquid soap informed us that the soap contained 3.9% cocamide DEA, but no lanolin or lanolin-related compounds such as lanolin alcohols.

In the 2nd patch test session, the patient was patch tested with the 5 components of the ICO. 1 of these, an extreme pressure (EP) additive (present at 2–5% in the ICO), was positive in a dilution series in pet. (1%–0.32% ++; 0.1% +; 0.032% −). The manufacturer then informed us that this EP additive contained 78% 2-ethylhexylzinc dithiophosphate (EHZDTP) (Fig. 1) and 22% mineral oil.

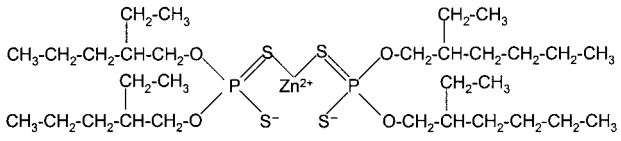

Fig. 1. Chemical structure of 2-ethylhexylzinc dithiophosphate (EHZDTP).

For the 3rd patch test session, we had obtained the components of the ESCF. We also patch tested the patient again with EHZDTP (without mineral oil), which was positive in a dilution series (1%–0.32%–0.1%–0.032% +; 0.01% −). Only 1 of the components of the ESCF, Texamin PD 1, was positive (1%–0.32% ++; 0.1% +; lower %s NT). 20 controls were negative on patch testing with 1% EHZDTP and Texamin PD 1.

Discussion

It was concluded that the patient had been occupationally sensitized to components of 2 cutting fluids, 2-ethylhexylzinc dithiophosphate (EHZDTP) in the ICO and fatty acid polydiethanolamide (FAPDEA, Texamin PD 1) in the ESCF. To our knowledge, neither EHZDTP nor FAPDEA have previously been reported to cause allergic contact dermatitis.

Cocamide DEA was also relevant, in the liquid soap used at work. Sensitization to lanolin may also have been occupationally induced. Amerchol L-101 is the trade name of a product containing lanolin alcohols (2), which may have been present in anticorrosives or cutting oils to which the patient had been exposed.

Metal dialkyldithiophosphates act as antioxidants, corrosion inhibitors, and, as in our case, EP-additives (3).

The chemical formula of the allergenic FAPDEA is $RCO\text{-}N(CH_2CH_2OH)_2$ in which R is C16-18 (CAS 68603-38-3). This chemical differs from cocamide DEA (CAS 68603-42-9) only in its fatty acid chain. According to the manufacturer, Texamin PD 1 was used as a corrosion inhibitor in the cutting oil. Cocamide DEA used as a surfactant, and a fatty acid ester used as an emulsifier, have previously caused sensitization (4, 5). Cocamide DEA has mainly caused sensitization in shampoos, soaps and cosmetics (6–9), but also in a hydraulic mining oil and metalworking fluid (4).

Our patient's patch test reaction to colophonium may also have resulted from previous occupational exposure (11–13), even though it was not present in the 2 cutting fluids analyzed.

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Active sensitization by epoxy in Leica® immersion oil

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Key words: active sensitization; epoxy resin; occupational allergic contact dermatitis; laboratory technician; patch test technique; plastics and glues.

A Leica® immersion oil containing epoxy resins (Table 1) caused a worldwide epidemic of allergic contact dermatitis in the late 1990s (1–11). In many clinics, the patients' own immersion oil was tested as is, which carried the risk of active sensitization.

Case Report

12 out of 36 laboratory technicians in a bacteriology laboratory, using immersion oil for microscopy, developed skin symptoms. Eventually, it was shown that at least some of these patients (11) had been sensitized by a Leica® immersion oil. A 35-year-old female laboratory technician, however, had had mild hand dermatitis, together with dermatitis on her face and neck (4, 8). She had been patch tested elsewhere with the immersion oil as is. At D2 and D5 readings, the patch test reaction was evaluated as slightly irritant. Then, after 2 weeks, a bullous reaction developed at the patch test site. In a modified European standard series, colophonium elicited a ++ reaction, and fragrance mix a ?+ reaction, whereas standard epoxy and a plastics and glues series were negative.

When retested by us 11 weeks later, the immersion oil patch test site was still eczematous, demonstrating a long-lasting patch test reaction (12). The patient was retested, according to the recommendations of the ICDRG, with an epoxy resin series, the epoxy chemicals of the immersion oil (Table 1), and the immersion oil in a dilution series (3%–1%–0.3%–0.1%–0.01%). Brominated epoxy resin (ER) containing 19% DGEBA-ER oligomer with a molecular weight (MW) of 340 (i.e., DGEBA), and 4.3% of an oligomer of MW 624, as well as 5% of unspecified derivative of dibromophenol (13) caused ++ patch test reactions. Leica® immersion oil 3% pet. was negative on D2 but ++ positive on D5 and D6, indicating previous active sensitization. The other epoxy chemicals in the immersion oil, namely cycloaliphatic epoxy resin (ERL 4221; 1%–0.5% pet.) and 1,4-butanediol glycidyl ether (0.25% pet.), were negative. A gas chromatographic analysis performed as previously described (14) showed that the patient's Leica® immer-

Table 1. The content of the Leica® immersion oil according to the material safety data sheet (MSDS), and according to gas chromatographic (GC) analysis, respectively; NA=not analyzed, MW=molecular weight

Name of chemical	MSDS; concentration	GC analysis	CAS-No.
modified cyclohexyl epoxy resins	45%	NA	2386–87–0
modified bisphenolic epoxy resins	35%	35%, DGEBA (MW 340)	25068–38–6
1,4-butanediol diglycidylether	10%	9%	2425–79–8
phthalates	4%	NA	117–81–7

Table 2. Recommended patch test concentrations patients' epoxy products (17)

Epoxy product	Recommended patch test concentration
adduct hardeners	1–10% pet.
DGEBA epoxy resins, liquid	1–2% pet.
DGEBA epoxy resins, solid	10% pet.
non-DGEBA epoxy resins	0.5% pet.
paints, lacquers, glues, etc., solvent-based	1–10% pet. or acet.
paints, lacquers, glues, etc., without solvent	1–2% pet. or acet.
polyamine hardeners	0.1–1% pet.
powder paints	5–10% pet or acet.

pet.=petrolatum; acet.=acetone.

sion oil contained 35% DGEBA and 9% 1,4-butanediol glycidyl ether.

Discussion

Active sensitization was confirmed by re-patch testing (15). The standard epoxy, i.e., diglycidyl ether of bisphenol A (DGEBA), remained negative, whereas a brominated epoxy resin containing DGEBA was positive. Perhaps the patient did not become strongly allergic to DGEBA and therefore did not react to 1% DGEBA, though might have reacted to higher concentrations. There are other explanations for false-negative patch-test reactions, such as a lower concentration than declared (16). Our experience is that brominated ER reacts more strongly than 1% standard ER, possibly because it contains irritants that accentuate the reaction. This might also explain why the 3% immersion oil in which the final concentration of DGEBA was about 1% – but which also contained other chemicals which probably increased penetration, e.g., the reactive diluent 1,4-butanediol glycidyl ether – did elicit a positive reaction. The immersion oil and the brominated epoxy might have contained other (epoxy) impurities, i.e., allergens that reacted or cross-reacted on patch testing.

Epoxy products containing liquid low-molecular-weight DGEBA-ER should usually be patch tested at 1 to 2% pet. (Table 1) (17). The final concentration of the strongest allergen should usually not exceed that of commercial patch test series or the concentration otherwise recommended (18). The Leica® immersion oil has elsewhere been patch tested as is (4, 8) or at 50% (1). Accordingly, the final-patch test concentration clearly exceeds the concentration generally recommended for epoxy resins (17, 18), and this induced active sensitization in our patient. In previous studies in which strong immersion oil has been used for patch testing (1, 4, 8), the patients had already been occupationally sensitized to at least 1 epoxy compound, and therefore active sensitization did not necessarily occur. However, it cannot be excluded that the patients in these studies were sensitized to other epoxy compounds to which initially they were not allergic. The manufacturer stated that the immersion oil contained 35% "modified bisphenolic epoxy resins". Our analysis showed that this "modified bisphenolic epoxy resin" was mainly DGEBA (MW 340) (Table 1).

We have previously reported inappropriate patch or use testing performed by dermatologists and dentists resulting in active sensitization or other side-effects (19–21). In such studies, patch testing was performed with undiluted dental resins (19–21). Patch testing with patients' own materials is an important part of the diagnosis of contact allergy, but does need to be performed skilfully.

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Allergic and irritant occupational contact dermatitis from alstroemeria

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Key words: Alstroemeria; occupational; allergic contact dermatitis; irritant contact dermatitis; plants; florists; α-methylene-γ-butyrolactone; calcium oxalate crystals.

We report 2 cases of contact dermatitis from alstroemeria in 42- and 23-year-old female patients who had worked as florists, respectively, for 15 and 2 years. The 1st patient, who was the owner of large plant houses, also worked on picking. They had had for 12 and 2 months, respectively, a pruriginous dry pulpitis with hyperkeratosis and fissuring localized to the 1st 3 digits of both hands, extending to the palmar aspect of the right hand in the 1st patient. Occasional episodes of pruriginous vesiculation of the fingers had also been experienced by both.

The 1st patient, patch tested with the GPEDC standard series, pesticide and plant series (Chemotechnique or Trolab allergens) and several plants brought in by her, had positive reactions (++ or +++) to fresh pieces of the flower, stem and leaf of alstroemeria and to α-methylene-γ-butyrolactone [αMγBL] at 0.01% pet. (Chemotechnique). The 2nd patient, who reacted only to αMγBL in the 1st set of patch tests, also had positive reactions to the pieces of alstroemeria, a plant that she worked with, even though she had not suspected it. Both patients reacted to ketonic and alcoholic extracts of alstroemeria, extemporaneously prepared and incorporated at 1% pet. The plants were identified in the Botanical Department of the University of Coimbra as *Alstroemeria ligtu*, which is a cultivar increasingly popular among florists (1–3).

Although both patients improved considerably on reducing skin contact with alstroemeria and protecting themselves with vinyl and latex gloves, complete clearing of the dermatitis has not been achieved, very probably because, as stated in previous reports, the allergen penetrates rubber and vinyl gloves (3). These are typical cases of occupational allergic contact dermatitis from alstroemeria due to α-methylene-γ-butyrolactone or tulipalin A, the allergen also in tulip bulbs, which elicits the characteristic pattern of dry pulpitis of the 1st 3 digits in florists – also known as tulip fingers - extending to the right palm in workers who pick the flowers (4–7), as did our 1st patient.

Nevertheless, the clinical picture of dry fissured pulpitis and palmar dermatitis also suggests an irritant contact dermatitis from plants, due to the chemical activity of plant enzymes or to the mechanical action of sharp plant structures, namely glochids or raphides (8). In search of a possible mechanical irritant mechanism, we optically microscoped fresh pieces of alstroemeria leaves and flowers and the sap of the plant, collected after breaking the stem like florists do. At 40× magnification, we saw multiple needle-shaped structures in the sap, either isolated or in large agglomerates, which were typical of calcium oxalate crystals at a higher magnification (100×). In confirmation of the nature of these crystals, we observed their dissolution when adding HCl to the preparation, while none such occurred on adding CH_3COOH (9). Such calcium oxalate crystals have been described in several plants (8), as well as in tulip bulbs (10), but we have found no previous description of their presence in alstroemeria.

We conclude that this occupational contact dermatitis is caused not just by delayed-type hypersensitivity to αMγBL, but by a non-specific inflammatory reaction caused by needle-shaped calcium oxalate crystals, which subsequently facilitates sensitization to αMγBL.

Acknowledgements

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Drug eruption induced by cefcapene pivoxil hydrochloride

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Key words: cutaneous adverse drug reaction; cefcapene pivoxil hydrochloride; antibiotics; medicaments; positive patch test.

A 64-year-old woman was seen in July 2000 with pruritic papules and erythema on the trunk and upper extremities that had started 1 day earlier. She had taken cefcapene pivoxil hydrochloride (Flomox®, Shionogi Pharmaceutical Co. Ltd., Osaka, Japan) 100 mg t.d.s. orally for the prevention of infection of the thigh skin, where an angioinfusion catheter had been placed for a hepatic cancer 2 days earlier. Topical corticosteroid application cleared her skin lesions within a week of stopping the oral antibiotic. Patch tests with cefcapene pivoxil hydrochloride 10% and 1% pet. showed erythema at D2 and erythema with papules at D3, 5 control subjects being negative to the same concentrations.

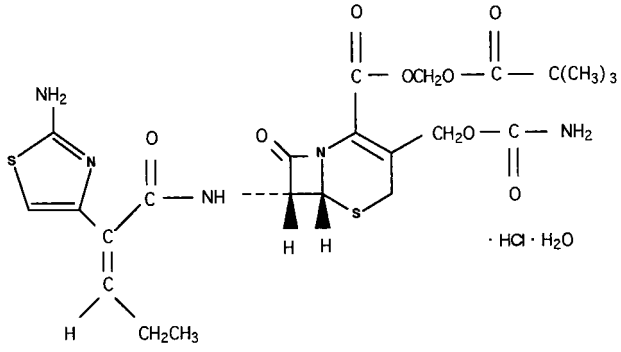

Fig. 1. Chemical structure of cefcapene pivoxil hydrochloride.

Discussion

Cefcapene pivoxil hydrochloride is an oral 3rd-generation cephalosporin with a wide spectrum of activity. It has been in use since 1997 only in Japan. As well as gastrointestinal symptoms, it has been reported to the manufacturer as causing rashes. There are 5 β-lactams that have a pivaloyloxymethyl base as a side chain, e.g., pivmecillinam, cefteram pivoxil, cefetamet pivoxil, cefditoren pivoxil, and cefcapene pivoxil hydrochloride. These 5 drugs rarely cause eruptions, although pivaloyloxymethyl esters have been associated with carnitine deficiency (1). Cefcapene pivoxil hydrochloride with a pivaloyloxymethyl base (Fig. 1) has a similar structure to ceftibuten. Drug eruptions due to cefcapene pivoxil hydrochloride or ceftibuten have not previously been reported in the literature.

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Periorbital allergic contact dermatitis from oxybuprocaine

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Key words: allergic contact dermatitis; oxybuprocaine; local anesthetics; eyedrops; ophthalmics; medicaments; elderly patients; periorbital skin; lack of cross-sensitivity.

Periorbital allergic contact dermatitis accounts for only 2% of all allergic contact dermatitis (1), being caused commonly by antibiotics, sympathomimetics, preservatives and local anesthetics (2, 3).

Case Reports

2 elderly women, aged 64 (patient no. 1) and 71 years (patient no. 2), underwent regular tonometry for long-standing glaucoma, using several local anesthetics. Both developed periorbital dermatitis. Patient no. 1 used Thilorbin® AT (oxybuprocaine, fluorescein, phenylmercuric borate, polysorbate 20, mannitol), Novesine® AT (oxybuprocaine, chlorhexidine diacetate, boric acid) and Conjucain® EDO (oxybuprocaine, sorbitol, sodium hydroxide), while patient no. 2 used Conjucain® EDO only. Patch testing, according to (4) and (5), gave the results shown in Table 1.

Table 1. Patch test results

		D1	D2	D3	D4
Patient no. 1					
phenylephrine	10% aq.	−	−	−	−
Thilorbin® AT	as is	++	++	++	++
Novesine® AT	as is	+	+	++	++
Conjucain® EDO	as is	+	+	++	++
oxybuprocaine	0.5% pet.	++	++	++	++
fluorescein	1% aq.	−	−	−	−
phenylmercuric borate	0.1% aq.	−	−	−	−
polysorbate 20	5% aq.	−	−	−	−
hydroxycellulose	10% aq.	−	−	−	−
chlorhexidine diacetate	0.5% aq.	−	−	−	−
boric acid	3% aq.	−	−	−	−
Patient no. 2					
Conjucain® EDO	as is	−	+	+	NT
oxybuprocaine	0.5% pet.	?+	++	+++	NT
tetracaine	1% pet.	NT	−	−	NT
cinchocaine	5% pet.	NT	−	−	NT
articaine	1% aq.	NT	−	−	NT
lidocaine	1% aq.	NT	−	−	NT
mepivacaine	1% aq.	NT	−	−	NT

Discussion

Oxybuprocaine (benoxinate; 4-amino-3-butoxybenzoate-2-(diethylamino)-ethylester; CAS 99–43–4) is a local anesthetic of the ester type frequently used for tonometry. Adverse reactions, such as fibrinous iritis (6) and keratopathy (7), are rare. 2 cases of immediate-type hypersensitivity reactions have previously been reported (8, 9). To our knowledge, except in the guinea pig (10), no delayed-type hypersensitivity reaction has previously been described. In patient no. 2, no cross-reactions with local anesthetics of ester or amide type were observed. We recommend routinely patch testing oxybuprocaine in patients with periorbital contact dermatitis.

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Primula dermatitis mimicking lichen planus

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Key words: primula; allergic contact dermatitis; lichen planus.

Case Report

A 61-year-old woman, with no prior history of skin disease, presented in March 2000 with a 7-month history of itchy erythematous, papular lesions, starting on her hands and wrists and spreading to her forearms and left cheek. She had already consulted 3 dermatologists and been treated with oral antihistamines and topical medicaments, with no benefit. She had no other medical history and did not take any medication.

Clinical examination revealed erythematous lichenoid papules on her thumbs and wrists. The lesions were arranged more linearly on her forearms and left cheek. No abnormalities of the mucosae or nails were found.

Histological examination showed a band-like lymphocytic infiltrate in the papillary dermis, with damage to the basal layer and necrotic keratinocytes, findings which were consistent with lichen planus. All laboratory tests were normal except for the ANF which was 1/80 (speckled).

Further history taking determined that she had several plants in the home, including *Primula obconica*. A patch test with primin 0.01% pet. was strongly positive. The lesions disappeared on treatment with topical corticosteroids and did not return after removal of her primulas.

Discussion

Primula obconica, first grown in China, is a member of the Primulaceae family, subgenus Cortusoides (1). The main sensitizer is primin, found in microscopic glandular hairs called trichomes, the density of which is highest on the calyces (2). Primin is a 2-methoxy-6-pentyl-1,4-benzoquinone (3). Other allergens are miconidin, a primin precursor, and primetin, a flavoquinone (3, 4). Cross-reactivity exists with other naturally-occurring quinones (5) in orchids and tropical woods. Patch tests are performed with primin 0.01% pet. (6). A positive patch test is seen in 1–1.8% (1, 7, 8) of patch-tested patients in appropriate countries.

Contact allergy to primula shows distinct clinical patterns. Most typical are linear erythematous lesions with vesicles or bullae, most common on the fingers, hands, arms and face. A generalized eruption can also occur (9, 10), as well as an urticarial eruption, erythema multiforme-like lesions (11), herpes simplex-like lesions (12), vitiligo (13) or a photodermatitis (14). To our knowledge, this is the 1st report of a lichen planus-like eruption, previously described from metals, tattoos, para-phenylenediamine and film developers (15).

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