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Short Communications

Allergic contact dermatitis at the application site of an electrosurgical earthing plate occurring in a windscreen repairer

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Key words: allergic contact dermatitis; electrosurgical plate; (meth)acrylates, windscreen repair; occupational.

Case Report

A 55-year-old man developed an itchy, erythematous oedematous well-defined plaque 12 h after the application of an electrosurgical earthing plate on the left thigh. He was self-employed and worked as a windscreen repair mechanic. He was right handed and had a chronic dermatitis involving the right-thumb pulp and index finger. His work involved the use of acrylic resins to repair cracks in windscreens, although he protected his hands with latex gloves.

Patch tests were performed to an extended European standard series, a (meth)acrylates series (Chemotechnique), his windscreen resin and the electrosurgical earthing plate (Niko). The reactions are shown in Table 1 and include several (meth)acrylates. There was a positive reaction to the patient's windscreen resin, suggesting that this exposure led to sensitization. (Meth)acrylates are present in the adhesive that attaches the electrosurgical earthing plate to the skin, which accounts for the acute allergic contact dermatitis that our patient developed at this site.

Table 1. Patch test results

Patch tests	D2	D4
windscreen resin 2% pet.	++	+
earthing plate (Niko)	+	?+
2-hydroxyethyl acrylate	+	+
2-hydroxypropyl acrylate	+	+
2-hydroxyethyl methacrylate	++	++
2-hydroxypropyl methacrylate	++	++
ethylene glycol dimethacrylate	++	++
triethyleneglycol dimethacrylate	+	?+
1,4 butanediol dimethacrylate	+	−
1,4 butanediol diacrylate	+	+
1,6 hexanediol diacrylate	+	+
diethyleneglycol diacrylate	++	+
tripropyleneglycol diacrylate	?+	?+
triethyleneglycol diacrylate	++	++

Discussion

Single-use electrosurgical plates are coated with an acrylic-containing adhesive, which keeps the aluminium foil in close contact with the patient's skin during the procedure. Our patient had been exposed to acrylic resins during his work of repairing windscreens. He had a chronic finger pulp dermatitis, predating the reaction to the earthing plate, that can be attributed to contact with (meth)acrylate resins. The occupational exposure to (meth)acrylates sensitized the patient and subsequent application of the adhesive-coated electrosurgical plate led to an acute contact allergic dermatitis.

There have been several reports of allergic contact dermatitis at the site of electrosurgical plates (1–3). 1 such report described 2 patients who were probably sensitized to (meth)acrylates from the use of sculptured nails (1). Allergic contact dermatitis from acrylic resin repair of windscreens has also been reported (4), and this patient also developed a dermatitis predominantly affecting the fingertips, as seen in our patient. This is the 1st report of allergic contact dermatitis from an electrosurgical earthing plate developing in a patient sensitized by occupational exposure to (meth)acrylates used in windscreen repair.

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Contact allergy to epoxy resin based on diglycidyl ether of bisphenol F

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Key words: epoxy resin; diglycidyl ether of bisphenol A; diglycidyl ether of bisphenol F; epoxy novolac resin; allergic contact dermatitis; occupational.

Epoxy resins based on diglycidyl ether of bisphenol A (DGEBA-R) (Fig. 1) are well-known causes of occupational allergic contact dermatitis (1–3). Besides bisphenol A, epoxy resins can be based on other substances, including bisphenol F (BF) (4). Epoxy resins based on BF (DGEBF-R) or phenolic novolac both contain diglycidyl ether of bisphenol F (DGEBF), which has 3 isomers (Fig. 2). DGEBF-R is less viscous than DGEBA-R, and is used when greater resistance is needed.

There have been several reports of contact allergy to epoxy resins other than DGEBA-R (5–11). In a Swedish aircraft plant, of 3 cases of contact allergy to a novolac-based epoxy resin, only 1 showed positivity to DGEBA-R (11). Contact allergy to DGEBF-R has also been acquired from epoxy resins in flooring materials and putty (12). A DGEBF-R was added to our standard series in 1997. The results from 1997 and 1998 in consecutively patch tested dermatitis patients are described here.

Materials and Methods

Substance

A DGEBF-R (Rütapox 0161) provided by Bakelite Gesellschaft mbH, Duisburg, Germany, was used as test substance.

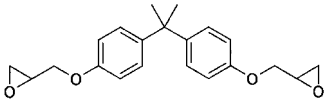

Fig. 1. Diglycidyl ether of bisphenol A.

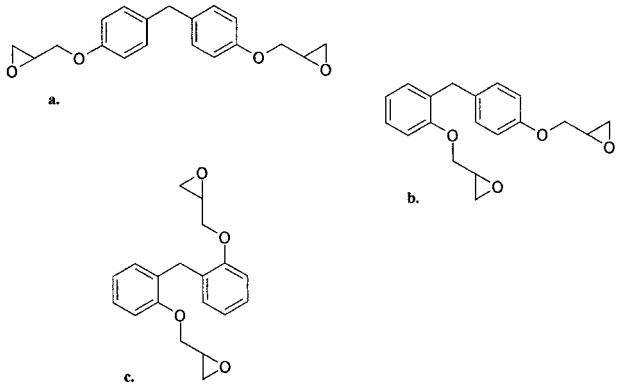

Fig. 2. (a) p,p′-diglycidyl ether of bisphenol F. (b) o,p′-diglycidyl ether of bisphenol F. (c) o,o′-diglycidyl ether of bisphenol F.

Patients

1299 patients tested with the standard series in our department were included, 40% of whom were male.

Patch testing

DGEBF-R 1% w/w in pet., the same concentration as DGEBA-R in the standard series, was applied in Finn Chambers® attached to the back with Scanpor® for 2 days (D), and read according to ICDRG criteria on D3 and D7.

High-pressure liquid chromatography

The DGEBF-R added to the standard series contained 0.6% DGEBA (and the test preparation, accordingly, 0.006%). The DGEBA-R in the standard series (Chemotechnique, Malmö) contained less than 0.01% of any of the 3 DGEBF isomers (Fig. 2).

Results

A total of 23/1299 (1.8%) patients reacted to either of the epoxy resins (Table 1). 22/1299 (1.7%) reacted to DGEBF-R, 16 of whom had suspected occupational contact dermatitis. 9 patients reacted to DGEBF-R without reacting to DGEBA-R. 4 patients were positive to DGEBF-R on D7 but not on D3. 1 patient (no. 14) was positive only to DGEBA-R and not to DGEBF-R, but she was read only on D3 and therefore a reaction by D7 to DGEBF-R cannot be excluded. 7 patients who reacted only to DGEBF-R had weak reactions, 1 of whom was not read on D7. 12 of the patients who reacted to DGEBF-R had equal or almost equal intensity of reaction to DGEBA-R, scored as +, ++ or +++. 18 patients had concomitant reactions to other substances in the standard series.

A clear occupational relevance was found in 6 of the patients allergic to epoxy resins. 1 of these (no. 15) worked with composite material, which, according to the material safety data sheet, was impregnated with epoxy novolac resin.

Discussion

Among our patients, contact allergy to DGEBF-R may be more common than to DGEBA-R. Patients with contact allergy to DGEBF-R, but not to DGEBA-R, had weak reactions in most cases. In a recent report, 9/178 (5.1%) patients reacted to an epoxy resin based on novolac, all of whom also reacted to DGEBA-R in the standard series (13). It has been suggested that reactions to DGEBF-R could be explained by its content of DGE-

Table 1. Patients reacting on patch testing to epoxy resins based on DGEBA or DBEBF; no. 11 had a ++ reaction to DGEBA-R when retested; NR: not read

Pat no.	Age (years)	Sex	DGEBA-R		DGEBF-R		Localization of dermatitis	Possible source of sensitization
			D3	D7	D3	D7		
1	52	f	−	−	++	++	hands	
2	50	m	++	NR	+	NR	extremities	glue, dental material
3	37	f	+	+	+	+	hands	
4	35	f	++	++	++	++	forearms	
5	31	m	+	?	+	−	eyelids	flooring material
6	28	m	−	NR	+	NR	hands	
7	25	f	−	−	+	−	atopy, no dermatitis	printed circuit board
8	24	m	+++	+++	+++	+++	thigh, hands	putty
9	72	f	+	(+)	+	+	hands	
10	64	f	+++	+++	+++	+++	hands	
11	61	f	−	?+	−	++	hands, face forearms	powder paint
12	57	f	++	++	−	++	hands	
13	52	m	+++	+++	+++	+++	hands	paint
14	46	f	+	NR	−	NR	paronychia	glue, dental material
15	45	m	++	++	+++	++	hands	paper/acrylates
16	44	f	−	−	+	?+	hands	epoxy composite
17	43	m	−	++	−	++	hands	paint, glue
18	42	f	++	++	−	++	hands	
19	42	f	−	−	+	+	fingers	
20	38	m	−	−	+	(+)	hands, body	concrete
21	34	m	++	+(+)	++	++	eyelids, forearms	flooring material
22	31	f	−	−	+	?	forearms	car polish
23	22	f	−	−	+	?	neck, arms	

BA. In our study, there were more patients reacting to DGEBF-R than to DGEBA-R, which excludes that interpretation. Furthermore, the concomitant reactions to DGEBA-R ought then to be stronger, which they were not.

The 3 patients who did not react to DGEBF-R until D7 and had a reaction to DGEBA-R on D3 may have metabolized a substance present in DGEBF-R into an allergen present or cross-reacting with an allergen in DGEBA-R.

In addition to the 22 patients reacting to DGEBF-R in this study, 3 patients reacted to DGEBF-R, but not to DGEBA-R, after more than 10 days. When retested with DGEBF-R, they reacted on D3. Patch-test sensitization was suspected and therefore patch testing with DGEBF-R 1% pet. cannot be recommended. At present, the test preparation in our department is 0.25% pet. No suspected patch test sensitizations have so far been reported (905 patients tested).

Further studies are required to elucidate contact allergy to the 3 isomers of DGEBF-R and its relationship to contact allergy to DGEBA-R.

Acknowledgements

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Contact dermatitis from white flower embrocation

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Key words: white flower embrocation; allergic contact dermatitis; lavender; camphor; herbal remedies; medicaments; Chinese medicine

Case Report

A 37-year-old women was stung by an insect on the anterior thigh and applied a Chinese herbal remedy, white flower embrocation, to the site. Within 2 days, she developed a 7-cm itchy, erythematous, vesicular reaction at the site, which resolved after several weeks leaving an area of hyperpigmentation. She had developed similar reactions 2 years earlier where she had applied the remedy to mosquito bites.

Prick testing to 13 common aeroallergens in the past had been negative. Patch testing was performed with our standard series, using standard methods as previously described (1). There were no reactions at 2 and 4 days (D), but + reactions to fragrance mix and colophonium at D7. An open test to the white flower embrocation revealed a + reaction by D2, which was still present at D7.

The patient provided the package for the embrocation, which indicated its ingredients as wintergreen oil (40%), menthol crystal (30%), eucalyptus oil (18%), camphor (6%), and lavender oil (6%). We then patch tested her with lavender oil, camphor, and 5 items known to cross-react with eucalyptus or benzoin: vanillin, orange oil, cinnamic alcohol, α pinene, and eugenol (Table 1). We did not have wintergreen oil or menthol available for testing.

Table 1. Patch test results

Allergen (pet.)	D2	D4
alpha pinene (15%)	−	−
camphor (10%)	+	++
cinnamic alcohol (5%)	+	+
eugenol (2%)	−	−
lavender oil (as is)	+	+
orange oil (2%)	−	+
vanillin (10%)	−	−

The patient's delayed reaction to colophonium was explainable on the basis of its cross-reaction to the later-applied lavender oil. In retrospect, she recalled having a rash at the site of a surgical bandage years earlier that was attributed to a "pressure effect". Furthermore, she also recalled previously using Tiger Balm, which contains 25% camphor, and which may have sensitized her years earlier to this. Finally, the patient noted that the rashes associated with the white flower embrocation worsened in sunlight, which may be explainable by lavender being a photosensitizer.

Discussion

There has been increased reporting of sensitization to herbal remedies and aromatherapy products, the latter both occupationally and non-occupationally (2, 3). This case illustrates the value of performing an open test to assess contact allergies to topical medicaments. More important, though, is identification of the individual ingredients of such medicaments, because many such can cross-react with each other, or with common allergens (4, 5).

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Fixed drug eruption due to scopolia extract

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Key words: fixed drug eruption; scopolia extract; anticholinergic; medicaments; cutaneous adverse drug reactions.

A 42-year-old woman was seen in January 2000 with brown pigmentation on the forehead. 5 months previously, she had bought Shin-Cyugai-Icyouyaku® (Cyugai Pharmaceutical Co. Ltd.) from a drugstore and taken 3 tablets for gastric pain. 2 h later, she developed pruritic erythema, followed by pigmentation. Afterwards, she had the same erythema when she took the drug.

She was patch tested on unaffected skin of the back with 10% and 1% pet., and on involved skin with 10% pet., of 8 constituents in Shin Cyugai-Icyouyaku®: azulene sulfonate sodium, L-glutamine, sodium bicarbonate, synthetic hydrotalcite, scopolia extract, sucralfate, lipase AP6 and diasmen SS. Only scopolia extract 10% pet. was positive on involved skin of the forehead at 2 and 3 days after application. As a control, scopolia extract 10% pet. was applied on 5 normal subjects, resulting in no response.

Discussion

Scopolia extract, extracted from dried rhizomes and roots of simple plants of the genus *Scopolia*, has anticholinergic actions, e.g., inhibition of gastric juice secretion and gastrointestinal motility (1). Scopolia extract contains alkaloids (0.90–1.09%) consisting mainly of hyoscyamine (1). It is widely used in medical therapy and frequently contained in over-the-counter drugs. Scopolia extract causes known adverse effects, e.g., mydriasis, nausea, vomiting, headache, vertigo, and dysuria. Atropine and hyoscine (scopolamine) analogues are antimuscarinic alkaloids like hyoscyamine. Only 1 case of fixed drug eruption from scopolamine has been reported (2, 3), and none from scopolia extract, hyoscyamine or atropine.

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Hyperpigmentation and contact dermatitis due to *Juglans regia*

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Key words: irritant contact dermatitis; contact hyperpigmentation; *Juglans regia*; plants; walnut juice; juglone; lawsone; henna.

The juice of walnut shells, the produce of the *Juglans regia* tree, has been used for centuries to colour the skin and hair and for its astringent properties. Juglone, the active ingredient from the green husk of walnuts, has been considered a strong sensitizer in guinea pigs (1), but contact sensitivity in man has rarely been reported, although juglone is known to be a strong irritant (1, 2).

Case Report

In September 1999, a 65-year-old woman presented, complaining of very intense skin hyperpigmentation and large tense blisters involving the palms and fingers (Fig. 1). Examination also revealed brown stains on the forearms, together with large erosions and eczematous lesions (Fig. 2). Our diagnosis of contact pigmentation and acute contact dermatitis due to walnut juice was immediately backed up by the patient, who confirmed that she had shelled 15 kilos of fresh walnuts in the 3 days before the onset of the complaint.

To check for a possible contact allergy, patch tests with the European standard series, a hydroalcoholic extract of walnut husk, and juglone (Sigma-Aldrich Co., St. Louis, Missouri, USA) (1% aq.) were carried out; lawsone (Sigma-Aldrich Co., St. Louis, Missouri, USA) (1% aq.), the active ingredient of henna, was also tested in view of a possible cross-reaction with juglone (Fig. 3). The tests were performed according to standard tech-

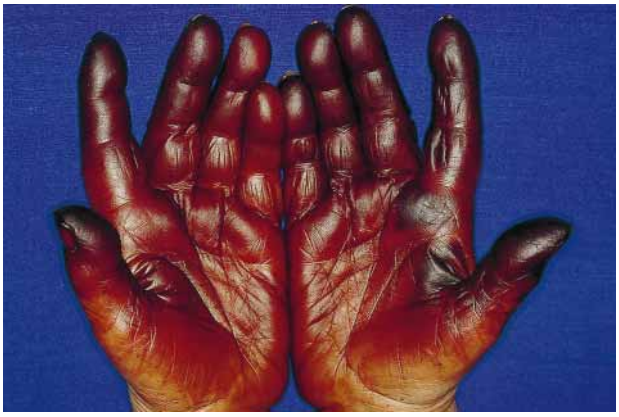

Fig. 1. Skin hyperpigmentation and large blisters of the palms and fingers.

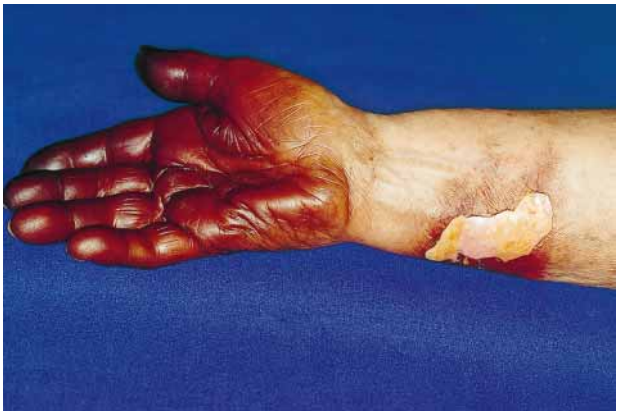

Fig. 2. Erosions and eczematous lesions on forearms.

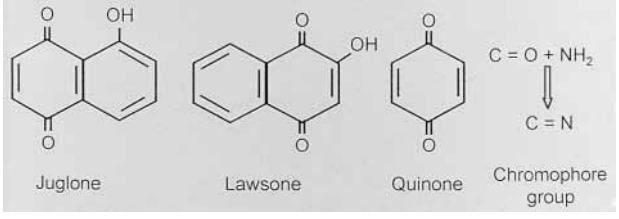

Fig. 3. Chemical structure of juglone (5-hydroxy-1,4-naphthoquinone) and lawsone (2-hydroxy-1,4-naphthoquinone) and mechanism of skin pigmentation.

nique, using Finn Chambers®, Scanpor® tape and 2 days (D) occlusion. Readings were made on D2, D3, D4 and D7. Only the hydroalcoholic extract of walnut husk elicited a bullous reaction of clearly irritant type, on D2.

Treatment with cool, weak aluminium acetate (Burow's solution) compresses was instituted, and by 5 days later, the irritant contact dermatitis had healed. 3 weeks later, the pigmentation had entirely cleared up.

Comment

Juglans regia, the European walnut, is a handsome, deciduous tree that grows up to 20 m in height. Thanks to their juglone content, walnut husks are used in semipermanent vegetable hair dyes, as is henna. On the same principle, they are used in so-called self-tanning products that do not require exposure to the sun or UVA rays.

A review of the literature shows that juglone can cause irritant reactions as well as skin hyperpigmentation (3), but, although it has been found to be a strong sensitizer in guinea pigs, contact allergy is considered a very rare event in man (1–4).

The pigmenting action of juglone is held to be primary and of exogenous type: in fact, juglone stains the skin with no involvement of the melanocytes. Walnut juglone, like henna lawsone, is a naphthoquinone (Fig. 3), the only difference being the position of the OH group. "Activated" ketone C=O groups (with an unstable electronic halo due to the banzene rings) have an elective affinity for the NH_2 group of keratin aminoacids. The resulting reaction gives rise to C=N chromophore groups with a strong pigmenting action, that absorb visible colours, especially violet, and reflect yellow and red. This results in the colouration ranging from red to deep brown that is induced by walnut or henna. Dihydroxyacetone, contained in various self-tanning products, works according to the same mechanism.

In our parts of Southern Italy, slight primary skin pigmentation due to walnut husk is quite commonly observed in the early autumn; this is the time when the outer green husk of fresh walnuts must be removed. The hyperchromia, involving the hands and particularly the palms, fingers and nails, lasts 1–4 weeks according to the intensity of the pigmentation. Housewives and agricultural workers are the subjects most at risk. These patients often come under dermatological observation for other reasons, and the disease is therefore only diagnosed by chance. In our patient, the intense pigmentation and the acute irritant contact dermatitis had undoubtedly been caused by the cumulative effect of 15 kilos of walnuts shelled in the 3 days before the onset of the complaint.

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Allergic nickel and chromate hand dermatitis induced by orthopaedic metal implant

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Key words: allergic contact dermatitis; systemic reaction; nickel; chromate; cobalt; stainless steel; orthopaedic implant; fracture; energy-dipersive X-ray analysis.

Case Report

A 35-year-old non-atopic diver, with no previous history of metal allergy, slipped on a wet pier and sustained a multiple compound trimalleolar fracture of the right ankle. The fibula and tibia were immediately surgically realigned and retained by metal plates and screws, and the ankle immobilized in plaster for 5 weeks. 1 month after the accident, the patient developed itching, scaling and vesiculopapular dermatitis on several fingers of both hands, mainly on their ventral and acral parts, which worsened over the next few months. 6 months after the accident he consulted a dermatologist.

Patch testing, performed according to the recommendations of the ICDRG, was positive to nickel sulfate (+++), chromate (+), cobalt (?+), budesonide (++) and 4-tert-butylphenol-formaldehyde resin (+). The patient was advised to have the metal removed and, thereafter, 8 metal screws and 1 plate were analyzed by energy-dispersive X-ray analysis (1, Technical Research Centre of Finland, Research report VAL 24–992184). The screws and the plate contained 62.0–63.7% iron, 17.4–18.0% chromium, 14.1–14.9% nickel, 1.5–1.8% molybdenum and 0.2–0.6% silicon. The dermatologist considered the sensitization to metals, as well as the hand dermatitis, to have been induced by the orthopaedic implant.

The patient's insurance company then referred the patient to us for a second opinion. A 2nd patch-test session was performed, confirming the metal sensitivity. Budesonide was also positive (++), whereas 4-tert-butyl-phenol formaldehyde resin was now negative. The metals gave the following reactions in dilution series: nickel sulfate 3–1%, ++; 0.32%, +; 0.1%, negative; potassium dichromate 1–0.5%, +; 0.32%, ?+; 0.1%, −; and cobalt chloride 3–1%, +; 0.32%, ?+, 0.1%, −.

It was concluded that the patient had become sensitized to nickel and chromate in the orthopaedic metals. It was also apparent that sensitization to cobalt had occurred, even though no cobalt could be shown on analysis. The patch-test reaction to budesonide was unclear as the patient gave no history of using corticosteroids. The hand dermatitis improved after removal of the metal from the ankle, but nevertheless continued to relapse. The insurance company accepted the claim for compensation.

Discussion

The clinical significance of nickel release from surgical implants remains controversial (2). The most commonly used alloys in orthopaedic implants are stainless steel and vitallium (3). Vitallium contains mainly cobalt and chromium and also some nickel (3). Stainless steel contains at least 12% chromium (4), and often also contains nickel, as well as carbon, nitrogen, manganese, magnesium, phosphorus, sulfur, cobalt, copper, silicon and molybdenum (4). There are many types of stainless steel, the main types, with their nickel content in parentheses, being: martensitic (0–2.5%), ferritic (0–4.5%) and austenitic (8–34%) (8, 17). Austenitic stainless steels are the most widely used (4). The commonly used 18/8-stainless steel contains 18% chromium and 8% nickel. The stainless steel used in implants and prostheses normally contains 9–14% nickel, up to 20% chromium and small amounts of manganese and molybdenum (3), as did the screws and plates analyzed in the present study.

Stainless-steel prostheses can release nickel, chromium or cobalt ions (3), but most metal-sensitive patients can have orthopaedic metal implants without risk (2, 3, 5). High-quality stainless steel is usually not regarded by dermatologists as a hazard (4), though some types release enough nickel to elicit dermatitis in nickel-sensitive patients (4, 6–11). Metal-allergic patients have developed eczema over the operation site (5, 13, 14), which has prompted removal of the implant for improvement or cure (5). Eruptions associated with orthopaedic implants may also be generalized (3), eczematous (15, 16), as in our patient, urticarial (3, 17) or vasculitic (13). These may clear upon removal (15, 16) but, as with metal allergies in general, may instead relapse and become chronic. Chromates are well-known sensitizers, but metallic chromium does not induce contact allergy (12). However, it is believed that plasma or other body fluids can transform metallic chromium into allergenic chromate salts.

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Allergic contact dermatitis from benzocaine ointment during treatment of herpes zoster

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Key words: allergic contact dermatitis; local anaesthetics; benzocaine; herpes zoster; medicaments.

Case Report

During treatment of herpes zoster throracis with oral acyclovir and Anaesthesin® (benzocaine) 20% ointment, a 72-year-old woman developed a painful pruritic erythematous dermatitis in the area of the herpetic lesions on the right trunk, spreading to the right upper arm. This led the practitioner to misdiagnose acyclovir resistance. On admission, resolving vesiculobullous lesions were seen within a sharply demarcated dermatitis. There was no previous history of skin disease or allergy and she had rarely used cosmetics or medicaments.

Polymerase chain reaction (PCR) for varicella zoster and herpes simplex virus was negative. Patch tests to an extended European standard series, plus Anaesthesin® 20% ointment and its ingredients, showed +++ reactions to the ointment and to benzocaine. Other ingredients of the ointment, such as myristyl myristate, polysorbate 80, and softisan 649, and other local anaesthetics, such as lidocaine, bupivacaine, and procaine, were all negative.

The dermatitis faded after changing the topical mediament to a class-III corticosteroid cream, in combination with an oral antihistamine.

Discussion

The "caine" anaesthetics have been known as a common cause of allergic contact dermatitis since the 1920s (1, 2). Benzocaine is used topically in painful conditions such as herpes zoster, insect bites, lumbago, burns and perniosis.

Our case illustrates the difficulty in diagnosing allergic contact dermatitis in areas of the skin that are already affected by other lesions. Our report emphasizes the importance of patch testing in tracking down the allergen under such conditions. Furthermore, patch testing can exclude other potential sensitizers in a medicament, other allergens, such as thiuram (3), or cross-sensitizations to other local anaesthetics (4).

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Unusual clinical presentation in a case of contact dermatitis due to corticosteroids diagnosed by ROAT

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Key words: allergic contact dermatitis; corticosteroids; ROAT; hydrdocortisone aceponate; medicaments; cross-sensitivity.

Contact allergy due to topical corticosteroids may be well-known (1, 2), but in some cases, the diagnosis remains difficult to establish.

Case Report

A 50-year-old woman, with no history of atopy, was referred when eczema developed on her legs while applying Efficort lipophile® (hydrocortisone aceponate) to psoriatic lesions strictly limited to her lower back. There was no eczema on or around the site of application of the corticosteroid ointment, but it was present on the backs of the legs, mainly in the popliteal fossae. The same adverse reaction, in the same location, occurred when using Diprosone cream® (betamethasone dipropionate) on the back.

Patch tests were performed with the European standard series, a corticosteroids series (Table 1), preservatives and excipients series (Trolab – Hermal), Efficort® cream and Diprosone cream® as is and at 10% and 1% pet. Patch tests were also performed with tixocortol pivalate, budesonide, hydrocortisone-17-butyrate, betamethasone and aclomethasone at serial dilutions from 0.1 to 0.0001% pet. All these patch tests were negative on day (D) 2, 4 and 7. A repeated open application test (ROAT) with Efficort cream® was done, eliciting on D3 an annular positive reaction surrounding the site of application of the ointment. ROATs performed with the vehicles contained in Efficort cream® were negative, but a ROAT with hydrocortisone aceponate 0.127% was positive on D4. As patch tests with tixocortol pivalate, budesonide, betamethasone-17-valerate, betamethasone and amcinonide remained negative, it was necessary to perform ROATs with some of these compounds to determine the corticosteroid classes to which the patient had been sensitized.

Table 1. Results of patch tests and ROATs performed with corticosteroids

Tests	Results D2	D4	D7
Patch tests			
budesonide 0.1%; 0.01%; 0.001%; 0.0001% pet.	−	−	−
betamethasone 0.1%; 0.01%; 0.001% pet.	−	−	−
triamcinolone acetonide 0.1% pet.	−	−	−
tixocortol-21-pivalate 1%; 0.1%; 0.01% pet.	−	−	−
aclomethasone-17,21-dipropionate 0.1%; 0.01%; 0.001% pet.	−	−	−
clobetasol-17-propionate 0.25% pet.	−	−	−
dexamethasone-21 phosphate disodium salt 1% pet.	−	−	−
hydrocortisone-17-butyrate 0.1%; 0.01%; 0.001% pet.	−	−	−
hydrocortisone 1% pet.	−	−	−
prednisolone 1% pet.	−	−	−
amcinonide 0.1% pet.	−	−	−
Efficort® cream as is ; 10%; 1% pet.	−	−	−
Diprosone® cream as is; 10 %; 1% pet.	−	−	
ROATs			
Efficort® as is	−	+	−
hydrocortisone aceponate 0.127% pet.	−	+	
cetearyl alcohol 10% pet.	−	−	−
benzyl alcohol 10% pet.	−	−	−
tixocortol-21-pivalate 1% pet.	−	−	+ D15
betamethasone 0.1% pet.	−	−	−
Tridesonit® (desonide at 0.1% pet.)	−	−	−

As adverse reactions had occurred with betamethasone dipropionate belonging to class D1 (halogenated and with C16 substitution esters) (3) and hydrocortisone aceponate belonging to class D2 (labile esters) (3), we contra-indicated corticosteroids belonging to class D without performing further tests. As budesonide can induce active sensitization, we did not use this molecule to investigate potential allergy to class B corticosteroids (acetonides). Nevertheless, we performed a ROAT with a commercialized form of desonide 0.1% pet, with negative results on D7. The ROAT with tixocortol pivalate 1% pet. was positive on D15. The ROAT with betamethasone 0.1% pet. remained negative on D7 reading.

Comment

Contact allergy to topical corticosteroids was observed in 2.5% of 7238 patients (1) and in 2% of 5432 patients (2) in 2 European multicentre studies. To our knowledge, this is the 1st such case with eczema at sites distant from the site of application of the corticosteroid, without any annular dermatosis surrounding the site. This case also emphasizes the difficulties in diagnosing corticosteroid allergy. Patch tests have to be read on D2, D4 and D7. When negative, according to Isaksson et al. (4), it may be necessary to test with serial dilutions. Even with such dilutions, patch tests remained negative in our patient, though using ethanol as vehicle might have enhanced their sensitivity.

This case emphasizes that ROATs can be of value in diagnosing corticosteroid allergy, when patch tests performed with standard and serial dilutions have been negative. It may also be necessary to perform ROATs to identify all the sensitizing classes of corticosteroids. In

our patient, this was the only way to determine that she was sensitized to classes A (hydrocortisone type), D1 and D2 of corticosteroids, according to the Goossens classification (3).

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Eczema herpeticum in parthenium dermatitis

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Key words: eczema herpeticum; Kaposi's varicelliform eruption; parthenium dermatitis; allergic contact dermatitis; plants; airborne.

Case Report

A 34-year old shopkeeper was diagnosed as having parthenium dermatitis on the basis of clinical features and patch test results. Lesions had been present for the last 6 months, confined to the face and cubital fossae. He was treated with systemic prednisolone 40 mg daily, reduced to 20 mg within 2 months, after which he presented with multiple papulovesicular lesions on the face, with the dermatitis subsiding to some extent. There was no previous history of herpes labialis or genital herpes. On examination, there were vesicular lesions and multiple erosions with brownish-colored crusts on the forehead, cheek and face. The face was oedematous. Tzanck smear from the vesicular lesions and erosions showed multinucleated giant cells. Direct immunofluorescence from the vesicle floor was positive for the presence of HSV antigen. His anti-HSV antibody titre was 1:10 at the time of presentation, but we could not record the 2nd reading as the patient was lost to follow-up. With a diagnosis of eczema herpeticum, he was treated with acyclovir 200 mg 5× a day for 7 days, with which the lesions subsided.

Discussion

Eczema herpeticum (Kaposi's varicelliform eruption) has been associated with various dermatoses, including atopic dermatitis, seborrhoeic dermatitis, neurodermatitis, Darier's disease, pemphigus foliaceus, mycosis fungoides, Wiskott-Aldrich disease, benign familial pemphigus, congenital ichthyosiform erythroderma and Hailey-Hailey disease (1–3, 4). It has also been associated with 2nd degree burns and sun exposure (5, 6).

Bork et al. (1) in Germany reported an increase in the incidence of eczema herpeticum from 1 to 3,000,000 to 1 in 600,000–750,000 per year between the 1960s and the 1980s. Recently, Vestey et al. (7) found HSV-specific cell-mediated immunity to be deficient in 3 out of 7 patients with eczema herpeticum. Eczema herpeticum has been seen to occur in irritant contact dermatitis (8), but it has not previously been reported in airborne contact dermatitis or parthenium dermatitis.

Eczema herpeticum occurring during the course of corticosteroid withdrawal has also been reported in a few cases of atopic dermatitis and erythroderma (6, 9).

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Aziridine hardener – a new sensitizer in the dyeing of leather

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Key words: aziridine (PFA) hardener; trimethylpropane triacrylate; propyleneimine; dimethylethanol amine; wool wax alcohols; leather; dyeing; tannery; chronic sulfate; patch test; allergy; allergic contact dermatitis; asthma.

Polyfunctional aziridine (PFA) hardeners (or cross-linkers) are used to harden many surface coatings, finishes and adhesives (1–3). They are potent skin and respiratory sensitizers (1–5).

Patients and Methods

Patch testing was carried out in 4 workers with work-related dermatitis and respiratory symptoms, out of a total of 50 workers, in the same tannery (Table 1), using standard methods (6), with a modified a modified European standard series (Chemotechnique Diagnostics AB, Sweden), a (meth)acrylates series (patient nos. 1, 2, 4) or 2 relevant acrylates (patient no. 3, Table 2), other relevant series and 2 commercial PFA hardeners (Table 2, Fig. 1), dimethylethanolamine (2-dimethylaminoethanol, Sigma, D-4250) and propyleneimine (Fluka Ab, Bucks SG, 82310) (Table 2). Dilution series were deployed for potassium dichromate, chromium chloride, cobalt chloride, nickel sulfate and commercial PFA hardener 1 (2%, 1% and 0.5% pet.) (Table 2).

Prick tests were also done and included a standard series (Allergologisk Laboratorium AS, Denmark), other relevant series and a PFA hardener, dimethyletha-

Table 1. Characteristics of the 4 patients sensitized to an aziridine (PFA) hardener in a tannery

Patient no.	1	2	3	4
sex/age (years)	M/43	M/44	M/34	F/57
occupation	dye mixer	leather worker	leather worker	leather worker
duration of occupation (years)	6	26	9	6
duration to dermatitis (years)	1.5	10	5	5
localization of dermatitis	hands, arms, thighs, legs	hands, arms, face, trunk, thighs	hands, arms, neck, legs	hands, arms, face, neck
use of gloves (occasional)	rubber, PVC	rubber, textile	textile	rubber
atopy own/family	no/no	no/no	no/no	no/no

Table 2. Results of patch tests in the 4 patients sensitized to aziridine (PFA) hardeners in a tannery

Patient no.	1	2	3	4
commercial PFA hardener 1				
(2%)*	++	++	++	+
(1%)*	++	++	++	+
(0.5%)*	+	++	+	−
PFA hardener 2 (2%)*	++	++	NT	+
trimethylpropane triacrylate (0.1%)*	−	−	−	−
pentaerythritol triacrylate (0.1%)*	−	−	−	−
propyleneimine (0.1%)*	NT	NT	−	−
dimethylethanol amine (1%)*	−	NT	−	−
standard series	nickel sulfate + wool wax alcohols ++	dichromate ?+ fragrance mix ++	dichromate ++ cobalt chloride ++	dichromate +

*Petrolatum.

nolamine (DMEA), trimethylol triacrylate (TMPTA), and propyleneimine as human serum albumin (HSA) conjugates and in water, as well as potassium dichromate 1 mg Cr^{6+}/ml, chromium chloride 1 mg Cr^{3+}/ml, nickel sulfate 10 mg $NiS0_4$/ml, cobalt chloride 1 mg Co^{2+}/ml, all in water (1, 6, 7).

Polyfunctional aziridine (PFA) (Fig. 1), a reaction product of propyleneimine and TMPA, was analyzed with gas chromatography using mass selective detector with the 2 commercial PFA hardeners (Table 2), to verify whether they were of the same type as those used by our previous patients (1, 5).

An otolaryngorhinological examination was conducted on all 4 patients. In addition, nasal challenges with PFA hardener 1 and dichromate 0.01, 0.1 and 1 mg Cr^{6+}/ml to patient no. 1 and bronchial challenge with PFA hardener 1 to patient nos. 3 and 4 were performed as chamber exposure tests (1, 8).

Results

Patient no. 1, as a dye mixer (Table 1), made a complex mixture of a water dispersion of polyurethane, a water-based latex-type dye and a commercial hardener (Table 2, Fig. 1). The leather workers (patient nos. 2–4) were exposed to both wet tanned and dyed, but unfinished, hides and dusts from dry-dyed finished hides. Patient no. 3 had also handled finished hides in the warehouse.

On patch testing, patient nos. 1–3 were ++ to the 2 commercial PFA hardeners, and also ++ or + to a dilution series of hardener 1 (Table 2). Patient no. 4 was + to the hardeners. Analysis of the 2 PFA hardeners showed 92% (hardener 1) and 38% (hardener 2) PFA (Fig. 1). 2 leather workers (patient nos. 2, 3) with long-standing and extensive dermatitis were also ++ to chromium chloride and potassium dichromate in dilution series (9). Patient no. 4 was a + to potassium dichromate, but only ?+ to chromium chloride. Patient no. 1 also reacted (++) to wool wax alcohols and had a non-occupational allergy to nickel. Patient no. 2 reacted to fragrance mix and patient no. 3 also to cobalt chloride, possibly from metal complex dyes. When seen 3–6 months later, all were clear: patients nos. 2–4 had to stop working in the tannery.

The rhinitis of patient no. 1 was considered to be non-occupational after negative nasal challenge. Patient no. 2 had no rhinitis when examined, but developed intrinsic asthma having stopped working in the tannery. Chamber challenge confirmed occupational asthma in patient nos. 3 and 4, with delayed rhinitis in patient no. 3.

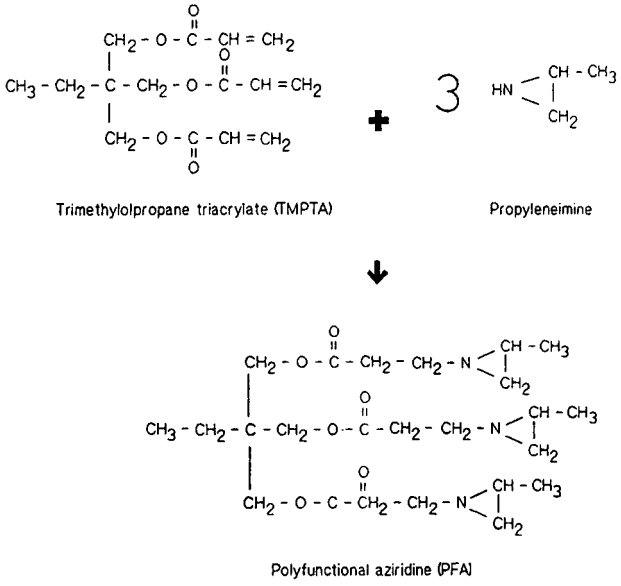

Fig. 1. Chemical structure of a polyfunctional aziridine (PFA).

Discussion

Analysis of the 2 commercial hardeners used in the tannery confirmed that they were synthesized from propyleneimine and TMPTA as in our previous cases (Fig. 1; 1, 5). Some unhardened PFA may have been left on the surface of the hide. TMPTA residues in such hardeners may also sensitize (10). Analysis of a previous PFA hardener detected 0.3% TMPTA (5). Neither our previous nor present patients were allergic to TMPTA (or PETA). The hardener may also contain minute amounts of DMEA and propyleneimine. DMEA has caused asthma (11), but not dermatitis. Propyleneimine has not been reported as inducing dermatitis, though the chemically related ethyleneimine has (12). Patch testing with DMEA and propyleneimine was negative in the patients tested (Table 2).

Allergy to chromium had been reported in tannery workers as well as from leather shoes (9, 13, 14). Although the representative of the factory was aware of the carcinogenic and sensitizing properties of chromium (13), he was unaware of the risk of allergy associated with PFA hardeners, because this was missing from the material safety data sheets, thus delaying diagnosis.

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Occupational allergic contact dermatitis from formaldehyde resin in clothing

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Key words: occupational; allergic contact dermatitis; textile finishes; formaldehyde; quaternium-15; ethylene urea melamine formaldehyde; clothing resins.

Formaldehyde-resin dermatitis from textiles (1–3) occurs occasionally where clothing is in close contact with the skin (4) and is only rarely occupational (2, 5).

Case Report

A 30-year-old man presented with a 4-year history of hand dermatitis. He had worked in a clothing warehouse for the previous 8 years, handling new ready-made clothing. He occasionally wore rubber-backed cotton gloves at work. The dermatitis improved at weekends and cleared completely on holidays. He had been treated with topical betamethasone valerate 0.1% cream and Diprobase® emollient cream (paraffin 15%, paraffinum liquidum 6%, cetearyl alcohol 7.2% and cetomacrogol 2.25%). There was no personal or family history of atopy. On examination, he had an erythematous scaly vesicular eruption on both palms, the right (dominant hand) being worse than the left. There were also scaly patches on the dorsa of all the fingers.

He was patch tested to the European standard, preservative, vehicle, plasticizer and glue, clothing and dye series and samples of his gloves. Patch tests were read at 2 and 4 days (D). He had positive reactions to formaldehyde (+), primin (++), quarternium-15 (++) and ethylene urea melamine formaldehyde (EUMF) (+) at both D2 and D4. An allergen-specific IgE test for natural rubber latex was negative.

Discussion

The cause of textile-resin dermatitis is usually free formaldehyde released from the resin. Patients are usually positive on patch testing to both formaldehyde and a formaldehyde resin (1–3), occasionally to formaldehyde resin alone (2). The 9 main types of formaldehyde resins used in durable-press fabrics can be classified into high, medium and low formaldehyde releasers (1, 2). The amount of high-formaldehyde-releasing resin in durable-press fabrics in the US has fallen from 55% in 1980 to 27% in 1990 (1, 6), but allergic contact dermatitis has still been reported occasionally (7).

Our patient reacted to EUMF, which is a mixture of ethylene urea formaldehyde (EUF) and melamine formaldehyde (MF), both of which are high formaldehyde releasers. EUMF had been thought to be the best patch test screening agent for clothing dermatitis (1), though more recently, dimethylol dihydroxyethylene urea (DMDHEU) has been suggested to be better (7). DMDHEU is a low formaldehyde-releasing resin but has become much more widely used of late and may now represent the main cause of textile allergy (7). However, our patient did not react to DMDHEU, which highlights the difficulty in selecting screening agents without losing test specificity.

Our patient also reacted to primin (probably not relevant) and quarternium-15, a formaldehyde-releasing preservative. Reactions to formaldehyde-releasing preservatives are a common finding in formaldehyde-related textile dermatitis and are important to recognize, as they may also be clinically significant (2).

When sensitization to textiles is occupational, subsequent clothing dermatitis is unlikely (5, 6). However, it is probably best to advise patients to wash all new clothes before wearing them. The potential for formaldehyde-release from resins usually decreases with the number of washes, washing powders usually being alkaline. Chlorine bleaches will increase formaldehyde release and should not be used (4, 6, 7).

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Localized aquagenic urticaria dependent on saline concentration

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Key words: localized aquagenic urticaria; facial contours; sea water; hypertonic saline; tap water; distilled water; osmolarity.

Case Report

A 37-year-old non-atopic woman had a 4-year history of recurrent erythema and whealing of the face and neck elicited by contact with water, particularly sea water. The lesions were intensely pruritic and strictly localized to the ears, preauricular zone, mandibular and sub-mandibular areas, and the anterior aspect of the neck. The forehead and central zone of the face were spared. The urticarial rash initially used to develop only when the patient went swimming in the sea: it appeared within about 10 min of immersion and cleared spontaneously about 30 min after rinsing and drying her skin. With time, her symptoms had worsened and the flare and itching had become so annoying that she completely stopped sea bathing. Tap and swimming pool water at first caused no problems, but recently she had also experienced similar, though attenuated, symptoms when going to the swimming pool and when taking a shower or bath, if she stayed in contact with water more than 10 min. The water temperature was irrelevant. The patient reported no other skin symptoms. She had never applied retinoids nor any other irritant topical drug. On the other hand, she used everyday cosmetic products without any problem. She could still wash her face without discomfort but, as she feared further progression of her symptoms, she preferred not to use rinse-off detergents.

Patch testing to the Italian standard series was negative. An ice cube test was also negative. Water challenge tests were performed with fresh sea water as is, ultrafiltered sea water (to eliminate micro-organisms), hypertonic NaCl solution (3.5 g%, approximately reproducing the salt concentration of the Mediterranean sea), tap water and distilled water. These liquids were tested 2 by 2, on different days, by means of soaked gauze pads applied to the patient's mandibular regions and, as controls, to the antecubital fossae. The pads were left in place for 20 min. On one occasion, sorbic acid 5% pet. and pet. as is were applied to the right and left preauricular area, respectively, to check the patient's reactivity to a non-aqueous solution of a common non-immunological contact urticant. The patient knew that we were testing different water solutions, but she took no note of which was which. Readings were performed by a dermatologist who was also unaware of which test was which.

The sea water as is, the ultrafiltered seawater and the hypertonic saline solution elicited intense erythema, scattered with distinct small wheals, after 20 min of contact with the skin of the mandibular and submandibular region. Localized pruritus and discomfort were severe. The rash cleared spontaneously within 60 min. Tap water elicited patchy erythema and mild discomfort, while distilled water elicited only a tiny follicular wheal and no subjective symptoms. Control tests in the antecubital fossae were all negative. Sorbic acid 5% pet. caused intense erythema and a burning sensation, but no whealing. Petrolatum as is had no effect.

It was not possible to investigate the urticant effect of ethanol, acetone or a hypertonic non-ionic water solution, such as a glucose solution, because the patient refused to undergo further testing.

Discussion

Our patient has a peculiar form of localized aquagenic urticaria apparently dependent on the ionic concentration and/or osmolarity of water. Her symptoms are much more intense on contact with hypertonic saline than with tap or swimming pool water, which have a low ionic concentration and are hypotonic as compared to body fluids. The urticant effect of distilled water is almost negligible.

Aquagenic urticaria is a rare form of physical urticaria characterized by the appearance of wheals at the site of contact of skin with water, regardless of its temperature, within 2 to 30 min of exposure. To the best of our knowledge, 28 cases have so far been described in the literature (1–3). Although the restriction of aquagenic wheals to only certain parts of the body has sometimes been reported (2, 4, 5), our case is unique as to the strict localization of the urticarial rash to the facial contours and neck.

The pathogenic mechanism of aquagenic urticaria is obscure. There is some evidence that it is, at least in part, histamine-mediated and dependent upon mast cell activation (4, 6). It has been proposed that water does not act as the primary trigger of mast cell degranulation, but rather as a solvent vehicle of some epidermal antigen that would then diffuse into the dermis causing histamine release from sensitized mast cells (4). In some cases, organic solvents, such as acetone or ethanol, have been shown to enhance the urticant effect of water (3, 4, 6, 7).

Hide et al. (3) have recently described a patient in whom 5% saline was more effective than distilled water in eliciting the wheal-and-flare reaction (4). Our case confirms their observation and supports the hypothesis that the salt concentration and/or osmolarity of water may influence the pathogenic process of aquagenic urticaria, possibly by enhancing the solubilization and penetration of a hypothetical epidermal antigen, in the same way as has been postulated for enhancing organic solvents.

Acknowledgement

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Dermatitis around tracheostomies due to cleansing tissues

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Key words: irritant contact dermatitis; tracheostomized patients; tracheostomy; patch testing; solvents

Case Reports

59-year-old and 56-year-old female, and a 60-year-old male, tracheostomized patients were referred because of dermatitis around their tracheostomies. Complaints of severe itching had persisted for several months. On examination, there was diffuse erythema with scaling and crusting in all 3 patients.

They were patch tested with the European standard series, their own topical materials, and additional series if appropriate, using van der Bend patch test chambers affixed with Fixomull Stretch tape. All 3 patients reacted to the cleansing tissues that they used to remove glue from the skin around the tracheostomy: + at D2 and D3 in the 1st patient; ++ at D2 and +++ at D3 in the 2nd; and +++ at D2 and D3 in the 3rd. In the last patient, a + reaction to methyldibromo glutaronitrile (0.3% pet.) was also seen at D3. The dermatitis cleared when the patients stopped using these particular cleansing tissues.

We then performed patch testing with the tissues, as is, and with a 10% concentration of an extract in alcohol in 5 healthy subjects. 2 of these developed a contact urticarial reaction at the tissue test site, with severe itching and erythema. This is likely to have been due to isopropyl alcohol impregnated in the tissue (1). In the other 3, the tissue also had to be removed because of burning sensations and severe erythema after several hours. The 10% concentration of the extract caused an itchy reaction with erythema after several hours in the 2 healthy subjects who experienced contact urticaria with the tissue itself. In the other 3 subjects, there was no reaction to the 10% concentration after 3 days

In addition, we tested another 20 healthy subjects with 5% and 10% of the extract. In 10 (50%) of these, there was a + reaction to the 10% concentration after 3 days.

Discussion

We found 1 previous case report of dermatitis in a tracheostomized patient, which was due to a rubber disc (2).

After testing healthy control subjects, we concluded that the cleansing tissue that these 3 patients used was irritant and the likely cause of the dermatitis around their tracheostomies. The ingredients of these tissues are isopropyl alcohol, benzyl alcohol, fragrances, isoparaffin, dipropylene glycol methyl ether and Aloe Vera Extract. The tracheostomized patients could not be retested with the 5% or 10% dilutions of the extract, or with the separate ingredients, because of their poor general condition.

Patch testing cleansing tissues as is can cause severe irritant reactions. However, these materials, containing several solvents, are used on fragile and susceptible skin around tracheostomies. We recommend testing the cleansing material at an appropriate dilution of an extract, depending on the ingredients, in our case, with a 5% concentration of the extract in alcohol.

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Allergic contact dermatitis from estradiol and norethisterone acetate in a transdermal hormonal patch

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Key words: estradiol; norethisterone acetate; transdermal therapeutic systems; medicaments; allergic contact dermatitis.

Allergic contact dermatitis from transdermal therapeutic systems (TTS) is mostly due to components such as ethanol (1, 2), hydroxypropylcellulose (3) or colophonium (4). With estradiol TTS, although about 20% of patients report side-effects (5), Type-IV allergic reactions to topical estradiol, proven by patch tests, are rare (6–9).

Case Report

A 50-year-old postmenopausal woman began using Estragest TTS® (Ciba-Geigy) in September 1999. The patches contained 5 mg estradiol and 15 mg norethisterone and were applied 2× weekly. She developed itchy discoid indurated erythema under the 3rd patch applied, followed by a bullous reaction. Because of this, treatment was switched to the estradiol-containing gel Gynokadin® (Kade). However, acute eczema also developed on sites of application of this gel, which then regressed with oestrogen suspension.

Table 1. Patch test results

	Patch tests	D1	D2	D3
Separate components of Estragest TTS®				
17-β-estradiol	1% eth.	+++	+++	+++
	0.1% eth.	+++	+++	+++
norethisterone acetate	1% eth.	+++	+++	+++
	0.1% eth.	+++	+++	+++
hydroxypropylcellulose	pet.	–	–	–
paraffin	as is	–	–	–
polyisobutylene		NT	NT	NT
Separate components of Gynokadin gel®				
estradiol	0.5% pet.	–	–	–
Carbopol	1% pet.	–	–	–
triethanolamine	1% pet.	–	–	–
ethanol 96%	as is	–	–	–
petrolatum	as is	–	–	–

eth: ethanol 96%.
Carbopol is a polyacrylic acid, a separate component of the gel.

Patch tests were performed with the DKG standard series, as well as the separate components of the TTS system and Gynokadin® gel. All test substances were applied for 24 h using Finn Chambers® on Scanpor® tape (Epitest Ltd. Oy, Tuusula, Finland) on the patient's upper back and fixed with Mefix® (Mölnlycke, Hilden, Germany). Readings were performed after 1, 2 and 3 days (D). Patch test reactions were read according to the criteria of the DKG.

Strongly positive results were recorded with estradiol and norethisterone acetate 1% eth. The respective vehicles failed to elicit positive reactions (Table 1). However, polyisobutylene, which is soluble only in chloroform according to information from the manufacturer, was not tested.

The same concentrations of estradiol and norethisterone were negative in 20 controls.

Comment

Estragest TTS® shares the basic structure of all TTS: an outer impermeable membrane, a reservoir of the solubilized drug (17-β-estradiol and norethisterone acetate in ethanol and the gel-forming hydroxypropylcellulose), a rate-limiting membrane and an adhesive (polyisobutylene). Considering the wide use of estrogen TTS, allergic

contact dermatitis from 17-β-estradiol is very rare, though several cases of immune or autoimmune reactions to estrogens have been reported (10).

Oral administration of oestrogens in patients with allergic contact dermatitis due to estradiol may result in systemic contact dermatitis (8, 9), or may be tolerated (7). According to Gonçalo et al. (9), the ideal vehicle for testing estradiol is probably ethanol. Petrolatum was effective for estradiol patch testing only in the report of El Sayed et al. (8). Estradiol 0.5% pet. failed to elicit a positive reaction in our strongly sensitized patient. High concentrations of estradiol (10% pet.) were also needed to elicit a week reaction in the 2 cases of Gonçalo et al. (9).

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Erythema-multiforme-like eruption from amoxycillin and allopurinol

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Key words: erythema-multiforme-like eruption; amoxycillin; allopurinol hypersensitivity syndrome; systemic contact dermatitis; adverse cutaneous drug reactions; antibiotics; medicaments.

Case Report

A 70-year-old woman, with no previous history of drug allergy, who had asymptomatic hyperuricaemia and hypertension under treatment with enalapril and hydrochlorothiazide, was hospitalized with generalized erythematous maculopapular plaques, as well as multiple vesicles on the arms, facial oedema, oral ulcers, fever, vomiting and diarrhoea. She had been treated with allopurinol for the previous 10 days and, in the last 24 h, had received amoxycillin for an upper respiratory tract infection. 9000 leukocytes/mm^3 (9.3% eoxinophils), abonormal liver function (GOT 46, GPT 62 U/l), and 40 ml/min creatinine clearance was documented. Red cells, platelets urine analysis coagulation tests, CXR, ECG, and serology for infections were normal or negative. Skin biopsy of an arm lesion showed significant dermal oedema with a large subepidermal bulla; superficial dermal vessels were surrounded by an inflammatory infiltrate in which lymphocytes were predominant. The biopsy was compatible with the diagnosis of erythema multiforme (EM) (1).

Amoxycillin and allopurinol were withdrawn. Trimethoprim-sulfamethoxazole (TMP-SMX) treatment was initiated but, since clinical deterioration was observed, these drugs too were stopped. Finally, she received cyclosporin with resolution.

Prick and intradermal tests with benzyl penicilloyl polylysine (6×10^{-5} M: Allergopharma, Germany), minor determinant mixture (1×10^{-2} M: Allergopharma, Germany) and penicillin G (PNG) (10.000 IU/ml: Antibióticos Pharma, Spain) were negative. Immediate skin test with amoxycillin (20 mg/ml: Beecham, Spain) was negative but 24 h later, she developed local erythema and induration. Biopsy of the intradermal test showed dermal oedema, and an inflammatory infiltrate with lymphocytes, histiocytes and eosinophils surrounded by dilated superficial and deep blood vessels. Focal areas of spongiosis without vesicles were found in the epidermis. Direct immunofluorescence did not demonstrate any deposits of IgG, IgA, IgM, C3 or fibrinogen. The biopsy was compatible with a Type IV hypersensitivity reaction.

Patch tests with amoxycillin (5% aq.: Beecham, Spain) and ampicillin (5% aq.: Normon S.A, Spain) were positive, with erythema, oedema, induration and vesicles, and negative to allopurinol (10% DMSO: Glaxo Wellcome, Spain), PNG (10.000 U/g pet.) and TMP-SMX (10% DMSO: Guinama, Spain).

Simple, blind placebo-controlled oral challenge with allopurinol (12.5 mg) produced, 4 h later, severe generalized erythema and pruritus, fever (38°C) and nausea that

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disappeared over several days with antihistamine and high doses of systemic corticosteroids. Serum analyses at this point were normal. Oral challenge with TMP-SMX was negative.

Discussion

Numerous drugs, including sulfonamides, penicillins and allopurinol, have been implicated in the aetiology of EM. In addition to drugs, many others factors may cause EM, such as viral and bacterial infections, histoplasmosis, systemic lupus erythematosus and malignant tumours (2). Systemic contact dermatitis and allopurinol hypersensitivity syndrome (AHS) may both provoke a similar clinical and histological reaction (3–5). AHS includes EM or TEN as major criteria (6–8) and has been found to occur most frequently in patients with renal failure or taking diuretics (especially thiazides), as in our patient.

Our patient was diagnosed as having concomitantly developed AHS (confirmed by oral challenge) as well as a Type IV reaction to amoxycillin (confirmed by intradermal and patch tests) (9, 10). Other similar but uncommon clinical cases have been described where 2 different drugs have been implicated in the same skin reactions, including phenytoin and amitriptyline (11), but, to our knowledge, this is the 1st report of AHS and Type IV amoxycillin hypersensitivity occurring in the same patient at the same time.

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Acute generalized exanthematous pustulosis induced by amoxycillin with clavulanate

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Key words: acute generalized exanthematous pustulosis; adverse cutaneous drug reaction; amoxycillin/clavulanate; positive patch test; antibiotics; medicaments.

Case Report

A 28-year-old man presented with a generalized pustular eruption 2 days after starting oral amoxycillin/clavulanate (Augmentin®) and ketorolac trometamol (Taradyl®) following appendectomy. He had no personal or family history of psoriasis or previous drug reaction. On examination, he had a temperature of 39 °C and severe malaise, and was admitted to the intensive care unit. Dermatological examination showed a generalized erythematous eruption scattered with numerous pinhead-sized pustules, associated with buccal erosions and oedema of the face and extremities. The antibiotic was substituted with a combination of clindamycin and gentamycin and systemic corticotherapy was prescribed.

Bacteriological and mycological cultures of pustules were negative. There was hyperleucocytosis (WBC $46\times10^3/mm^3$) with lymphocytosis (40%), hypocalcemia (8.2 mg/l), hypoproteinemia (5.6 g/l), and elevated CRP (13.8 mg/dl) and fibrinogen (444 mg/dl). Blood cultures, throat swab, and investigations for viral infections were negative. Skin biopsy showed subcorneal or intraepidermal pustules, with papillary oedema, perivascular inflammatory cell infiltrate containing eosinophils and capillary thrombosis. Some necrosis of keratinocytes was also noted. In view of this pattern invoking acute generalized exanthematous pustulosis (AGEP), the antibiotics and corticosteroids were stopped after 3 days. The fever and pustulosis resolved after 1 week, followed by a desquamative phase. After 10 days, blood abnormalities returned to normal.

Due to the severe malaise and leucocytosis with

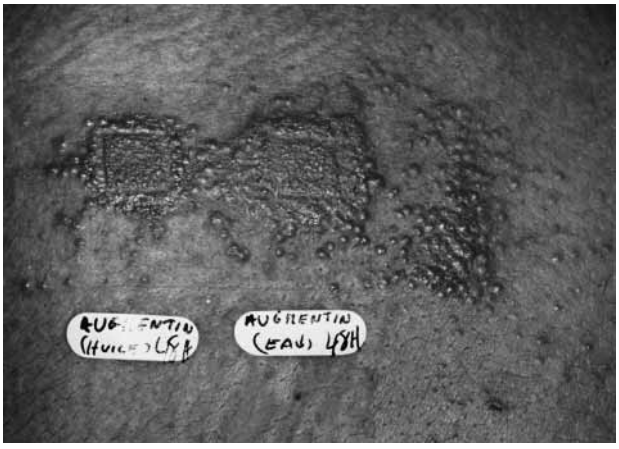

Fig. 1. Positive patch tests with Augmentin® at D2.

lymphocytosis, further investigations were performed to exclude a lymphoproliferative process. CXR and CT scan, medullar scintigraphy, medullogram and monoclonality research were all negative. Lymphoblastic transformation test performed 1 month later with Augmentin® and Taradyl® was positive only for Augmentin®. Patch testing with a solution of Taradyl® and a crushed tablet of Augmentin® in water or olive oil was positive after 2 days only to Augmentin®, and showed vesicles and pustules on an erythematous base (Fig. 1).

Comment

The main cause of AGEP is drugs, particularly β-lactam and macrolide antibiotics (1). 2 facts made this particular case interesting: 1st, the marked leucocytosis with unusual lymphocytosis suggesting a lymphoproliferative process; 2nd, the positive patch test result. In a series of 14 patients with AGEP, Wolkenstein et al. (2) have shown relevant positive patch tests in $^1/_2$ the cases. Reinduction of adverse cutaneous reaction has been described on patch testing in exfoliative dermatitis or generalised exanthema (2). Though patch-test reactions spreading beyond the test area have been reported in AGEP, no full-scale relapses have been described. Positive patch-test results in AGEP have now been reported with amoxycillin, buphenine, carbamazepine, chloramphenicol, dexamethasone, diltiazem, dihydroquinidine, isoniazid, metronidazole, nystatin, nifuroxazide, paracetamol, phenobarbital, pristinamycin, propicillin, spiramycin, streptomycin, terbinafine, ticlopidine and virginiamycin (2–11).

Patch testing appears, therefore, to be a relatively safe, easy and valuable alternative to a potentially dangerous provocation test to assess the culpability of a drug in this condition.

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Allergic contact dermatitis due to guava tea

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Key words: allergic contact dermatitis; atopic eczema; medicaments; herbal remedies; guava; *Psidium guajava*; tannic acid; tannins; 45 kD protein.

Guava (*Psidium guajava*) grows widely in Central and South America. Its fruit is used to make guava jelly, a type of jam, and its bark and roots are astringent from the tannin that they contain. Guava tea was recently introduced into Japan for the treatment of skin diseases, especially atopic dermatitis, some patients bathing with the powder and leaves of guava (1, 2).

Patient, Methods and Results

Case Report

A 17-year-old high school student had had atopic dermatitis since the age of 5 years, treated previously with topical corticosteroids and recently with guava tea extract. He would put a 30 g guava tea bag into his bath tub in about 50 litres of water. When his eczema spread, he stopped this and started using *Muto Happu*, a sulfur-containing bath liquid. He also applied shark oil and a moisturizer to his skin. His eczema improved when he restricted further treatment to moisturizers.

He was patch tested with the Japanese standard series, guava tea extract and other contactants. Positive reactions were observed at D2 and D3 to guava tea extract 0.25% aq, *Muto Happu*, soap (1% aq.) shampoo (1% aq.), hair treatment (1% aq.), moisturizer (as is) and lanolin (as is). 9 healthy subjects patch tested as controls with 0.25% guava tea extract were negative.

Extraction of allergen from guava leaves

30 g dry leaves of *Psidium guajava* were extracted with 500 ml phosphate-buffered saline (PBS) for 2 days at 4°C. The extract was concentrated 10× under reduced pressure. The concentrated extract was applied to a Sephadex G 100 column and eluted with PBS into 50 fractions.

Patch testing with 10 fractions

The patient was patch tested with the major 10 fractions and with tannic acid 0.25% aq., contained in guava leaves at 10%. Positive reactions were observed at D2 and D3 to 5 out of the 10 fractions and to 0.25% tannic acid.

SDS-PAGE

SDS-PAGE was performed on a 12.0% Tris-tricine SDS gel. The concentrated extract and fractions positive on patch-testing were applied to the gel and electrophoresed. The gel was silver-stained with a kit (Daiichi Chem, Japan). A 45 kD protein band was detected in the fraction of tube no. 20–27 and a faint 45 kD band in that of tube no. 28–34 (Fig. 1).

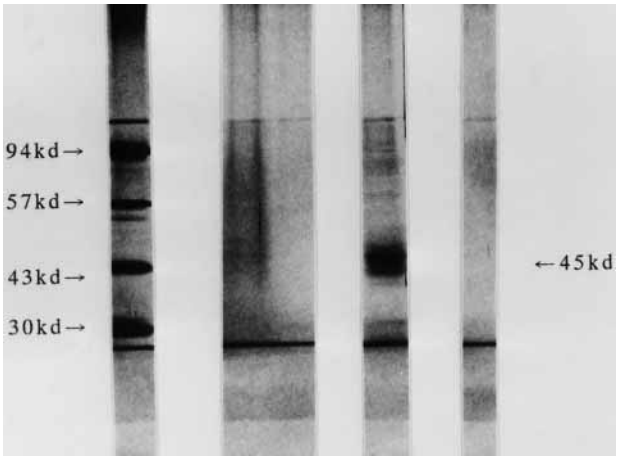

Fig. 1. SDS-PAGE of fractions of guava tea extract. Concentrated extract (A), Sephadex fraction of 20–27 (B) and that of 28–34: a 45-kD band was detected strongly on B and very faintly on C.

Discussion

There is no previous report of contact dermatitis from *Psidium guajava*. Its major allergens have now been identified as a 45 kD protein and tannin. Potter et al. (3) characterized a 62-kD allergen in *Verbena hybrida* leaves, against which their patient had specific IgE. There are 4 previous reports of contact dermatitis due to tannin (4–7). Tannin can penetrate easily through the normal skin, unlike a 45-kD protein, which may, however, penetrate through the compromised barrier of atopic dermatitis and exacerbate the condition.

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Optician's occupational allergic contact dermatitis, paresthesia and paronychia caused by anaerobic acrylic sealants

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Key words: occupational; allergic contact dermatitis; optician; paresthesia; paronychia; anaerobic sealant; adhesive; ethylene glycol dimethacrylate; 2-hydroxyethyl methacrylate; (meth)acrylates; material safety data sheets.

Opticians have very rarely been reported to develop occupational allergic contact dermatitis.

Case Report

A 46-year-old atopic man had been working for 20 years as an optician, when he started to develop redness and fissuring of the pulps of the thumb and index finger of the right hand. Within 1 year, this had spread to the flexor aspects of the thumb and index finger of both hands. It healed during a vacation but relapsed when working with anaerobic sealants. He also had paresthesia of the involved pulps and a work-related paronychia.

The optician spent 60–70% of his time grinding and shaping lenses made of polymethyl(meth)acrylate. Grinding solutions kept the digits wet throughout. Additionally, 2 anaerobic acrylics were used for 1 h per day to seal the screws of hinges and to stick lenses to metal frames (Screw Lock Hilco and Screw Securing No. 317800). Dust from detaching old screws also elicited dermatitis, as did handling the contaminated surfaces of bottles containing anaerobic sealants. Metal frames caused him no problems.

The rest of his work (30–40%) involved customer service: selling spectacles, performing examinations of vision and contact lens fittings.

2 patch test sessions were performed according to the recommendations of the ICDRG. In a modified European standard series, methylchloroisothiazolinone/methylisothiazolinone elicited a ++ reaction. Several (meth)acrylates reacted positively in an extensive (meth)acrylate series (Table 1). A dilution series of Screw Securing No. 317800 gave the following reactions: 2%, ++; 1%, ++; 0.5% ?+. Screw Lock was negative. Both anaerobic sealants were then analyzed for (acetone-soluble) (meth)acrylates by gas chromatography/mass spectrometry (3), showing them to contain mainly ethylene glycol methacrylates (Fig. 1) with some others (Table 2).

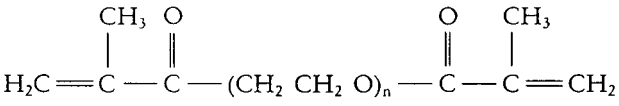

Fig. 1. The structural formula of polyethylene glycol dimethacrylate (PEGDMA). The anaerobic sealants used by the patient were composed of PEGDMA in which *n* was 2–6.

Discussion

Anaerobic sealants are widely used in the engineering and electronic industries (1–10), where they typically cause allergic contact dermatitis of the pulps of the digits (9). They are based on polyethylene glycol dimethacrylates (PEGDMA, Fig. 1), where *n* in this formula has been stated to be usually 4 (8), though one manufacturer informed us that PEGDMA contained about 40% triethyleneglycol dimethacrylate (TREGDMA), i.e., $n=3$ (10). In our previous study, an anaerobic glue which, according to the material safety data sheet (MSDS), contained about 70% TREGDMA, actually comprised 13% TREGDMA and 58% larger oligoethyleneglycol dimethacrylates (3).

Patients sensitized to anaerobic sealants have previously shown patch test reactions to 2-hydroxyethyl methacrylate (2-HEMA) and 2-hydroxypropyl/methacrylate (2-HPMA) (9, 10), due to cross-reactivity, contamination or bioconversion. 2-HEMA seems a good screen for anaerobic sealants as well as (meth)acrylates used elsewhere in dentistry (9, 11, 12). Occupational allergic contact dermatitis has also been caused by 2-hydroxyethyl acrylate in contact lenses (13).

Paresthesia is unique to the contact dermatitis caused by acrylic monomers. It manifests as a burning sensation, tingling, and slight numbness (14) and may per-

Table 1. Patient's patch test reactions with an extended (meth)acrylate series

	(Meth)acrylate series	Source	Abbreviation	Patch-test concentration (%) (w/w) (all allergens in pet.)	Patch-test reactions
1	glycidyl methacrylate	O	GMA	0.1	−
2	butyl acrylate	C	BA	0.1	−
3	2-ethylhexyl acrylate	C	2-EHA	0.1	−
4	ethyl acrylate	C	EA	0.1	−
5	ethyl cyanoacrylate	O	ECA	10	−
6	ethyl methacrylate	C	EMA	2	−
7	n-butyl methacrylate	C	BMA	2	−
8	2-hydroxyethyl methacrylate	T	2-HEMA	1	++
9	2-hydroxypropyl methacrylate	C	2-HPMA	2	++
10	2,2-bis[4-(2-methacryloxyethoxy)phenyl] propane	C	BIS-EMA	1	−
11	1,4-butanediol diacrylate	C	BUDA	0.1	−
12	1,6-hexanediol diacrylate	C	HDDA	0.1	?+
13	diethyleneglycol diacrylate	C	DEGDA	0.1	−
14	tripropyleneglycol diacrylate	C	TPGDA	0.1	−
15	trimethylolpropane triacrylate	C	TMPTA	0.1	−
16	pentaerythritol triacrylate	C	PETA	0.1	−
17	oligotriacrylate 480	C	OTA 480	0.1	−
18	epoxy diacrylate= (2,2-bis[4-(2-hydroxy-3-acryloxypropoxy)phenyl] propane	C	BIS-GA	0.5	−
19	urethane diacrylate (aliphatic)	C	al-UDA	0.1	−
20	urethane diacrylate (aromatic)	C	ar-UDA	0.05	−
21	ethoxyacrylate	O	EtA	0.1	−
22	1,4-butanediol dimethacrylate	C	BUDMA	2	−
23	ethyleneglycol dimethacrylate	T	EGDMA	2	++
24	triethyleneglycol dimethacrylate	T	TREGDMA	2	+
25	urethane dimethacrylate	C	UDMA	2	−
26	2,2-bis[4-(methacryloxy)phenyl] propane	C	BIS-MA	2	−
27	2,2-bis[4-(2-hydroxy-3-methacryloxypropoxy) phenyl]propane	T	BIS-GMA	2	−
28	methyl methacrylate	T	MMA	2	−
29	N,N-methylenebisacrylamide	C	MBAA	1	−
30	tetrahydrofurfuryl methacrylate	C	THFMA	2	−
31	2-phenoxyethyl acrylate	O	2-PEA	0.1	−
32	isobornyl acrylate	O	IBA	0.1	−
33	dipropyleneglycol diacrylate	O	DPGDA	0.1	−
34	ethoxylated bisphenol A dimethacrylate	O	EBADMA	2	−
35	N,N-dimethylaminoethylmethacrylate	C	DMAEMA	0.2	−
	Screw Securing No. 317800	O		2%, 1%	++
	Screw Securing No. 317800	O		0.5%	?+
	Screw Lock	O		2%,1%,0.5%	−

Source of methacrylates: C=Chemotechnique Diagnostics AB, Malmö, Sweden; T=Trolab; O=manufactured by ourselves. NT= not tested.

Table 2. Quantitative analysis of acetone-soluble (meth)acrylates

Methacrylate*	Abbreviation	Screw Lock	Screw Securing No. 317800	Patch test reaction to methacrylate (Table 1)
ethyleneglycol dimethacrylate	EGDMA	ND; <0.05%**	ND; <0.05%**	++
diethyleneglycol dimethacrylate	DEGDMA	3.0	2.7	NT
triethyleneglycol dimethacrylate	TREGDMA	15.0	9.8	+
tetraethyleneglycol dimethacrylate	TETEGDMA	31.0	13	NT
pentaethyleneglycol dimethacrylate	PEGDMA	18.0	12	NT
hexaethyleneglycol dimethacrylate	HEGDMA	8.2	8.3	NT
dodecyl methacrylate (lauryl methacrylate)		ND	4.1	−
tetradecyl methacrylate		ND	2.0	NT
hexadecyl methacrylate		ND	1.2	NT
octadecyl methacrylate		ND	1.8	NT

ND: not detected.
NT: not tested.
** 0.05% detection limit.

sist for up to 6 months (15) after the dermatitis has subsided. Paresthesia may also develop from acrylics in the absence of allergic contact dermatitis (16). Paronychia has previously been reported in association with dental (17) and nail acrylics (18), which may also cause allergic onycholysis (9).

The patient did not react to one sealant even though it contained dimethacrylates to which he was allergic (19): occlusion during patch testing may have been inadequate. The MSDS of Screw Securing No. 317800 did not declare any harmful agents, as we have found before (3, 20).

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Allergic contact dermatitis from zinc ricinoleate in a deodorant and glyceryl ricinoleate in a lipstick

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Key words: allergic contact dermatitis; zinc ricinoleate; glyceryl ricinoleate; sulfated castor oil; cosmetics; deodorants; lipsticks; cross-sensitivity.

Ricinoleates, e.g., zinc ricinoleate, magnesium ricinoleate or glyceryl ricinoleate, are metal soaps of ricinoleic acid. They are used in adhesives, corrosion inhibitors, cosmetics, greases, varnishes, print pigments and for deodorizing of various products (1). Ricinoleic acid is a mixture of fatty acids obtained by the hydrolysis of castor oil (syn. Ricini oleum, Rizinusöl, Castoröl) (2). The proportion in castor oil is 80 to 85%. It is also a component in several other seed oils (1).

Castor oil is a slightly yellow, viscous, flammable, indigestable oil extracted from the seeds of *Ricinus* spp. (Euphorbiaceae). It is used externally for its emollient effect (2). In comparison with other vegetable oils used for cosmetic purposes, castor oil has the best ability to penetrate to the intercellular spaces of the stratum corneum (8). Besides that, it has, like ricinoleic acid, a well-known purgative effect (7). Among coffee workers with occupational allergic respiratory symptoms, Romano et al. (4) found the castor bean to be a major cause of occupational sensitization.

Table 1. Summary of positive patch test results

Allergen		D2	D3
Vichy deodorant (as is)		−	+
Vichy deodorant mixture A: zinc ricinoleate 76%, triethanolamine (TEA) 20%, lactic acid 1%, 2.5% propylene glycol and water		−	+++
BeBe lipstick (as is)		−	+
BeBe lipstick, mixture 1		+	+++
Ingredients of BeBe lipstick, mixture 1			
glyceryl ricinoleate	30% pet.	−	+
cetyl alcohol	5.0% pet.	−	−
cetyl alcohol	1.0% pet.	−	−
octyldodecanol	30% pet.	−	−
parrafinum liquidum	as is	−	−
parrafinum liquidum	5.0% pet.	−	−
Candellila cera	40% o.o.	−	−
carnauba	50% o.o.	−	−
Cera microcrystallina	as is	−	−
Cera alba	as is	−	−

Table 2. Results of re-patch testing with further substances

Allergen			D2	D3
zinc ricinoleate		76% pet.	−	?+
zinc ricinoleate		30% pet.	−	−
zinc ricinoleate		15% pet	−	−
zinc ricinoleate		1.0% pet.	−	−
oleyl alcohol		10% pet	−	−
PEG-35 castor oil	(Eumulgin R035)	20% pet	−	−
hydrogenated castor oil	(Cutina HR)	5.0% pet.	−	−
glyceryl ricinoleate	(Cithrol GMR)	20% pet.	−	+
oleic acid		5.0% pet.	−	−
sulfated castor oil	(Sykanol DKM45)	20% pet.	+	++
glyceryl-PEG-ricinoleate	(Cremophor EL)	20% pet.	−	−
castor oil	(Rizinusöl)	as is	−	−
oleyl alcohol		as is	−	−
glyceryl ricinoleate		30% pet.	−	+

After removing the oil from the seeds of *Ricinus* spp., a residual pulp remains, which contains a higly toxic protein called ricin (3). The fatal dose by intravenous injection in experimental animals has been reported to be as low as 300 ng per kg body-weight (2).

Sulfated castor oil is a non-irritating detergent and wetting agent, which may be used for skin cleansing instead of soap. It was formerly used as an emulsifying agent. Turkey red oil is a commercial variety of sulfated castor oil used in the dyeing industry (2).

Case Report

A 51-year-old woman developed a pruritic erythema in both axillae after the use of a new deodorant (Vichy dermo tolerance herb würzig®; Vichy France, 92400 Courbevoie). The use of another deodorant led to complete remission, and the renewed use of the first deo caused a recurrence of the contact dermatitis, with spread to the upper arms. Furthermore, 1 week later, she developed an acute contact dermatitis of the lips after using a previously-tolerated perfumed lipstick (BeBe Lippenpflegestift zartrosè®; Johnson & Johnson, Bad Honnef).

Patch testing with the European standard series, perfume constituents and the vehicle series of Trolab/Hermal was negative; only her own deodorant and her lipstick elicited + reactions at D3 and D4. Further patch testing with the ingredients of the deodorant and the lipstick showed the positive results in Table 1. The manufacturer of the deo supplied 5 coded mixtures, of which only 1 was strongly positive. This mixture contained 76% zinc ricinoleate, 20% triethanolamine (TEA), 1% lactic acid and 2.5% propylene glycol. In the vehicle series, propylene glycol 20% aq. and 2.5% TEA had already been negative. 17 control patients were patch-test negative with mixture A of the deodorant.

The manufacturer of the lipstick provided 12 materials for patch testing, of which only 1 mixture was strongly positive. The breakdown testing of this mixture of 10 substances revealed only a + reaction to 20% and 30% glyceryl ricinoleate.

Dooms-Goossens et al. (3) described positive patch-test reactions to hydrogenated castor oil, sulfated castor oil, glyceryl ricinoleate, and PEG 400 monoricinoleate, which are possible cross-reactions. To confirm the patch test reactions and to detect possible cross-reactions with other substances, the patient was tested again after 1 month (17 months after the initial testing). Details are found in the Table 2. She reacted weakly to zinc ricinoleate 76% pet. (negative to lower concentrations). There was a ++ reaction to sulfated castor oil and a + reaction to 20% and 30% glyceryl ricinoleate.

Discussion

This was a clear case of sensitization to zinc ricinoleate (deodorant) and glyceryl ricinoleate (lipstick). The patient was probably sensitized by using the deodorant, and afterwards she could not tolerate the previously-used lip stick.

We observed a very strong reaction to mixture A of the deodorant containing zinc ricinoleate. This was probably due to TEA, lactic acid and propylene glycol enhancing penetration. TEA and propylene glycol were both negative on previous testing. Lactic acid was not tested, but is not known as an allergen. Dooms-Goossns et al. (3) reported a strong reaction to a similar mixture in a deodorant (Grillocin HY-77, which is a mixture of 88% zinc ricinoleate, TEA, propylene glycol, sodium lactate, zinc resinate, isostearic acid, abietic acid and toc-HY-77).

In the lipstick of our patient, the sensitizer was glyceryl ricinoleate. It did not contain castor oil, TEA or propylene glycol.

The final series of patch testing showed that the patient also reacted to sulfated castor oil. Castor oil as is and 2 modifications of it were patch test-negative, as were oleic acid and oleyl acohol. 1 patient of Dooms-Goossens et al. (3) was also tested with a similiar series and showed reactions not only to glyceryl ricinoleate, but also to hydrogenated castor oil, sulfated castor oil,

PEG 400 monoricinoleate and sodium sulphoricinoleate. Glycerin-PEG ricinoleate was negative, while castor oil produced a doubtful reaction (ROAT negative). Tan et al. (6) described an allergic contact dermatitis from a lipstick. The findings on patch testing were a ++ reaction to castor oil, a dose-dependent ++ reaction to ricinoleic acid, a + to ++ reaction to pigments in castor oil and a +++ reaction to oleyl alcohol. The authors considered the positive reactions to oleyl alcohol and ricinoleic acid to be cross-reactions.

The above shows that cross-reactions between the various types of ricinoleates and sulfated castor oil might occur. Sulfated castor oil is widely used in cosmetics. Our patient had never reacted before to a cosmetic. As sulfated castor oil was neither an ingredient in the deodorant nor in the lipstick, this may represent a true cross-reaction. Sulfated castor oil should be a candidate for the vehicle patch test series. In the German computer information network on ingredients of cosmetics and common dermatologic preparations, we have found sulfated castor oil as a component in 9 products, of which 8 are used for skin protection, and 1 as a face cream. Castor oil itself was present in a total of 26 products listed, hydrogenated castor oil in 29 products and PEG 40 hydrogenated castor oil in 33 products, mainly for face, body and skin care, sun protection and other topical products (5).

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182 patients with occupational allergic epoxy contact dermatitis over 22 years

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Key words: cycloaliphatic epoxy resin; dipropylenetriamine; epoxy resin; methylhexahydrophthalic anhydride; non-DGEBA epoxy resin; polyamine hardeners; reactive diluents; tetraglycidyl-4,4′-methylene dianiline; triglycidyl-4-aminophenol; allergic contact dermatitis; occupational.

Since the early 1970s, epoxy resin compounds (ERCs) have become one of the most common causes of occupational allergic contact dermatitis in Finland (1, 2).

Patients and Methods

Data on patient referral, patch-testing methods, including with ERCs, and criteria for the diagnosis of occupational skin disease have been published earlier (2–4). In the present report, we have included all patients with occupational allergic contact dermatitis from ERCs seen at our clinic over 22 years.

Results

A total of 182 patients were diagnosed to have occupational allergic contact dermatitis from ERCs during the 22 years. The ERCs were divided into 5 categories: DGEBA epoxy resin (ER), non-DGEBA ER, reactive diluents, polyamine hardeners, and other ERCs (Table 1). Based on our previous findings, patients who were allergic to reactive diluents concomitantly reacted on patch testing to non-DGEBA ERs, and vice versa (2). Thus, those patients who reacted to both reactive diluents and non-DGEBA ERs without known exposure to either non-DGEBA or reactive diluents, respectively, were included in only 1 exposure category (Table 1). 146 of the 182 patients (80%) were sensitized to DGEBA ER. Contact allergy to polyamine hardeners occurred in 42 patients (23%).

Of the 182 patients, 130 (71%) had an isolated epoxy allergy to 1 of the ERC categories (Table 1), and 52 (29%) had simultaneous contact allergy to 2 or more categories. 95 patients (52%) had an isolated contact allergy to DGEBA ER, 16 (9%) to non-DGEBA ERs (5–8), 6 to polyamine hardeners (9–10), 6 to reactive diluents (11–12) and 7 to other ERCs (Table 2).

43 of the 182 patients had an allergic contact dermatitis from epoxy hardeners, 42 from polyamines and 1 from a phthalic anhydride (Table 3). Diaminodiphenylmethane, followed by diethylenetriamine, were the most common amine sensitizers (Table 3). Cycloaliphatic epoxy resins (6) and aniline epoxy resins were the most common causes of allergic contact dermatitis from

Table 1. Causes in 182 patients with epoxy resin compound (ERC) allergy

ERC category	No. cases
DGEBA ER	146
polyamine hardener	42
reactive diluent	29
non-DGEBA ER	17
other ERCs	7
triglycidyl isocyanurate	6
phthalic anhydride hardener	1

Table 2. Isolated contact allergy to ERCs in 130 out of 182 patients with ERC allergy

ERC	No. cases	Refs.
DGEBA ER	95	(5–8)
non-DGEBA ER	16	(5–8)
polyamine hardener	6	(9, 10)
reactive diluent	6	(11, 12)
other ERCs	7	
triglycidyl isocyanurate	6	(13)
phthalic anhydride hardener	1	(14)

Table 3. Contact allergy to ER hardeners in 43 out of 182 patients with ERC allergy

Causative hardener	No. cases
diaminodiphenylmethane (MDA/DDM)	14
diethylenetriamine (DETA)	10
isophoronediamine (IPDA)	8
triethylenetetramine (TETA)	5
tris-(dimethylaminomethyl)phenol (tris-DMP)	5
trimethyl hexamethylenediamine (TMD)	3
xylylenediamine (XDA)	3
ethylenediamine (EDA)	2
dipropylenetriamine (DPTA)	1
tetraethylenepentamine (TEPA)	1
methylhexahydrophthalic anhydride (MHHPA)	1

Table 4. Contact allergy to non-DGEBA ERs in 17 out of 182 patients with epoxy resin compound allergy

Non-DGEBA ER	No. cases
cycloaliphatic ERs	12
aniline ERs	6
N,N′-tetraglycidyl-4,4′-methylenedianiline (TGMDA)	1
triglycidyl-4-aminophenol (TGPAP)	1
brominated ER	1
phenol novolac ER	1
dimethylhydantoin ER	1
unknown non-DGEBA ER	1

non-DGEBA ERs (Table 4). Only solitary cases were caused by other non-DGEBA ERs, e.g., triglycidyl-4-aminophenol (TGPAP, Table 4, refs. (5, 8)). Most patients sensitized to reactive diluents were allergic to phenyl glycidyl ether (PGE) and cresyl glycidyl ether (CGE) (Table 5).

Table 5. Contact allergy to reactive diluents in 29 out of 182 patients with ERC allergy

Reactive diluent	No. cases
phenyl glycidyl ether (PGE)	25
cresyl glycidyl ether (CGE)	16
butanediol diglycidyl ether (BDDGE)	12
hexanediol diglycidyl ether (HDDGE)	6
butyl glycidyl ether (BGE)	5
allyl glycidyl ether (AGE)	4
neopentyl glycol diglycidyl ether (NPGDGE)	2

Discussion

In the course of 22 years, we have encountered altogether 182 patients with occupational allergic contact dermatitis from ERCs. It was not possible to verify a patient's exposure to individual amines and reactive diluents, and thus cross-reactions between amines (Table 3, i.e., 1 patient might react to several amines even though possibly exposed to only 1) and reactive diluents (Table 5) apparently occurred. Our study confirmed that DGEBA ER is very important in screening for ERC allergy (2, 4). However, 35 out of 182 patients, i.e., nearly 20% (Table 2), had an isolated epoxy allergy to an ERC other than DGEBA ER, and would not have been detected if only DGEBA ER had been used for patch testing (5–14).

Aromatic compounds, especially PGE, have been noted to react on patch testing in most patients allergic to reactive diluents. Butanediol diglycidyl ether (BDDGE) was found to screen for contact allergy to aliphatic reactive diluents (2, 11, 12). In some cases, non-DGEBA ERs, e.g., cycloaliphatic ER (6), tetraglycidyl-4,4′-methylenedianiline (TGMDA, refs 5, 8) or triglycidyl-4-aminophenol (TGPAP; 8), may cause isolated epoxy allergy, and thus need to be included in patch testing. Phthalic anhydride hardeners very rarely cause allergic contact dermatitis (14), but may more often induce immediate allergy, such as contact urticaria (15, 16). A number of different hardeners are used to cure ERs, and many of them need to be included in patch testing because they do not necessarily cross-react (9, 10).

In conclusion, epoxy resin allergy has been known for decades, but it is still common. Extensive patch testing is needed if the allergen is not DGEBA epoxy resin. Recommendations on how to patch test with ERCs have recently been summarized (4).

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Increase in hydration and protective function of horny layer by glycerol and a W/O emulsion: are these effects maintained during long-term use?

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Key words: moisturizers; glycerol; W/O emulsion; horny layer; hydration; prevention; skin-care products; long-term use.

Moisturizers improve stratum corneum (SC) regeneration (1–5). Emulsions, especially W/O, produce SC hydration via occlusion and/or active release of water. Their protective effect is due to the protective film on the skin rather than to improved SC regeneration (1, 4). Long-term studies of a glycerol- and urea-free emulsion, a glycerol emulsion, 2 urea emulsions, and 1 emulsion containing both glycerol and urea have been published (5, 6). While these studies suggest that improved barrier function was maintained over a 3-week (wk) study period, the respective effects of the active ingredient and the vehicle are hard to differentiate. The primary aim of this study was to determine whether the hydration and regeneration afforded by glycerol, previously demonstrated by us (1–4), persist for 6 weeks, as compared to vehicle.

Materials and Methods

Subjects

10 female and 3 male volunteers with a mean age of 37.8 years (range, 23–57): exclusion criteria, skin conditions, pregnancy, and age <16 years. Subjects gave informed consent and were instructed not to use anything on the skin areas used for the study during the 2 weeks before and during the study. Instead, they performed standardized washing (3 min; 0.01 mol/l sodium lauryl sulfate-Texapon® K 12, Caesar & Lorenz, Hilden, Germany; rinsing with tap water) of the entire skin area under study after 1 and 3 weeks.

Study products and study product application

4 60-cm^2 skin areas used as test sites, 2 on the right forearm and 2 on the left. Treatments A and B administered to symmetric test sites, as were treatments C and D; 50% of the subjects received treatment A on the left forearm and treatment B on the right; the other half received treatment A on the right forearm and treatment B on the left. 0.4 ml of study product uniformly applied to each test area 2× daily. Following treatments were administered:

(A) *Untreated*
(B) *Wasserhaltige Wollwachsalkoholsalbe* [oily cream], *DAB*
(wool wax alcohols 3.0, cetearyl alcohol 0.25, white petroleum jelly 46.75, water ad 100.0)
(C) *Nichtionische hydrophile Creme* [nonionic hydrophilic cream], *DAB*, without glycerol

(polysorbate 60 5.0, cetearyl alcohol 10.0, white petroleum jelly 25.0, sorbic acid 0.1, water ad 100.0)

(D) *Nichtionische hydrophile Creme* [nonionic hydrophilic cream], *DAB,* with increased glycerol content (polysorbate 60 5.0, cetearyl alcohol 10.0, glycerol 85% 15.0, white petroleum jelly 25.0, sorbic acid 0.1, purified water ad 100.0).

Measurements

Made at baseline, 3 weeks, and 6 weeks, always between 9:00 and 11:00 a.m. At 3 weeks, made before washing. Time between last application and measurement always 12 h. Study variables transepidermal water loss (TEWL), using a TEWA-Meter TM 210 (Courage & Khazaka, Cologne, Germany), and SC water content, using a Corneometer CM 820 (Courage & Khazaka, Cologne, Germany) and the Skicon instrument (IBS, Japan). Applicable guidelines complied with (7–9).

Statistical analysis

Treatment A compared with B, and treatment C with D, calculating the differences A–B and C–D at baseline, 3 weeks, and 6 weeks. A–B and C–D compared statistically between baseline, 3 weeks, and 6 weeks. Wilcoxon & Wilcox multiple comparison of correlated samples used (10).

Results

A–B comparison found insignificant reduction in TEWL with the W/O emulsion versus untreated (Table 1). SC water content, as determined by corneometry and the Skicon, showed significant increases at 3 and 6 weeks versus baseline.

C versus D comparison showed significant reduction in TEWL with the glycerol-containing O/W emulsion at 3 and 6 weeks versus baseline. Corneometry and Skicon

Table 1. Results of the measurements at baseline, 3 weeks, and 6 weeks: medians and, in brackets, 25% and 75% percentiles. Results of the statistical comparisions of A–B and C–D at the 3 points of measurement time

	Comparison W/O-emulsion (B) versus untreated (A)		
	Baseline	3 weeks	6 weeks
TEWL			
W/O emulsion	5.3 (4.5/6.2)	4.5 (4.0/5.8)	4.7 (4.0/5.4)
untreated	5.2 (4.5/6.2)	5.3 (3.8/5.7)	5.0 (4.3/5.6)
difference	0.5 (−0.7/1.1)	0 (−0.9/0.9)	−0.5 (−0.9/0.3)
stat. results			
Corneometry			
W/O emulsion	59.5 (55.25/62.75)	72 (68/75)	68 (66/70)
untreated	62.5 (58/65)	61 (60/62)	60 (58/63)
difference	−2 (−5/0)	8 (5.5/13)	9 (6/11.5)
stat. results	$p<0.01$		
	$p<0.01$		
Skikon			
W/O emulsion	35 (31.5/40)	66 (58/75)	55 (47/75)
untreated	37 (31/52.8)	35 (30/44)	31 (28/49)
difference	−3 (−6/3)	28 (12.7/42.5)	26 (15.5/41.5)
stat. results	$p<0.01$		
	$p<0.01$		
	Comparison glycerol emulsion (D) versus vehicle (C)		
TEWL			
glycerol emulsion	5.3 (4.1/6.1)	4.3 (2.9/4.8)	3.6 (2.8/4.2)
vehicle	4.6 (3.3/5.2)	5.3 (4.4/5.9)	5.3 (3.7/5.8)
difference	0.9 (−0.4/1.5)	−0.7 (−1.3/0.1)	−1.0 (−2.3/−0.1)
stat. results	$p<0.01$		
	$p<0.01$		
Corneometry			
glycerol emulsion	64 (58.5/65.5)	78 (73/83)	77 (74/80)
vehicle	62 (53.5/64.75)	64 (62/69)	66 (61/70)
difference	1 (−0.5/2)	11 (7/17.5)	10 (5.5/18.5)
stat. results	$p<0.01$		
	$p<0.01$		
Skikon			
glycerol emulsion	39 (29.3/47.5)	143 (98/156)	87 (78/140)
vehicle	35.5 (27.3/44.5)	50 (38/54)	48 (34/65)
difference	6 (−2.5/7)	95 (56/118.5)	55 (23/80)
stat. results	$p<0.01$		
	$p<0.01$		

data showed significant increases at 3 and 6 weeks versus baseline.

Discussion

Conclusions from study results.

Compared to vehicle, glycerol had a significant hydrating effect on both deeper (corneometry) and superficial layers (Skicon) of the SC, which was maintained over the entire 6-week treatment period.

Wasserhaltige Wollwachsalkoholsalbe [oily cream], *DAB*, also produced significant improvement in SC hydration in both deeper (corneometry) and superficial layers (Skicon). The hydrating effect of this W/O emulsion has thus been demonstrated for long-term use as well.

Long-term use of glycerol reduced TEWL. As SC hydration showed no increase between 3 and 6 weeks, this effect cannot be explained by its hygroscopic properties, but would rather suggest improved barrier function (regenerative skin protection), which has been a frequent finding during its short-term use (1–4). Consistently with previous studies (5, 6), regenerative skin protection persisted long-term.

This study confirmed earlier results of short-term treatment, showing that the occlusive effect of W/O emulsions was relatively small. Hydration would appear to be due not only to occlusion, but also to the release of water from the emulsion, as also demonstrated by us earlier (11).

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Chemical load as a factor in skin sensitization risk assessment: rodent versus man

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Key words: allergic contact dermatitis; models; risk assessment; body load.

There are many and various tests used in skin sensitization risk assessment (1–9). The classic tests include the LLNA, typically in 3 mice, the MEST, the Buehler test in guinea pigs (10–20), and the Draize RIPT in man (200 subjects). It is immediately clear that there are differences in population sizes from model to model. Regardless of the species utilized, most allergenic compounds demonstrate dose-response characteristics, the local concentration of the chemical being critical. Several factors influence the skin sensitization risk from a material, including dose, bioavailability, skin site, skin condition, presence or absence of an enhancer in the formulation, duration of exposure, open or closed application.

Typically, allergen exposure is expressed as a % of the chemical and assumes that, in any situation, the same % exposure will induce or elicit an equal sensitization response. It has been demonstrated, however, that rather than the % weight/volume, a more important factor in risk assessment is the dose/unit area (10–15). The higher the dose/unit area, the greater the incidence of sensitization. Regardless of how the exposure is expressed, the varying responses observed between the species have

Table 1a. Chemical load in man and guinea pig for various patches, expressed as a % of body area

Species	% body area		
	plastic chamber*	plastic chamber**	small Finn chamber***
man (20,000 cm^2)	1.4×10^{-4}	2.5×10^{-4}	3.2×10^{-5}
guinea pig (200–700 cm^2)	0.4–1.4	0.7–2.5	0.09–0.32

* 2.8 cm^2; ** 4.9 cm^2; *** 0.64 cm^2.

Table 1b. Chemical load in man and mouse estimated from actual volume of material applied on each species in risk assessment tests

Species	Drug load per unit surface area ($\mu l/cm^2$)
man (20,000 cm^2) (300 μl) in plastic chamber 2.8–4.9 cm^2	1.5×10^{-2}
mouse (36–54 cm^2) (10 μl) in open application	$1.85–2.78\times10^{-1}$

Table 1c. Chemical load in man and mouse exposed to equal volumes of material

Species	Drug load per unit surface area ($\mu l/cm^2$)
man (20,000 cm^2) (10 μl)	5.0×10^{-4}
mouse (36–54 cm^2) (10 μl) in open application	$1.85–2.78\times10^{-1}$

previously been attributed to immunological differences, but there are clearly size (weight/body size ratio) differences between the species used in skin sensitization risk assessment.

Therefore, an issue arising from this size difference is the body load of chemicals applied in each species, which until now has not been considered. It is evident from comparison between the other species and man, as shown in Tables 1a–c, that the % body area covered by a chemical-impregnated patch or estimated chemical loads in the animal models relative to body size, are far greater than in man. It would therefore appear that this load difference may impact upon the outcome of a risk assessment test, and represents a further factor to be considered in risk assessment.

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Contact allergy to miripirium chloride in Depo-Medrol

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Key words: contact allergy; Depo-Medrol; methylprednisolone; miripirium chloride; myristyl-γ-picolinium chloride; rheumatoid arthritis; medicaments; preservatives; biocides; antimicrobials.

Depo-Medrol is a methylprednisolone acetate suspension used for intramuscular, intra- or periarticular and intradermal injections. Its ingredients are methylprednisolone 40 mg/ml, polyethylene glycol 3350 NF 29 mg/ml and myristyl-γ-picolinium chloride (=miripirium chloride) 0.2 mg/ml as a preservative.

Case Report

A 53-year old woman with rheumatoid arthritis was referred to our clinic due to eczematous reactions on several fingers, which had developed after intra-articular injections of Depo-Medrol in those fingers. She had no previous history of eczema and had had Depo-Medrol injections previously without any skin problem.

Her eczema was cleared when she came to us. We suspected contact allergy to methylprednisolone and she was patch tested with a screening corticosteroid series (Chemotechnique Diagnostics, Malmö, Sweden), and the Depo-Medrol suspension as is. On the 1st test reading, Day (D)3, there was 1 papule to Depo-Medrol, but on a 2nd reading on D7, she showed a +++ reaction to Depo-Medrol, but no reactions to the steroids of the screening series. She was then tested with the ingredients of Depo-Medrol, supplied by the manufacturer, and on the 2nd reading on D7, showed strong positive reactions to myristyl-γ-picolinium chloride 0.1% and 0.03%, while there had been only a tiny papule to the preservative 0.1% on the 1st reading D3. 10 controls, who had never been exposed to Depo-Medrol, were tested with myristyl-γ-picolinium chloride 0.1 and 0.03% and were all test negative at both D3 and D7.

Discussion

Contact allergy to methyl prednisolone due to intra-articular injections has previously been described (1) and allergy to corticosteroids was also our 1st suspicion. Testing with the ingredients of Depo-Medrol showed, however, that the preservative of the suspension was the cause of the allergy. Contact allergy to myristyl-γ-picolinium chloride from injections of Depo-Medrol has also previously been reported (2, 3). Related to the frequent use of Depo-Medrol injections, it seems, though, to be rare. According to the manufacturer and the Medical Products Agency in Sweden, Depo-Medrol is the only medical preparation in our country to contain myristyl-γ-picolinium chloride and our patient has been able to continue steroid injections using another steroid preparation. This case shows the importance of testing not only with the suspected product, but also with the ingredients. It also demonstrates the value of late test readings.

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Contact dermatitis from sodium metabisulfite in a baker

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Key words: sodium metabisulfite; baker; dodecyl gallate; allergic contact dermatitis; occupational; antibacterials; preservatives; biocides.

Case Report

A 23-year-old baker presented with an 8-month history of a rash that began on her left ventral wrist and spread to involve both dorsal hands. She described blisters and fissuring which completely cleared on holidays. She had a past history of asthma and hay fever, but no history of eczema. She was patch tested, using Finn Chambers on Scanpor, to a modified European standard series, a cosmetics series, various bakery allergens, diallyl disulfide (in garlic), sodium metabisulfite and her own samples. She also had prick tests to her own flours,

spices and foods. She had relevant positive patch test reactions at day (D) 2 and D5 to sodium metabisulfite (1% pet), and at D5 to dodecyl gallate (0.25% pet). Prick tests were negative.

Discussion

Bakers are at high risk for the development of hand dermatitis caused by both contact dermatitis and contact urticaria (1, 2). Irritant contact dermatitis results from repeated exposure to wet dough, flours, detergents and cleaners (1, 3). Contact urticaria from flours, spices and essential oils causes immediate reactions, which may evolve into chronic dermatitis (1, 3, 4). Less commonly, bakers are affected by allergic contact dermatitis from flavourings and spices, including cinnamon (5), flour improvers (such as benzoyl peroxide) and antioxidants (lauryl gallate) (1, 5).

Sulfites are used for their antibacterial, bleaching and antioxidant effects (6). Sodium metabisulfite, $Na_2S_2O_5$, is a potent reducing agent and antioxidant used in the food and beverage industry, pharmaceutical preparations and photography (7, 8). It is well recognized as a cause of asthma and anaphylactoid reactions through exposure in foods and medications, including local anaesthetic preparations (6, 9). It has recently been described as an allergen in topical ketoconazole, corticosteroid, and anti-haemorrhoidal creams (10–15). In food handlers, it has been reported as a cause of allergic contact dermatitis in a salad maker (16), pastry and biscuit maker (17), and a baker (6), where it was found in the flour the baker used.

Dodecyl gallate is an antioxidant that inhibits the breakdown of lipids by atmospheric oxygen (18). It is used in fats in the cosmetics and food industries, especially bakery goods and cooking oils (3).

In our patient, sodium metabisulfite was utilized in the bread improvers. Dodecyl gallate was added to fresh apples to prevent discolouration. She has changed to sodium metabisulfite-free bread improvers and tinned apples, and her dermatitis has improved significantly. We recommend that sodium metabisulfite be routinely tested in bakers who present with hand dermatitis, and therefore be included in bakery series.

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Recalcitrant allergic contact dermatitis from azathioprine tablets

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Key words: azathioprine; contact allergy; patch test; proliferation test; medicaments; carers.

Case Report

An otherwise healthy 44-year-old woman developed eczema on her face, neck, hands and soles. After symptoms had worsened for 5 months, she sought medical help. She was treated for 2 months with betamethasone valerate, mometasone furoate and fusidic acid creams, chlorhexidine baths, 3 courses of oral methyl prednisolone, cephalosporin antibiotic and itraconazole antifungal without permanent resolution. It turned out that she had been handling azathioprine tablets at home for 1 year. Her son had had leukaemia and, after a successful marrow transplantation, he had been taking azathioprine. To help him swallow the tablets, his mother had been crushing them.

On patch testing, azathioprine tablet (Azamun®, Leiras, Finland) crushed and diluted 1:1 with water gave a positive reaction, confirmed on serial dilution of azathioprine tablet from 1:3 to 1:333 in water. On further testing, serial dilution of pure azathioprine (Sigma) at 0.1%, 0.1% and 0.01% pet. also gave a dose-dependent response. An attempt was made to demonstrate in vitro proliferation of peripheral blood mononuclear cells (PBMC) to azathioprine. However, a dose-dependent suppression of proliferation at 0.01 to 1 μg/ml azathioprine, when compared to untreated cells, was seen. PBMC studied showed a normal proliferative response to phytohemaglutinin (PHA). Similar proliferation profiles were seen in PBMC depleted of either CD4+ or CD8+ T cells by the immunomagnetic method.

The patient was instructed to arrange for her home to be cleaned of all remaining azathioprine debris, as well as to stop crushing them. Successful initial treatment response was achieved by oral prednisone 15 mg/day, but not at a lower dose. Reduction of the dose to 5 mg/day was not achieved until after 3 months' such treatment, with the help of topical corticosteroids. Ultraviolet light B (UVB) treatment was then given for 7 weeks, during which prednisone was stopped, finally clearing her dermatitis. During a 6-month follow-up, she continued to be in remission.

Discussion

Suppression, rather than induction, of PBMC proliferation in vitro can be explained by azathioprine's immunosuppressive properties. Azathioprine is relatively well-tolerated, though its allergenic potential has recently gained attention (1), including cases of occupational dermatitis in pharmaceutical manufacture (2, 3). This case emphasizes the potential risk to patients and their relatives.

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Occupational sensitization to methoxysilane in fibreglass production

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Key words: allergic contact dermatitis; [3-(2-aminoethyl)aminopropyl]trimethoxysilane; occupational; fibreglass; material safety data sheets.

Case Report

A 54-year-old man was admitted with severe generalized eczema. He gave a past history of intermittent episodes of a similar rash. He had received one prescription for Tri-Adcortyl® cream, 9 months before this eruption, without any reported adverse effects.

He had been working as an electrician/fitter for many years in a factory that produced fibreglass insulation. The day before the onset of the widespread rash, he stated that he had been cleaning out some blocked pipes at his works and that he had been covered in dust. The blocked pipes apparently contained the raw materials that would combine to make the end-product. This

would have been a rare job for him to carry out, but he stated that his works usually tended to be dusty.

Weeks later, he was patch-tested to a standard and medicaments series of allergens and there was a positive (+) reaction to ethylenediamine on D4. He was also patch tested to the separate constituents of the binder material that bonds onto the glass fibres before curing in an oven. There was a positive (+) reaction to a silane component of the binder, tested at 10% in both pet. and aq., on D4. Tests in 10 controls were entirely negative.

Discussion

The material safety data sheet (MSDS) of the silane material identifies its components as being (a) 13-(2-aminoethylamino)-propyltrimethoxysilane and (b) methanol. The CAS registry number of (a) is given as 11760–24–3. Reference to the Aldrich Chemical Catalogue (1), however, identifies the holder of this number as being [3-(2-aminoethyl)aminopropyl]trimethoxysilane and directs to another page where an alternative name is used, namely N-[3-(trimethoxysilyl)propyl]ethylenediamine. I understand that the latter chemical is referred to as a substituted ethylenediamine: this would apparently explain the positive patch test results. It appears then that some incorrect detail was transcribed onto the MSDS. It is known that such problems can occur and indeed, when COSHH (2) risk assessments are carried out, it is up to the assessor to check the correctness of the information that is given.

The MSDS warns that the silane may cause skin sensitization: reference is made to standard animal testing. To the best of my knowledge, this is the 1st reported clinical case of such a problem.

The methoxysilane chemical has uses other than in an industrial setting. Indeed, a reference was found to a fairly recent (1997) patent application for a simulated skin tan lotion that contained N-[3-(trimethoxysilyl)propyl]ethylenediamine. Ethylenediamine itself is considered to sensitize rarely, other than when it is applied in products such as Tri-Adcortyl® cream, where it acts as a stabilizer. It would be reasonable to assume that there could be similar scope for developing allergic problems from the topical use of methoxysilane.

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