

Short Communications

Contact allergy to Psorigon®

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Key words: allergic contact dermatitis; Psorigon®; PS-98®; psoriasis; *Azadirachta indica*; neem oil; medicaments; plant extracts. © Munksgaard, 2000.

Case Report

A 35-year-old man had had psoriasis from age 7 years. He had used various topical corticosteroids and, more recently, topical calcipotriol, with little benefit. He then tried a proprietary non-prescription cream called Psorigon®. His psoriasis improved during the 1st month of treatment, but thereafter, the cream appeared to worsen his psoriasis and cause pruritus. After 5 weeks of treatment, he stopped using Psorigon®.

On examination, he had widespread psoriasis with superimposed eczema. A potent topical corticosteroid was prescribed and he was patch tested to the European standard series, a corticosteroid series and Psorigon® cream as is. On D4, he showed a ++ reaction to Psorigon®, all other allergens being negative. Subsequently, he was patch tested to serial dilutions of Psorigon® (as is, 50%, 25% and 12.5%) and also to a new formulation of Psorigon® (PS-98®). Positive patch test results were obtained with both formulations at all dilutions. 12 volunteer controls demonstrated negative patch tests to Psorigon®.

He was then further patch tested against the ingredients of this formulation. Samples of the herbal ingredients (*Cistus labdaniferus*, *Salmo*, *Melia azadirachta*, *Oenothera biennis* (evening primrose), *Quercus robur* (oak) and *Cereus* (syn. *Cactus*) *grandiflorus*) were obtained from the manufacturer. Dilutions of 1%, 2%, 5%, and

10% were tested against. He showed a positive reaction to all concentrations of *Melia azadirachta*.

Comment

Melia azadirachta (syn. *Azadirachta indica*, Indian lilac, neem tree or margosa tree) is a tree long used in both agriculture and medicine (1). Its extracts are used as insect repellents, insecticides, soil fertilizers, dyes, waxes, lubricants, soaps and oral hygiene products. In traditional medicine, it has been used as a tonic, as an astringent, to treat malaria and for skin disease. It has been shown to have immunomodulatory and anti-inflammatory effects. Neem tree has many unique compounds, some of which have not yet been characterized. *Azadirachta indica* seed oil intoxication has been reported to cause Reye's syndrome in infants after oral doses of 5–30 ml (2). No previous reports of contact allergy to extracts of this tree have been published.

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Oral tolerance of nickel in patients with dyshidrosis

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Key words: dyshidrosis; oral challenge test; nickel. © Munksgaard, 2000.

During our research, 74 patients with various types of eczema have been orally challenged with nickel. 68 turned out to be positive to nickel on patch testing, while the remaining 6 persons with a history suggesting sensitivity to this metal had negative patch tests. At the be-

ginning of our study, patients received a dose 10× the dose recommended in the literature (1, 4). Later, depending on the results, patients received higher or lower doses than that. Following each oral challenge, patients were observed for 2 to 3 h. The condition of their skin

Table 1. Global results of oral challenge test with nickel for 2 groups of patients with and without dyshidrosis

Oral challenge test	Patients with dyshidrosis		Patients with other types of eczema	
	n	(%)	n	(%)
negative	5	25	24	44
positive	15	75	30	56

Table 2. Response to lower doses of nickel

Oral challenge test	Patients with dyshidrosis	Patients with other types of eczema
negative to 11.2 mg	5	24
positive to 11.2 mg	6	12
5.6 mg	2	1
2.24 mg	4	4
1.12 mg	3	5
0.56 mg		
0.224 mg		3
0.112 mg		4
0.056 mg		1

was also checked after 1 and 2 days. Positive results of oral challenge tests were obtained in 45 persons. All patients were divided into 2 groups, with (20 persons) and without dyshidrosis (54 persons), i.e., symmetrical ves-

icular eczema on the palms, and palmar surfaces and sides of the fingers (1).

Results are shown in Table 1. It should be noted that, although the difference was not statistically significant, the % of positive oral challenge tests for patients with dyshidrosis was higher (75%) than for patients with other types of eczema (56%). Moreover, we also investigated whether patients with dyshidrosis responded to lower doses of nickel than patients with other types of eczema. Data obtained are displayed in Table 2. Results indicate that patients with dyshidrosis were not more sensitive to small doses of nickel than patients of the other group.

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Occupational contact dermatitis in fishermen of Cumbuco beach, Ceará, northeast Brazil

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Key words: occupational contact dermatitis; fishermen; friction; nickel. © Munksgaard, 2000.

Jangadeiros are fishermen who work in boats similar to caravels, with broad bows, a high narrow poop and lateen sails, but smaller, and supporting 2 or 3 men. The boat is hand-crafted in local wood (*Apeiba tibourbou*). The ropes, fishing nets and bows, in the old days, were made of *Agavea americana*, a native plant. Today, transparent synthetic material is used, artificially coloured blue. *Jangadeiros* are exposed to the following risk factors for dermatoses: intense ultraviolet radiation, contact with sea organisms and repeated trauma in the manipulation of boats and ropes. Most *jangadeiros* also work as gardeners, housekeepers, carpenters or salesmen to supplement their income.

Patients and Methods

21 *jangadeiros*, who live and work in Cumbuco, a beach of Ceará, northeast Brazil, volunteered for interview and physical examination to identify dermatoses. Fishermen

presenting with erythema, edema, scaling or lichenification were patch tested to a standard series (FDA-Allergenic Laboratory, Rio de Janeiro) composed of 51 substances. Readings were made after 2 and 4 days, according to ICDRG recommendations (1, 2).

Results

Palmar hyperkeratosis was observed in 9 (43%) fishermen, scaling and lichenification in 2 (9.6%), in 1 in an area of contact with blue rope, and other dermatoses as follows: dermatophytosis (3, 14%), folliculitis (2, 9.6%), solar elastosis (1, 4.7%), actinic keratosis (1, 4.7%) and epithelioma (1, 4.7%). No dermatitis caused by sea organisms was seen.

Patch tests of these first 11 fishermen revealed hypersensitivity to: para-phenylenediamine (1, 4.7%), pyrethrin (1, 4.7%), nickel sulfate (1, 4.7%), nitrofurazone

(1, 4.7%) and promethazine (1, 4.7%). The other 6 were negative.

Discussion

Palmar hyperkeratotic scaling, the most common clinical finding, probably occurs due to repeated trauma in the manipulation of boats and ropes. No lesions caused by sea organisms were observed, as reported in the literature (3), and, in some fishermen, only old scarring. This occurs because *jangadeiros* start fishing in childhood and soon learn, from their parents, how to avoid the organisms that spell danger. The fisherman who was sensitive to nickel sulfate presented with erythema, scaling and lichenification in an area of contact with the blue rope used on the boats, which may possibly have nickel in its pigment or paint (4). Hypersensitivity to

other substances probably corresponds with their other activities and everyday contacts.

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Delayed allergic skin reactions to subcutaneous heparins. Tolerance of 2 recombinant hirudins

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Key words: heparin; low-molecular-weight heparin; heparinoids; pentosanpolysulfate; adverse drug reactions; delayed hypersensitivity; recombinant hirudins; tolerance; medicaments. © Munksgaard, 2000.

Heparin-induced non-necrotic skin reactions caused by subcutaneous (s.c.) administration of unfractionated heparins (UFH) or low-molecular-weight heparins (LMWH) are due to delayed hypersensitivity (1–3).

Case Report

A 63-year-old woman, undergoing radiotherapy for relapse of uterine carcinoma, was administered the LMWH nadroparin-calcium (Fraxiparin®) 0.6 ml daily by s.c. injection into the abdominal wall. 15 days after beginning therapy, she developed erythematous, infiltrated, pruritic and painful plaques at the injection sites. Switching to dalteparin-sodium (Fragmin P®) had similar effects 2 days after its 1st injection. Anticoagulation was then achieved with the recombinant hirudin desirudin 15 mg 2× daily s.c. over 4 days, followed by 15 mg for a further 7 days, without any side-effects.

Intradermal (i.d.) tests with various heparin preparations were performed 2 weeks after discontinuing therapy with desirudin. I.d. tests were performed on the flexor forearm with 0.05 ml of undiluted brands of UFH, LWMH, heparinoids and lepirudin (Table 1). Readings were taken after 20 min, and 1, 2 and 3 days (D), and considered indicative of delayed-type hypersensitivity when erythematous and papular or eczematous reactions were noted at D1, D2 or D3. Patch tests were not performed because, in our experience, they do not reveal the complete spectrum of heparin hypersensitivity (4).

Cross-reactions were observed to all the UFH and LMWH tested, including the latest LMWH on the German market. Most of the heparins tested were preservative-free (Table 1). Pentosanpolysulfate and lepirudin were negative. S.c. tests were performed on the abdominal wall with 0.1 ml of pentosanpolysulfate and lepirudin, with negative readings up to D3. Therapeutic doses of pentosanpolysulfate (1 ampoule) and lepirudin (1 ml of 5 mg/ml solution) were then injected s.c. into the abdominal wall, without any side-effects. Intravenous (i.v.) provocation with lepirudin was performed using a 5 mg/ml solution prepared according to the manufacturer's instructions. A therapeutic bolus containing 0.4 mg/kg of lepirudin was then injected i.v. over a 2-min period. The patient was subsequently observed for 1 day, and no side-effects were observed.

Discussion

Delayed-type hypersensitivity reactions to heparins are probably common and related to the heparin molecule itself (4). However, the heparin fractions which induce sensitization have not been determined. Skin biopsies of lesions and test reactions typically reveal eczematous changes (1, 2, 4). When i.d. and s.c. tests are performed, most patients react to both fractionated and unfractionated heparin as well as to the heparinoid danaparoid. However, as reported previously (4–6), some patients with delayed hypersensitivity to UFH and LMWH may

Table 1. Test results

	Test	2 min	D1	D2	D3
<i>Unfractionated heparins</i>					
heparin-calcium (25000 IE/ml) (Calciparin®)	i.d.	—	—	—	+
heparin-sodium (5000 IE/ml) (Heparin-Natrium Braun®)	i.d.	—	—	+	+
<i>Low-molecular-weight heparins</i>					
certoparin-sodium®	i.d.	—	+	+	+
dalteparin-sodium (Fragmin D®)	i.d.	—	—	?	+
enoxaparin-sodium (Clexane 20®)	i.d.	—	—	?	+
nadroparin-calcium (Fraxiparin®)	i.d.	—	—	+	+
reviparin-sodium (Clivarin®)	i.d.	—	—	?	+
tinzaparin-sodium (Innohep®)	i.d.	—	—	—	+
<i>Heparinoids</i>					
danaparoid-sodium (Orgaran®)	i.d.	—	—	?	+
pentosanpolysulfate (Fibrezym®)	i.d.	—	—	—	—
	s.c.	—	—	—	—
<i>Recombinant hirudin</i>					
lepirudin	i.d.	—	—	—	—
	s.c.	—	—	—	—
	i.v.	—	—	NT	NT

+: positive, erythema and papules, —: negative, ND: not tested.

i.d.: intradermal tests with 0.05 ml of the undiluted heparin, heparinoid or recombinant hirudin preparation, s.c.: subcutaneous test, i.v.: intravenous test.

All the heparins and danaparoid-sodium are derived from porcine intestinal mucosa.

Pentosanpolysulfate is derived from beech wood. Heparin-sodium Braun® and Tinzaparin-sodium contain benzyl alcohol as a preservative. Certoparin-sodium is preserved with chlorocresol. The other heparin preparations are preservative-free.

tolerate some LMWH without side-effects, indicating extended skin testing.

Recombinant hirudins (r-hirudins) may be administered by i.v. (lepirudin) or s.c. (desirudin) routes, and have been shown to be safe, effective and well-tolerated (7). S.c. desirudin is used in Germany in the prevention of thrombotic disorder and i.v. lepirudin for the treatment of heparin-induced thrombocytopenia type II. Lepirudin also appears to be a therapeutic alternative for haemodialysis patients with heparin necrosis (8).

Our results indicate that both desirudin and lepirudin may be safe therapeutic alternatives in patients with delayed hypersensitivity to heparins. To the best of our knowledge, this has not been reported previously for desirudin. Lepirudin was tolerated without side-effects after i.v. challenge or therapy in 9 other patients (4, 9). However, this r-hirudin may also induce immediate, as well as delayed-type hypersensitivity reactions (10, 11).

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Eruption caused by a deep-sea cnidarian

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Key words: Cnidaria; Siphonophora; Physonectae; deep-water marine organisms; occupational; seaman; cutaneous eruption. © Munksgaard, 2000.

The phylum Cnidaria (formerly Coelenterata) is the largest and most diverse group of toxic marine invertebrates. Their toxins are found in cellular organelles, nematocysts, exclusive to this phylum. Nematocysts are discharged by chemical stimulus or contact with the victim or prey (1, 2). Direct tentacle contact and injection of venom results in direct action of toxins or indirect immunological reactions to the venom (3).

Case Report

On 30 May 1999, a 51-year-old crew member of the O/V Justo Sierra of the Universidad Nacional Autónoma de México, during the BATO I deep-sea sampling campaign, was winding the rope attached to a deep-sea crus-

tacean trap (630 m). As it was being winched from its collecting site in the Gulf of Mexico (22° 24.5'N and 91° 33'W), an entwined gelatinous mass appeared at the 300 m mark. This material touched the subject on his left hand and leg. He immediately felt severe pain and burning sensation and later pruritus on the affected areas, which also subsequently became reddened and inflamed (Fig. 1).

Washing with fresh water intensified the pruritus, with the appearance of skin lesions in less than 1 h after contact. The pruritus continued throughout the evening, and awakened him frequently. He applied an 0.75-mg isothipendyl ointment throughout the next day without relief. That evening, 34 h after the initial contact, he washed the lesions and surrounding areas with vinegar and continued this treatment with progressively notice-



Fig. 1. (A) Sting on the hand. (B) Cutaneous eruption on the leg.

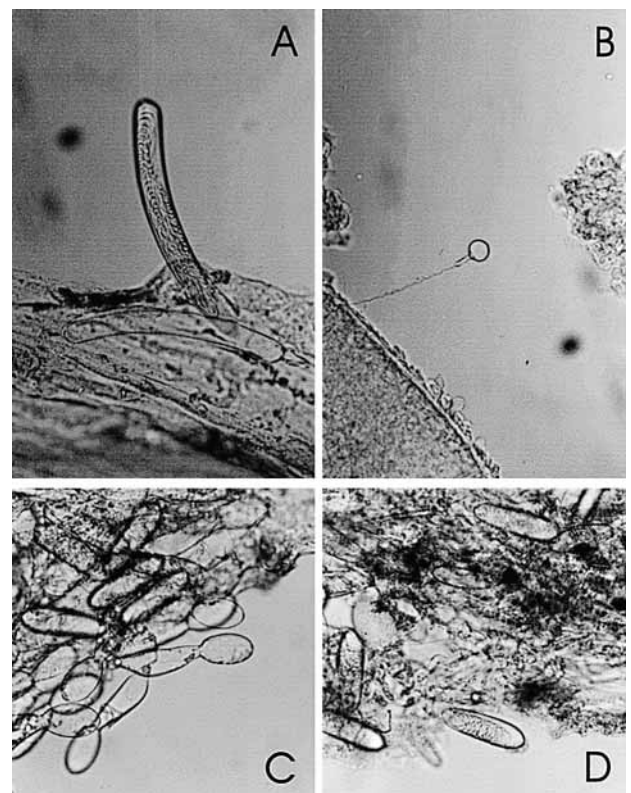


Fig. 2. 4 types of nematocysts (A) 240×, (B) 500×, (C) acroporae (120×), (D) 120×.

able relief of the pruritus. The itching and burning sensation completely subsided 48 h after contact and all lesions disappeared after 1 week.

After the stinging, the trap and collecting rope were again submerged and retrieved. Again, more gelatinous material adhered to the line at the 300 m mark, thus corroborating the depth of the offending animal.

Discussion

Vinegar irreversibly deactivates nematocysts from some cnidarians and prevents further stinging by inhibition of additional nematocyst discharge (4).

The gelatinous material was fixed in 5% formaldehyde for microscopy. A large quantity of 4 types of nematocysts (Fig. 2) were present, 3 of which could not be characterized by light microscopy. Of particular interest was the presence of the acrophores, which are found solely in subclass Siphonophora of the Cnidaria phylum (5). Having 4 types of nematocysts is characteristic of the order Physonectae, species of which include deep-water representatives, many yet to be described (R. Gasca, personal communication).

Physalia physalis, the Portuguese man-o'-war, is a toxic floating siphonophore, contact with the tentacle of which causes an intense sting, with redness, blistering and urtication, and even fatalities (4). Other free-floating siphonophores such as *Agalma okenia* and *Forskalia ed-*

wardsi, which belong to the order Physonectae, sting severely, causing pain, erythema and whealing (4). Although the exact identity of the stinging animal remains unknown, it is highly unlikely that this white (not blue) material came from *Physalia*, a jellyfish which is usually a surface floater.

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Protein contact dermatitis: aimed testing with foods

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Key words: protein contact dermatitis; prick testing; scratch-chamber testing; foods; occupational; atopy; fruit; vegetables; (shell)fish; meats; cheese. © Munksgaard, 2000.

Since the original description of protein contact dermatitis by Hjorth & Roed-Petersen (1), patients in our department with occupational hand eczema related to food contact have been prick tested and scratch-patch (chamber) tested with fresh fruits, vegetables, (shell)fish, meats and cheese.

Hannuksela & Lahti (2) used the scratch-chamber method in detecting immediate reactions to fresh fruit and vegetables. Niinimäki (3) recommended the scratch-chamber method to detect Type-I allergy to fruits and vegetables in food handlers with hand eczema. Cronin (4) used prick testing and found that the most common Type-I allergy in caterers was to fish. The hand eczema of such patients most often continues despite change of occupation (4, 5).

The results of aimed testing in 138 patients with occupational and 79 with non-occupational food contact and hand eczema, and in 87 patients with other skin diseases suspected of worsening upon contact with or ingestion

of foods, during the 5-year period from 1993 to 1997 are presented in Table 1. The test material and number of positive reactions appear in Tables 2 and 3. Prick tests gave more frequent positive reactions than scratch-patch tests, which were only rarely positive if the prick test to the same food was negative (Table 4). Positive reactions were more frequent in atopics than in non-atopics (Table 5). Relevance of positive reactions was more frequent among patients with occupational exposure (Table 6).

Prick tests in 20 non-atopic controls, without occu-

Table 1. Characteristics of 304 patients tested (1993–1997)

female	232 (76%)
male	72 (24%)
atopic	96 (32%)
occupational	138 (45%)
hand eczema	217 (71%)

Table 2. Results of prick and scratch-patch testing with fruit and vegetables

	Prick		Scratch-patch	
	no. tests	Pos.	no. tests	Pos.
kiwi	283	44	246	4
apple	284	25	256	0
potato	281	24	255	1
tomato	288	23	260	0
garlic	284	20	253	3
orange peel	288	19	258	3
carrot	283	19	255	2
lemon peel	294	17	256	0
celery	271	15	257	1
onion	283	15	258	3
lettuce	286	13	258	1
water cress	283	13	257	1
cress	282	12	255	0
chives	276	12	252	0
parsley	271	11	252	0
chicory	275	10	250	1
pineapple	216	7	195	1
prune	280	1	258	1
total	5008	300	4531	22

Table 3. Results of prick and scratch-patch testing with (shell)-fish, meats and cheese.

	Prick		Scratch	
	no. tests	Pos.	no. tests	Pos.
plaice	252	9	245	6
salmon	255	8	247	2
codfish	252	7	244	0
herring	252	7	245	1
chicken	255	6	248	2
veal	255	5	248	1
calf's liver	253	5	243	5
pig's liver	256	4	248	1
beef	253	4	245	1
Greenland halibut	254	3	246	0
pork	254	2	247	0
shrimp	252	2	244	2
cheese	254	1	247	0
total	3297	63	3197	21

pational food contact, showed in 1 individual positive reactions to apple, garlic and carrot and in another a positive reaction to kiwi. None of these reactions were clinically relevant.

Protein contact dermatitis is a clinical entity, describing patients with hand eczema aggravated or provoked by contact with fresh food, and generally related to occupational exposure. It appears from our results that scratch-patch testing is a less sensitive test procedure

Table 4. Overall comparison of results of prick and scratch-patch testing.

Fruit and vegetables prick tests	5008 tests	300 (6%) pos. reactions
scratch-patch tests	4531 tests	22 (0.5%) pos. reactions
pos. scratch-patch/neg. prick test		14 reactions
(Shell)fish, meats and cheese prick tests	3297 tests	63 (1.9%) pos. reactions
scratch-patch tests	3197 tests	21 (0.7%) pos. reactions
pos. scratch-patch/neg. prick test		18 reactions

Table 5. Frequency of positive reactions in atopics and non-atopics (χ^2 test: $p < 0.01$)

	Non-atopics	Atopics
patients without positive reactions	157	58
patients with 1 or more positive reactions	51	38
total	208	96

Table 6. Relevance of positive reactions among 217 patients with hand eczema

	No.	Relevance
non-occupational	79	6 (8%)
occupational	138	28 (20%)

than prick testing in these patients. Scratch-patch testing can only be recommended as a supplementary test if the prick test reaction to a suspected food is negative.

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Allergic contact dermatitis from dibucaine hydrochloride

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Key words: local anesthetics; amide-type; dibucaine hydrochloride; antipruritic jelly; medicaments. © Munksgaard, 2000.

Case Report

A 23-year-old, otherwise healthy, woman presented with 1-week history of pruritic lesions on the right forearm. She had been bitten by insects on the right forearm several days before the onset. After she had repeatedly applied Una-Kowa A[®] (Kowa Pharmaceutical Co., Nagoya, Japan), an over-the-counter (OTC) antipruritic jelly, the lesions increased in size and became more pruritic. She showed a 50×120 mm, dark-reddish lesion, consisting of edematous erythema and vesicles, on the flexor aspect of the right forearm, with millet-seed-sized serous papules and vesicles around this.

She was patch tested with Una-Kowa A[®] (as is), its ingredients, 0.1% dibucaine chloride, and a caine mix (5% benzocaine, 1% dibucaine hydrochloride and 1% procaine hydrochloride in pet. (Sunwhite P-1, Nikko SC): Japanese Society for Contact Dermatitis), using a 2-day application on the back with vinyl plaster (Mini-plaster, Torii Pharmaceutical Co., Ltd. Japan). Positive reactions to Una-Kowa A[®] as is, caine mix, and 0.1% dibucaine hydrochloride were seen (Table 1).

Discussion

Dibucaine hydrochloride is an amide-type anesthetic, a rare sensitizer either topically or by injection (1), though

allergic contact dermatitis from amide anesthetics has been reported (2–6). Dibucaine hydrochloride, in particular, is a cause of allergic contact dermatitis in Japan (4), because of its wide use in OTC medicaments, e.g., antiseptics, antipruritics and antifungals, although 33 now contain it (7), rather than 66 as in 1981 (4). Dibucaine is a strong experimental allergen in the Draize human repeat insult patch test (8).

Acknowledgement

We gratefully acknowledge the help of Professor Howard I. Maibach.

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Table 1. Results of patch testing

Materials	Concentration	Results
Una Kowa A [®]	as is	++
dibucaine hydrochloride	0.1%	++
diphenhydramine	1%	–
crotamiton	10%	–
caine mix		++

Reaction to cocamidopropyl hydroxysultaine, an amphoteric surfactant and conditioner

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Key words: cocamidopropyl hydroxysultaine; surfactants; shampoos; cosmetics; allergic contact dermatitis; lack of cross-sensitivity. © Munksgaard, 2000.

Cocamidopropyl betaine, as commercially supplied, is known sometimes to cause allergic contact dermatitis, though it is claimed that the chemical itself is not responsible (1–3), shampoos or shower gels being its main sources (4). Use of cocamidopropyl hydroxysultaine is also widespread in the USA.

Case Report

A 54-year-old stockbroker presented with an eczema of 2 months' duration on the forehead, back of neck, ears and surrounding areas. He had used 2 different shampoos that included botanical materials, and recalled previous reactivity to a massage product.

Patch tests to 40 screening agents and corticosteroids revealed ++ reactions to formaldehyde (1% aq.), quaternium-15 (1% pet.), DMDM hydantoin (2% aq.), and methylchloro- and methylisothiazolinone (0.02% aq.), all Chemotechnique, plus cocamidopropyl hydroxysultaine (1% aq.). 5 controls tested to this last were negative. He also had + reactions to cobalt chloride (1% pet.), potassium dichromate (0.5% pet.) and a ?+ reaction to carba mix, all Chemotechnique. Tests were read at 2 and 5 days (D) and all were positive by the D2 reading. He was negative to cocamidopropyl betaine as well as to 33 other screening allergens, 5 additional preservatives, and the 10 topical corticosteroids to which he was tested.

Because of the difficulty in finding a shampoo lacking all agents to which he was sensitive, the patient used a synthetic detergent bar as a shampoo, and the eruption cleared, except for mild residual erythema, after only 3 days.

Comment

The CTFA Dictionary (5) gives the structures of cocamidopropyl hydroxysultaine and cocamidopropyl betaine shown in Fig. 1, and the CTFA Handbook (6) describes cocamidopropyl hydroxysultaine as an amphoteric surfactant and conditioning agent. It has uses in hair conditioning, skin conditioning, viscosity increasing and surfactant foam boosting. It is found in (non-coloring) shampoos, cleansing agents (e.g., creams, lotions, and pads), bath soaps and baby shampoos (6).

This patient was allergic to 2 categories of shampoo ingredients, the amphoteric surfactant and multiple preservatives, making suitable alternatives difficult to find. He was patch-test negative to cocamidopropyl betaine, like other patients whom I have tested, not reacting to both chemicals, suggesting a lack of cross-sensitivity. Both agents should therefore be tested in patients suspected of allergy to hair-care products containing amphoteric surfactants.

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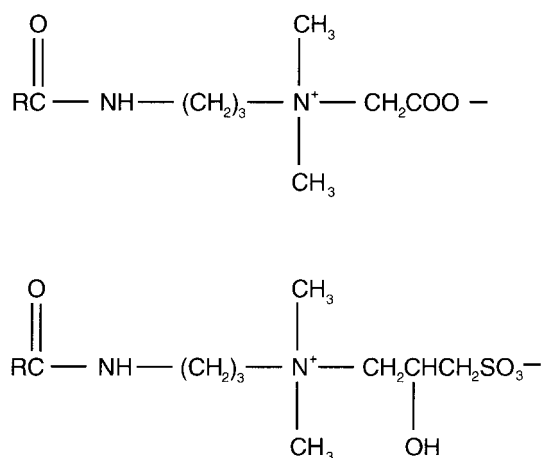


Fig. 1. Structures of cocamidopropyl betaine (top) and cocamidopropyl hydroxysultaine (bottom). RCO represents fatty acids from coconut oil.

Fixed drug eruption induced by tosufloxacin tosilate

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Key words: fixed drug eruption; tosufloxacin tosilate; new quinolone antibiotics; medicaments; positive open application test; negative patch test. © Munksgaard, 2000.

A 66-year-old woman presented with erythema of both loins. 3 days before, she had taken tosufloxacin tosilate (TFLX) (Ozex[®], Toyama Chemical Co. Ltd., Toyama) 150 mg orally and noted pruritic erythema. Since 1996, she had occasionally taken 150 mg of the same drug and had experienced erythema at the same sites.

She was patch tested with TFLX 20% and 10% pet. on the previously affected areas of the loins, and 20%, 10%, and 1% pet. on unaffected skin of the upper back. Positive reactions were observed on neither the previously affected nor the unaffected areas. We then performed an open application test with TFLX 20% pet. on a previously affected area of the left loin, 3 cm in diameter, which showed a positive response at 2 and 3 days after application. We also conducted an oral provocation test with 150 mg of TFLX, resulting in a positive response at 1 day after oral administration.

Discussion

New quinolones, in contrast to sulfonamides and tetracyclines, rarely induce a fixed drug eruption (FDE). Recently, the frequency of FDE due to new quinolones has increased with increase in their use (1–3). Only 3 cases of FDE from TFLX (4–6) have been reported and all showed a positive oral provocation test. A topical provocation test on the previously affected lesion is useful to confirm the cause of FDE with higher positive rates (59–87%) (7, 8). Of cases with FDE to new quinolones reported, 1 (2) had a positive patch test on the previously affected site, whereas all 6 cases in the Japanese literature showed no such response (5).

Open application testing on the previously affected area has been recommended for the diagnosis of FDE by Sugiura et al. (9). 50% pet. elicits positive responses to open application tests as well as, in previously affected lesions, to patch tests (9). However, 20% pet. on

the previously affected site in our case showed a positive response to open application test, but not to patch test. A larger amount of the causative drug may penetrate on open application test than on patch test and thus lead to a positive reaction, since, in our patient, the size of the previously affected lesion was much greater than that of the Finn Chamber used for the patch test. Open application testing may therefore be more useful for diagnosis, in the case of large lesions of FDE, than patch testing.

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Iodine allergy induced by consumption of iodine-containing food

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Key words: delayed-type hypersensitivity reaction; hyperthyroidism; iodine allergy; iodine restriction; oral iodine-containing food; seaweed. © Munksgaard, 2000.

Iodine is an essential trace element required for synthesis of thyroid hormones. Dietary sources include seaweed and fish, various medicines, and iodates added to bread (1). The Japanese commonly consume seaweed, such as kelp (*konbu*) and *wakame*, their average iodine intake thus being 0.1–20 mg per day (2). 1 case of maculopapular eruptions induced by the ingestion of iodine-containing food was reported by Adachi et al. (3). Iodine-induced hypothyroidism is not rare in Japan, about 50% of the patients with primary hypothyroidism becoming euthyroid under iodine restriction (4).

Case Report

A 60-year-old Japanese woman presented with a 3-day history of pruritic erythema on her face, neck and upper back, bilateral conjunctival congestion and a 30-min history of a strange feeling in her mouth after drinking *miso* soup with *wakame* seaweed in it. She had regularly consumed seaweed, such as *konbu* and *wakame*, since childhood and had experienced generalized pruritus after eating iodine-containing food for 30 years. She had developed erythroderma from iodine-containing X-ray contrast material at the age of 50 years. When she stopped eating iodine-containing foods after her 1st visit, she had no further eruptions or pruritus. However, she then mistakenly drank *konbu* tea and developed a burning sensation in the mouth 30 min later, with, 12 h later, edematous erythema appearing on her face and neck.

The results of prick testing, patch testing and lympho-

cyte stimulation testing (LST) are shown in Table 1. The prick test for *konbu* tea was negative, but after 5 min, she started to itch. The patch test for *konbu* tea was also negative, but 3 days later, a morbilliform erythema appeared on her extremities. Although the prick test for potassium iodide was also negative, 2 h later a nummular erythema appeared, and 2 to 3 days later both erythema and induration persisted at the same site. 3 control subjects were negative to both prick testing and patch testing.

Thyroid function studies showed her to be slightly hyperthyroid, which corrected itself after iodine restriction.

Discussion

100 g dry weight of kelp (*konbu*) contains as much as 170 mg of iodine, while 100 g of *wakame* seaweed contains 10 mg of iodine. Several patients have developed pustular eruptions after eating *konbu* in salad or vitamin supplements. Norwegian kelp tablets contain 0.225 mg of iodine. The ashes of kelp, a giant brown seaweed, are used as a source of both iodine and potash (6). Pustular eruptions or exacerbations of acne may be related to its ingestion (7). An early stage of delayed-type hypersensitivity seems to have played a rôle in the urticaria-like erythema seen in our patient. Labib et al. (8) reported a 4-year-old boy, put on a restricted diet for purported food sensitivity, who thereafter demonstrated both short stature and hypothyroidism. Excessive iodine intake may, in contrast, have caused mild hyperthyroidism in our case.

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Table 1. Results of LST, patch test and prick test

	LST ^{a)}	Patch test ^{b)}	Prick test
<i>konbu</i> tea as is	NT	—	—
potassium iodide in aq.	+ (186%)	—	—
povidone iodine as is	NT	+	—
amidotrizoic acid ^{c)} as is	+ (217%)	—	—
iopamidol ^{c)} as is	— (112%)	—	—
iomeprol ^{c)} as is	NT	—	—
minocycline in pet.	NT	—	NT
loxoprofen in pet.	NT	—	NT
Sedes G in pet.	NT	—	NT
Bufferin in pet.	NT	—	NT
Sennoside in pet.	— (143%)	—	NT
petrolatum	NT	—	NT
saline	NT	—	—

^{a)} As described previously (5).

^{b)} Readings D2 and D3, drugs 10% and 30%.

^{c)} Iodine-containing X-ray contrast medium.

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Maculopapular eruption from sertraline with positive patch tests

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Key words: sertraline; adverse drug reaction; positive patch test; psychotropic drugs; antidepressants. © Munksgaard, 2000.

Case Report

A 66-year-old man was admitted with a generalized pruritic maculopapular rash and fever (38–39°C) of 3 days' duration. The rash became confluent at the skin folds, with purpuric and scattered targetoid lesions at day 4, with a few pustules by day 5. The Nikolsky sign was negative, mucous membranes were spared and there was no lymphadenopathy, hepato- or splenomegaly. 3 weeks before, he had started Zoloft™ (sertraline 50 mg/day p.o.) for depression. At day 4, there was a leucocytosis (18.80 G/l) with neutrophilia (90.6%) and an elevated PCR (3.6 mg/dl). By the end of the 1st week, there was also eosinophilia (7.5% out of 12.20 G/l leucocytes). Skin biopsy at day 4 revealed an infiltrate in the superficial dermis, mostly of lymphocytes and histiocytes with a few eosinophils and extravascular erythrocytes, and focal degeneration of the basal cell layer. Sertraline was stopped, and oral methylprednisolone and hydroxyzine hydrochloride started, with complete resolution within 1 month. No rechallenge was attempted.

4 weeks thereafter, the patient was patch tested on the back with Finn Chambers™ on Scanpor tape, with the standard series of the Portuguese Contact Dermatitis Group (Chemotechnique or Hermal-Trolab), several psychotropic drugs (carbamazepine 5% pet., diazepam 10% pet., fluoxetine (Prozac™) and paroxetine (Seroxat™) 5% in aq. and pet.) and Zoloft™ (as is aq. and 10% pet.). Readings on days 2, 3 and 4, according to ICDRG guidelines, showed positive reactions (++) only to Zoloft™. 6 months later, patch tests with pure sertraline (kindly supplied by Pfizer) at 1, 5 and 10% aq., eth. and pet., were positive (++) at all concentrations and vehicles tested. Sertraline 10% eth. and 10% pet. was negative in 20 controls.

Comment

Adverse reactions to sertraline have involved mainly GI, CNS and sexual functions (1). Cutaneous adverse drug reactions are not common (<2%), not definitively attri-

buted to sertraline (2, 3) and rarely justify drug discontinuation (2–4). This is the 1st report of such an attribution at a high probability – I₃ – according to the criteria proposed by Moore et al. (5). The positive patch test reactions increase attributability to an even higher – I₄ – probability. Relevant positive patch test results are observed in only 20 to 37.5% of cases of cutaneous adverse drug reactions overall (6, 7), though in 45 to 59% of eczematous, exanthematic or delayed maculopapular reactions (7, 8). Certain drugs are particularly productive of positive patch test reactions, such as carbamazepine, β -blockers, tetrazepam, penicillins and sulfa derivatives (6, 7), and to these we can probably add sertraline.

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Allergy to rubber additives in orthopedic braces

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Key words: allergic contact dermatitis; rubber chemicals; thiourea derivatives; orthopedic braces; hockey; volleyball; elderly. © Munksgaard, 2000.

Thiourea and its derivatives (Fig. 1) have long been used as accelerators of vulcanization (1). Contact allergy to thiourea derivatives, used in the manufacture of neoprene, has been reported since 1960. Neoprene rubber is used, e.g., in running shoes, wet suits, swimming goggles and other waterproof materials (2). Another application is orthopedic devices like knee and ankle braces (3).

Case Reports

Case no. 1

A 52-year-old non-atopic man had used a knee brace for 5 years when playing hockey. Progressively, a vigorous vesicular eruption developed at the contact site of the brace. Simultaneously, a moderate dermatitis arose more-or-less all over the body. Patch testing with the European standard series (Trolab), supplemented with a rubber additives series (Chemotechnique), gave the following positive reactions: caine mix (+) (not relevant), thiuram mix (+) and diethylthiourea (+++) (Table 1).

The inner surface of the knee brace was lined with neoprene, presumably containing thiourea compounds.

Case no. 2

A 22-year-old non-atopic woman had used ankle braces on both legs for a few months when playing volleyball. Over several months, an itchy, sometimes exudative, erythematous squamous eruption developed on the ankles, its pattern coinciding with the impression of the ankle braces. Patch testing with a standard series, supplemented with a rubber additives series, showed a positive reaction to diethylthiourea (+) (Table 1). The inner surface of this brace was also lined with neoprene.

Case no. 3

A 62-year-old non-atopic man presented with an itchy dermatitis around his knee. The complaint arose after wearing a knee brace for several months. Patch testing (European standard series and rubber additives) revealed a positive reaction only to diphenylguanidine (+) (Table 1). In this patient also, the inner lining of the brace consisted of neoprene, presumably containing this rubber additive.

Comment

Thiourea derivatives can cause both allergic and photoallergic contact dermatitis. They have been reported in limb prostheses, photocopying materials, silver polish, neoprene attachment bands of a CPAP system, and other sources (4–6). Besides sensitization to these additives, allergy to the organic dye Disperse Blue 85 has also recently been reported as a cause of dermatitis from a knee brace (7). In our patients, the neoprene was substituted with leather and the patients then tolerated the modified brace.

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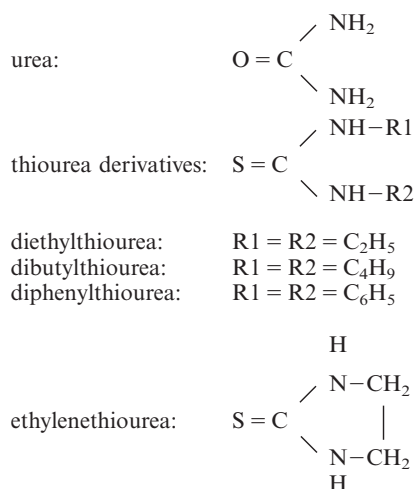


Fig. 1. Chemical structure of thiourea derivatives.

Table 1. Patch test result (D3)

Substance	Case no. 1	Case no. 2	Case no. 3
diethylthiourea	+++	+	—
dibutylthiourea	—	—	—
diphenylthiourea	—	—	—
diphenylguanidine	—	—	+
ethylenethiourea	—	—	—

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False-negative patch test reactions due to a lower concentration of patch test substance than declared

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Key words: false-negative; patch testing; methyl methacrylate; dental technician; occupational; allergic contact dermatitis; gingivostomatitis; acrylics; hand dermatitis; quality control. © Munksgaard, 2000.

A negative patch test does not necessarily mean that contact allergy has been excluded (1). The right patch test chemical may not have been used, or patch testing may have been improperly performed (Table 1) (1, 2). In protein contact dermatitis, patch test reactions are also negative (3, 4).

Case Reports

Patient no. 1 had previously been diagnosed as being very allergic to many (meth)acrylates (5). She developed an allergic gingivostomatitis from a temporary dental acrylic crown. A further patch test session was performed, according to the recommendations of ICDRG,

with (meth)acrylates to which she had earlier been negative. Methyl methacrylate (MMA) was patch tested with 2 commercial patch test substances, both at 2% pet. according to the manufacturer. One elicited a ?+ reaction and the other a ++ reaction (Table 2).

Patient no. 2 was a 37-year-old male dental technician who for 1 year had had hand dermatitis, first involving the fingerwebs, and later also the fingertips of the right hand. The dermatitis healed on vacations, but relapsed within 2 weeks back at work. He performed routine dental technician's tasks, involving considerable exposure to (meth)acrylates used in the manufacture of prostheses. He also washed his hands about 20× a day, and used vinyl protective gloves. He had previously had signs of

Table 1. Reasons for false-negative patch test reactions

- Too low a concentration of test substance:
 - correct patch test concentration not known;
 - actual patch test concentration lower than declared (present report);
 - final patch test concentration of allergen too low when patch testing patient materials;
 - degradation of allergen during storage.
- Too high a concentration of test substance with corticosteroids (or other immunosuppressants) (2).
- Influence of corticosteroids and other immunosuppressants (local or systemic medication).
- Failure to perform delayed readings (e.g., after D2).
- Wet or loosened patches.
- Inappropriate vehicle.
- Duration of contact too brief.
- Failure to perform photopatch testing.
- False anatomic location (e.g., thighs less sensitive than back).

Table 2. Variable patch test results with 2 commercial methyl methacrylates (MMA) (patient no. 1)

Patch test substance and declared concentration	Analyzed concentration	D2	D3	D4
MMA (manufacturer no. 1) 2%	0.5%	-	?+	?+
MMA (manufacturer no. 2) 2%	NT	++	++	++

Table 3. Patch test results and results of quantitative gas chromatographic analysis of dental acrylic products of patient no. 2; detection limit 0.05%

Product (dental acrylic product or patch test substance)	Amount of (meth)acrylates according to MSDS or product declaration	Results of quantitative analysis of methacrylates (%)			Patch test results
		MMA (methyl methacrylate)	EGDMA (ethylene glycol dimethacrylate)	BUDMA (butanediol dimethacrylate)	
Selecta plus liquid	MMA ~95%, BUDMA 4%,	95%	<0.05%	5%	+ (2% pet.)
Selectaplus powder	n.g.	n.a.	n.a.	n.a.	– (as is)
Vita Zeta cold curing polymer liquid	MMA 50–85%, EGDMA 10–40%	70%	30%	<0.05%	+ (2% pet.)
Forest acryl strong "S" (rosa) liquid	MMA >94%, EGDMA <5%	91%	9%	<0.05%	+ (2% pet.)
Forestacryl strong "S" powder	Polyethyl-methacrylate >99%, polyacryl-methacrylate <1%	n.a.	n.a.	n.a.	– (as is)
MMA of manufacturer 1	2%	0.5%	n.d.	n.d.	?+
EGDMA	2%	n.d.	n.d.	n.d.	?+
BUDMA	2%	n.d.	n.d.	n.d.	–

MSDS: material safety data sheet.

n.a.: not analyzed.

n.g.: not given.

n.d.: not done.

respiratory atopy but no skin problems. Currently he also complained of work-related rhinitis.

He was patch tested according to the recommendations of the ICDRG. In a modified European standard series, budesonide elicited a ++ reaction, a series of antimicrobials was negative, and (meth)acrylates gave the following reactions: ethyl acrylate (EA) 0.1% pet., +; ethyl methacrylate (EMA) 2% pet., +; 2-hydroxyethyl methacrylate (2-HEMA), 2%, ?+; 2-hydroxypropyl methacrylate (2-HPMA) 2% pet., ?+; ethylene glycol dimethacrylate (EGDMA) 2% pet., ?+, and MMA 2% pet., ?+. A dental screening series without (meth)acrylates was negative, but 3 of his dental products containing (meth)acrylates provoked + reactions (Table 3).

As there was discrepancy between the patch test results with MMA (with which 2% MMA elicited only a ?+ reaction), and the reactions of his own products (in which MMA at corresponding concentrations provoked stronger reactions) (Table 3), the content of the patch test substance of manufacturer 1 and the patient's dental products were analyzed using gas chromatography (6). Analyses revealed that the commercial patch test substance MMA contained only 0.5% MMA instead of 2%, as declared (Table 3). It was concluded that the patient had occupational allergic contact dermatitis (ACD) from MMA, and that the ?+ reaction to MMA was due to the inadequate patch test concentration of MMA (0.5%).

Discussion

(Meth)acrylates are common causes of occupational allergic contact dermatitis in dental technicians (7, 8). Patient no. 2, a dental technician, was sensitized to MMA and possibly to EGDMA present in products at work (Table 3), but which caused only a ?+ reaction. The allergic patch test reactions to EA, EMA, 2-HEMA and 2-HPMA may represent cross-reactivity. Details of the

clinical features of patient no. 1 have previously been reported (5): the discrepancy between her patch test results with 2 MMA products was a new finding.

We have previously emphasized that better MSDSs and product declarations are needed, as the patients' exposure data may not otherwise be determined (6, 9). There are many causes of false-negative patch test reactions (Table 1), e.g., testing a patient's dental composite acrylic resin at too low a concentration (10). Here, the concentration of a commercial patch test material was lower than declared. This had been adequately stored, so there were other reasons for the low concentration, raising questions as to quality control.

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Eyelid dermatitis: an evaluation of 232 patch test patients over 5 years

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Key words: allergic contact dermatitis; eyelid dermatitis; medicaments; cosmetics; relevance; seborrhoeic dermatitis; atopy; atopic dermatitis. © Munksgaard, 2000.

In 3 previous series evaluating eyelid dermatitis, the frequency of allergic contact dermatitis was 46% (1), 65.3% (2) and 72% (3). We have correspondingly reviewed our patch test data.

Patients and Methods

Using a computerized database, patients with eyelid dermatitis patch tested over a 5-year period from 1994 to 1998 were identified. We gathered information from hand-written patch testing records in addition to computerized records. Atopic status was ascertained by a personal history of asthma, eczema or hay fever, or 1 or more positive prick tests to common allergens. Patch test reactions were read at D2 and D4 and their relevance assessed at the final visit as current, past, or uncertain.

After patch testing, patients were classified into allergic contact dermatitis, irritant contact dermatitis, seborrhoeic dermatitis, atopic eczema, or diagnosis unknown.

All patients were patch tested using Finn Chambers on Scanpor tape. In all patients, an extended European standard series was used, plus a hand and face series (Table 1). Other test substances were applied if suspected. Prick tests were performed with 1 drop on the skin of the volar surface of the arm, using a standardized skin test needle and reading at 15 min. Positive and negative controls were performed. From 1994–1995, prick tests to house dust mite, grass, beech, birch, cat, dog, feathers, latex and moulds were made, but thereafter, the feathers prick test was discontinued.

Results

3115 patients were patch tested during the 5 years, of whom 232 had eyelid dermatitis, 197 (84.9%) female and 35 (15.1%) male, mean age 42.9 years. There were less men than in the patch test population as a whole (31%).

In these 232 patients, there were 171 positive results in 108 individuals, but only 67 patients (28.9%) had currently relevant positive tests. 120 patients had eyelid dermatitis alone, 65 had facial involvement and 47 had other areas affected. 35 (29.2%) of the 120 patients with eyelid eczema alone had currently relevant positive tests, 23 (35.4%) of the 65 patients with eyelid and facial involvement and 9 (19%) of the 47 with eyelid and other body parts affected.

119 patients (51%) in the eyelid dermatitis group were found to be atopic, the frequency of atopy in the patients with allergic contact dermatitis (49%) being similar to that in the group without (52%). The prevalence of atopy in the patch test population as a whole was 38.8%.

67 patients (28.9%) were diagnosed as having allergic contact dermatitis, 12 (5.2%) irritant contact dermatitis, 48 (20.7%) seborrhoeic dermatitis, 36 (15.5%) atopic eczema. 17 (7.3%) did not have eczema and in 52 (22.4%), it was not possible to make a firm diagnosis (Table 2). Overall, 5.7% of men and 27% of women had allergic contact dermatitis. The most common allergens are shown in Table 3.

Table 1. Face and hands series plus extended series extras 1994–1998

Test substances	Conc. (%)
2-bromo-2-nitropropane-1,3-diol	0.5
tosylamide/formaldehyde resin	10
polyester nail varnish resin	10
phosphorus sesquisulfide	0.5
diazolidinyl urea	2.0
cocamidopropyl betaine	1.0
BHA	2.0
BHT	2.0
benzyl alcohol	1.0
sorbic acid (1994–1996 only)	2.5
carba mix	2.0
DMDM hydantoin	1.0
propyl gallate (1994–1997 only)	1.0
acrylate copolymer (from 1996 onwards)	10.0
methylidibromo glutaronitrile	0.3
chlorphenesin (1998 only)	1.0
ethylenediamine	1.0
budesonide	0.1
cetearyl alcohol	20
imidazolidinyl urea	2.0
tixocortol pivalate	1.0

All tested in pet.

Table 2. Final diagnosis in patients with eyelid dermatitis

Allergic contact dermatitis	Seborrhoeic dermatitis	Atopic eczema	Irritant contact dermatitis	Unclassified	Not eczema
28.9%	20.7%	15.5%	5.2%	22.4%	7.3%

Table 3. Relevant patch test results in eyelid and all cases

Test substances	Eyelid cases (n=232)					All cases (n=3115)	
	No. positive	% positive	No. currently relevant	No. past relevance	No. uncertain relevance	No. positive	(%)
*nickel sulfate 5%	40	17.2	19	20	1	496	15.9
fragrance mix 8%	14	6.0	14	0	0	230	7.4
*quaternium-15 1%	11	4.7	10	1	0	48	1.5
*neomycin 20%	9	3.9	6	3	0	120	3.8
*diazolidinyl urea 2%	7	3.0	7	0	0	32	1.0
colophonium 20%	7	3.0	2	3	2	127	4.1
*thiuram mix 1%	6	2.6	4	0	2	96	3.0
*epoxy resin 1%	5	2.2	1	1	3	22	0.7
*tosylamide/formaldehyde resin 10%	5	2.2	5	0	0	18	0.6
*imidazolidinyl urea 2%	4	1.7	4	0	0	29	0.9
*methylchloroisothiazolinone and methylisothiazolinone 200 pm (aq.)	4	1.7	4	0	0	51	1.6
Myroxylon Perseirae 25%	4	1.7	3	1	0	92	3.0
formaldehyde 1% (aq)	3	1.3	3	0	0	43	1.4
p-phenylenediamine free base 0.5%	3	1.3	3	0	0	57	1.8
tixocortol pivalate 1%	3	1.3	3	0	0	50	1.6
*polyester nail varnish resin 10%	3	1.3	2	0	1	10	0.3
*PTBPF resin 1%	3	1.3	1	1	1	21	0.7
*phosphorus sesquisulfide 0.5%	2	0.9	1	0	1	11	0.4
primin 0.01%	2	0.9	1	1	0	35	1.1
wool wax alcohols 30%	2	0.9	2	0	0	48	1.5
*methyltribromo glutaronitrile 0.3%	2	0.9	2	0	0	11	0.4
parabens mix 12%	1	0.4	1	0	0	22	0.7
own glues/plastics	3	1.3	3	0	0	-	-
own products	9	3.9	9	0	0	-	-
benzalkonium chloride (aq.) 100 ppm	3	1.3	2	0	1	-	-
diaminophenylmethane 0.5%	1	0.4	1	0	0	-	-
n-butylglycidyl ether 0.25%	1	0.4	1	0	0	-	-
p-toluenediamine sulfate 1%	1	0.4	1	0	0	-	-
ethyl methacrylate 1%	1	0.4	1	0	0	-	-
gentamicin 2%	1	0.4	1	0	0	-	-
hydrocortisone (alc.) 2%	1	0.4	1	0	0	-	-
chloramphenicol 1%	1	0.4	1	0	0	-	-

All tested in pet. unless otherwise stated.

*Allergens more commonly positive in the eyelid dermatitis group compared to all patch-test patients

Discussion

A similar proportion to ours of Nethercott's (1) patch test patients had eyelids affected (7.2%). There were far more women in the eyelid dermatitis group than in the patch test population as a whole, reflecting greater cosmetic use.

Reactions to diazolidinyl urea, imidazolidinyl urea, quaternium-15, p-tert-butylphenol-formaldehyde resin, tosylamide/formaldehyde resin, epoxy resin and polyester nail varnish resin (4) were commoner in the eyelid dermatitis group (Table 3). Nethercott et al. (1) found diazolidinyl urea to be commoner and Valsecchi et al. (2) quaternium-15. The association between eyelid dermatitis and nail varnish allergy is well-established (5, 6). Just under 50% of the patients had the eyelids affected

alone, indicating their particular vulnerability (6, 7). Eyelid contact dermatitis can be caused by volatile allergens, airborne dusts or pollens (6), or by transfer of chemicals from the hands.

The frequency of allergic contact dermatitis in our study (28.9%) is significantly lower than in previous major studies (1–3), though in keeping with a much smaller study by Svensson & Möller (8). We also diagnosed seborrhoeic dermatitis in a larger proportion of patients (20.7%) than in other series (1, 2). The frequency of atopy was very high in the eyelid dermatitis group (51%). More patients with eyelid and facial involvement (35.4%) had allergic contact dermatitis than those with eyelid involvement alone (29.2%). Those with other areas affected were least likely to have allergic contact dermatitis (19%).

Nickel was the commonest allergen, being very slightly more frequent in the eyelid group (17.2%) than in the entire group (15.9%) (Table 3). Nickel sensitization has been described from eyelash curlers (9) and eye make-up (10, 11), though we could establish relevance in only just under 50% of such patients (47.3%). Allergic contact dermatitis of the eyelids from rubber chemicals has also been reported from eyelash curlers (12). Allergy to rubber chemicals was no more common in our eyelid group.

Factors contributing to our lower rate of allergic contact dermatitis may have been our policy to patch test *all* patients with eyelid eczema, and to diagnose allergic contact dermatitis *only* if current relevance of an allergen was definitely established.

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Very delayed reactions to β -lactam antibiotics

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Key words: hypersensitivity; antibiotics; late reaction; adverse drug reactions; late positive patch test reactions; patch testing technique; ampicillin; amoxycillin. © Munksgaard, 2000.

Type I reactions occur in 0.7 to 10% of all instances of immune-mediated adverse reactions to β -lactam antibiotics (1) and can be rapid and severe (2). Accelerated (after 1 h) and delayed reactions (after 24 to 72 h) have also been described, though pathogenetic mechanisms are often unclear (3). Fixed drug eruption has been described from amoxycillin (4). Patch tests (5), delayed positive skin tests (6), or both (7), suggest that over 40% of such delayed reactions are cell-mediated (8).

Materials and Methods

From 1996 to 1998, we studied 408 consecutive patients referred to our outpatient clinic for adverse reactions to β -lactam antibiotics. Only 30% of these had positive *in vivo* evidence of immune-mediated reactions: 18% with immediate skin tests (mainly *i.d.*, but also prick tests), 10% only to patch tests and 2% to both. Routine assessment of patch tests was made at day (D) 3, but 4 patients with negative immediate and patch test results returned later to report skin reactions at the site of either *i.d.* or patch test application. In 3 cases, the reaction was still

detectable by physicians 6 days after testing. These 4 cases, 3 female and 1 male, mean age 37 years, representing <10% of those with patch test positivity and 1% of all patients reporting such adverse reactions, were selected for repeat patch testing with readings extended up to D6.

In addition, all 4 patients were subjected to the following investigations.

In vitro tests: total serum IgE levels and specific IgE for penicilloyl G, penicilloyl V, amoxycillin and ampicillin, using the CAP System RAST FEIA (Pharmacia). Positive scores were assigned to >0.7 kU/l specific IgE (i.e., class 2 or higher).

In vivo tests: both prick tests and *i.d.* tests were performed, starting with the lowest dose and increasing every 20 min by 1 log₁₀. Allergens tested were benzylpenicilloyl-polylysine (PLL; starting dose 1.75 mcg/ml), minor determinant mix (MDM; starting dose 0.6 mcg/ml), penicillin G (PenG; starting dose 0.1 IU/ml), amoxycillin and ampicillin (starting dose 1 mg/ml) (all from Allergopen). Both negative (normal saline) and positive (histamine dihydrochloride 10 mg/ml) controls were added for prick tests. Assessment of the results was

performed after 20 min, 2 h, and 1, 2, 3, 4, 5 and 6 days.

Patch tests with amoxycillin, ampicillin and penicillin G (5% pet.) were applied on intact skin of the trunk, after application of ethyl alcohol, with Finn Chambers on hypoallergenic tape. Results were assessed at D3, D4, D5 and D6. In 1 case of reaction to cephradine, we applied a panel of cephalosporins (Firma SpA). 6 non-atopic healthy subjects, including 3 who had recently received full-dose β -lactam antibiotics (ampicillin or amoxycillin), were also tested by patch and i.d. tests, without positive reactions.

Results

The 1st patient (F, 49) had a diffuse morbilliform rash 12 h after amoxycillin+clavulanic acid, with intense itching and edema of the hands and feet. I.d. testing to Pen G and MDM was positive after 20 min, whereas ampicillin was positive after 6 days and amoxycillin after 4. Total serum IgE was 890 kU/l, and only class 1 positivity was detected by RAST for ampicillin. All patch tests were negative until D6, when both ampicillin and amoxycillin became positive.

The 2nd patient (M, 19) had a generalized intensely pruritic morbilliform rash 6 h after ampicillin. Ampicillin tested i.d., though negative at 20 min, was positive by D3. Total IgE was 12.9 kU/l, without positive specific IgE. Patch tests were negative at D3, but again ampicillin became positive by D6.

The 3rd patient (F, 55) had a generalized urticarial eruption and edema of the face and neck several hours after cephradine. I.d. tests were positive after 20 min to PPL, and at D3 and D6, respectively, to ampicillin and amoxycillin. Total serum IgE was 12 kU/l and specific IgE was negative by CAP RAST. Patch testing, also including cephalosporins, was initially negative, but at D6, there were positive reactions to both ampicillin and amoxycillin.

The 4th patient (F, 25 years) had a severe erythematous reaction of the head and neck, resembling a fixed drug eruption, accompanied by intense itching of the genital region, at a long unspecified time interval after an unrecorded oral antibiotic. I.d. tests were negative after 20 min, but amoxycillin became positive by D1 and ampicillin by D6. Total IgE was <4 kU/l, without specific IgE. Patch tests were positive at D4 to ampicillin and amoxycillin.

Discussion

Some authors define accelerated reactions as those occurring over 1 h after drug intake, and late reactions as those beginning after 48–72 h (9). However, there is now a consensus to unify the terms, referring to all reactions appearing later than 1 h as “non-immediate” (10). The pathogenesis of such reactions is thought to be T-cell-mediated (10), responding to glucocorticoids (11). In all 4 of our cases, tests for viral or bacterial infection (12, 13) were negative, excluding coincidental reactions (14), though non-immune delayed reactions to beta-lactam antibiotics are well-known (15).

The main finding in our patients was that both i.d.

and patch tests, which were negative at standard reading times, became positive long after the usual observation time, i.e., at D3 for i.d. and at D4 to D6 for patch test. This late positivity may also explain why so few patients with delayed cutaneous reactions to β -lactam antibiotics are reported to have positive patch tests (6), patch tests at D3 being still negative (16, 17). The number of delayed reactions diagnosed by such tests is not affected by the time delay in their application (18), in contrast to prick tests and specific IgE (19).

We therefore recommend that, in patients with delayed or late adverse cutaneous reactions to β -lactam antibiotics, all skin test sites should also be examined at D4 and D6 to detect these uncommon very late positive reactions.

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Eczematous plaques related to unfractionated and low-molecular-weight heparins: cross-reaction with danaparoid but not with desirudin

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Key words: heparin; low-molecular-weight heparin; heparinoids; recombinant hirudins; adverse drug reactions; medications; tolerance; delayed hypersensitivity. © Munksgaard, 2000.

When both unfractionated (UFHs) and low-molecular-weight heparins (LMWHs) cause eczematous plaques by (cross-) sensitization, danaparoid sodium (antifactor Xa) or hirudin (antifactor IIa) may sometimes be therapeutic alternatives (1), though cross-sensitivity may still occur (2).

therefore conducted with danaparoid (Orgaran®), a heparinoid, and desirudin (Revasc®), a recombinant hirudin (Table 1). Intradermal (i.d.) tests (1/100 and as is) were negative at 20 min, but an eczematous reaction (++) occurred at 4 days to danaparoid. All patch tests were negative at D2, D4 and D6.

Case Report

A woman who had had 3 episodes of eczematous plaques 36–48 h after subcutaneous (s.c.) calcium heparin and sodium dalteparin was referred for skin testing. S.c. challenge with 100 μ l each of sodium tinzaparin, sodium enoxaparin and calcium nadroparin, gave erythematous vesicular reactions at D2 to tinzaparin and enoxaparin and at D6 to nadroparin. Further tests were

Comment

Previous reports have identified cross-reactivity between s.c. danaparoid and heparins (3–6), featuring eczematous plaques, probably because both are of porcine intestinal mucosal origin. Our additional case, disclosing cross-reactions between UFH, LMWHs and heparinoid, illustrates the difficulty in identifying a safe heparin/heparinoid in cases of heparin-induced eczematous plaques,

Table 1. Results of prick, intradermal (id), subcutaneous (sc) and patch testing

	Prick 1/1 (20 min)	i.d.	s.c. 100 μ l (1/1)	Patch 1/1
<i>Innohep</i> ® No tinzaparin Na metabisulfite Na hydroxide	–	NT	– at 20 min ++ at D2	NT
<i>Lovenox</i> ® Na enoxaparin	–	NT	– at 20 min ++ at D2	NT
<i>Fraxiparine</i> ® Ca nadroparin HCl, Ca(OH) ₂	–	NT	– at 20 min ++ at D6	NT
<i>Orgaran</i> ® danaparoid Na Na sulfite	NT	– at 20 min ++ at D4 (1/100 and 1/1)	NT	– at D2, D4, D6
<i>Revasc</i> ® desirudin MgCl ₂ Na hydroxide mannitol 3%	–	– at 20 min – at D2, D4, D6 (1/100 and 1/1)	NT	– at D2, D4, D6

and reports a polypeptide hirudin sometimes being necessary.

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Eosinophilic cationic proteins in the peripheral blood of patients with contact allergy

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Key words: contact allergy; eosinophil cationic protein; blood eosinophil count. © Munksgaard, 2000.

Tissue damage in Type I allergy is due, among other things, to mediators released from eosinophil granules, and to eosinophil cationic protein (ECP) in particular (1, 2). Increased blood eosinophil counts have been reported in contact-sensitized laboratory animals (3).

Table 1. Patch test results

Allergen	No. positive reactions		total (n=89)
	male (n=27)	female (n=62)	
nickel sulfate 5%	4	27	31
formaldehyde 1%	12	13	25
cobalt chloride 1%	8	11	19
potassium dichromate 0.5%	10	7	17
fragrance mix 8%	4	9	13
thiuram mix 1%	2	9	11
thimerosal 1%	2	8	10
4-phenylenediamine 1%	5	2	7
glutaraldehyde 0.2%		7	7
Myroxylon Pereirae 25%	4	3	7
colophonium 20%	2	2	4
n-isopropyl-n-phenyl PPD 0.1%	2	1	3
acrylate		3	3
neomycin sulfate 20%	1	2	3
hydroquinone 1%		2	2
mercapto mix 2%	1	1	2
epoxy resin 1%	2		2
benzocaine 5%	2		2
MCI/MI 0.01%	1	1	2
quaternium-15 1%		1	1
Euxyl K 400 0.5%	1		1
parabens 12%	1		1
quinoline mix 6%	1		1

Materials and Methods

89 patients (62 women and 27 men, mean age 42.2 years) with contact dermatitis, without a history of atopy, with negative prick tests, total IgE below 100 kU/l, and with positive patch tests were studied. Controls comprised 25 healthy persons (16 women and 9 men), whose mean age was 41.7 years.

Patch tests with the European standard and additional series (Chemotechnique) were applied to the skin of the back. Readings were taken, after an application period of 2 days (D), at D2 and D4, according to the ICDRG (4). Prick tests were performed with vegetable pollen, house dust, mildew, goose and duck feathers, dog and cat hair, *Dermatophagoides pteronyssinus* and *Dermatophagoides farinae* (Allergopharma).

Total IgE was determined using Pharmacia ELKABE reagents and standards on a UniCAP-100 unit (normal values <100 kU/l).

Serum ECP was assayed with a double-antibody radioimmunoassay (Pharmacia & Upjohn). The limit level for ECP in healthy people was determined as 8.6 µg/l, the 95 percentile.

Eosinophilic granulocyte counts were obtained by

Table 2. Eosinophil count and ECP concentration in patients with allergic contact dermatitis

Eosinophil count	ECP concentration
from 27 to 1155/µl	from 1.48 to 74.278 µg/l
mean value 227.5/µl	mean value 12.854 µg/l
in 10 (11.2%) patients above 400/µl	in 57 (64.0%) patients above 8.6 µg/l

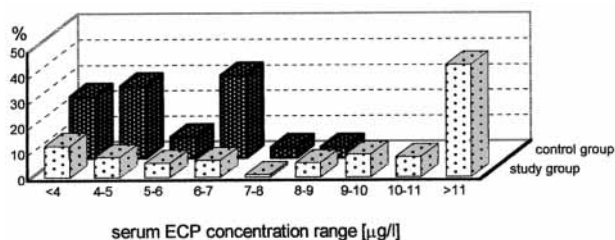


Fig. 1. Concentration of ECP in patients with allergic contact dermatitis and in controls.

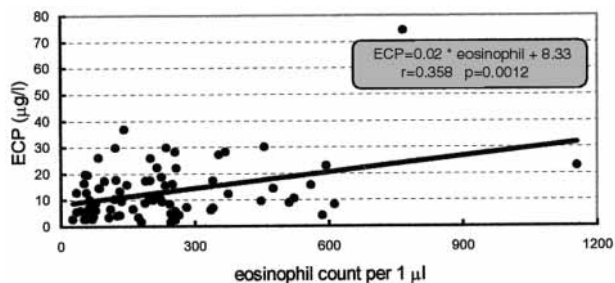


Fig. 2. The relationship between ECP concentration and eosinophil count in patients with allergic contact dermatitis.

counting total leucocytes on a Hemocell 1600 unit and calculating the % of peripheral blood eosinophils from their count in a specimen. Normal values ranged from 40 to 400 cells/ μ l.

Mean ECP concentrations were compared between the study group and controls, and the relationship between ECP concentration and eosinophil count determined. The likelihood ratio test was used in statistical calculations.

Results

Table 1 gives the results of patch tests.

Eosinophil counts in the blood of the study group ranged from 27 to 1155 cells/ μ l. In 10 patients, eosinophil counts were above 400 cells/ μ l (Table 2).

Mean ECP concentration in the study group was 12.854 μ g/l (1.48–74.278 μ g/l, SD-10.282 μ g/l) and differed ($p=0.0001$) from the mean concentration in the controls, which was 5.066 μ g/l (1.142–8.619 μ g/l, SD-1.798 μ g/l) (Fig. 1). In 57 (64%) patients with contact allergy examined, ECP values were above 8.6 μ g/l (mean value controls + 2 SD). Fig. 2 shows the relationship between ECP concentration and eosinophil count.

Discussion

Protein products released from eosinophils have been found in the serum of patients with asthma and atopic

dermatitis in particular (1, 2, 5–8), disease activity being found to be dependent on serum ECP levels (5, 9). We demonstrated no symptoms of the Type I allergy in our patients. In spite of that, the levels of eosinophil cationic protein in the serum of our patients were higher than those in healthy persons. This suggests that eosinophils and their mediators may contribute to the development of allergic contact dermatitis. In experiments on guinea pigs sensitized to various low-molecular-weight chemicals, we noted a considerable increase in blood eosinophil counts (10).

Acknowledgements

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Type I and Type IV immune responses to glyceryl thioglycolate*

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Key words: hairdresser; glyceryl thioglycolate; Type I immune reaction; Type IV immune reaction; contact urticaria; occupational; allergic contact dermatitis. © Munksgaard, 2000.

Type IV allergic contact dermatitis from glyceryl thioglycolate (GTG), a chemical used in "acid permanents", has been reported in hairdressers and their clients (1). GTG penetrates most protective gloves and remains on the hair long after it is permed (2).

Case Report

A 25-year-old woman attended beauty college for 1 year, after which she worked as a manicurist, and then as a hairdresser for 2 years. Her symptoms dated from a scissors injury to her left middle finger, which became infected and required treatment with systemic and topical antibiotics. Her hands did not clear completely until 7 months later, when she went on a 2-month maternity leave. Her hands were clear for 3 months after she returned to work, cutting hair only. Then, when she applied 2 permanents, the eczema recurred. Despite her not applying any more permanents, her hands continued to break out. For some duties, she wore vinyl gloves. She noted stinging and burning when she handled "dirty hair", shampooed hair, touched other cosmetics, or applied topical corticosteroid creams. She was suspended from work 3 months later. She had a previous history of asthma but not of eczema.

She presented with subacute dermatitis on the tops of and between the index and middle fingers of her left hand (between which she held hair while cutting it), extending to the ring finger. A milder dermatitis was seen on the right middle and ring fingers. She was patch tested with an extended NACDG screening tray, a hairdresser tray, her glove, her personal care items, and the cosmetics she used for her clients. She reported that several hours after the patch tests were applied, an erythematous streak developed at the site of the GTG patch test on the right side of her back and spread to the right elbow. She noted that this streak disappeared after several hours. At the D4 reading, she had a + reaction to GTG 1% pet. The same day, we applied GTG 1% pet.

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open on her left hand above the areas of dermatitis, and urticarial lesions developed at that site within 10 min.

2 weeks after being suspended from work, she returned to work for 1 day. Within hours of beginning work, her dermatitis flared on the left hand. She reported by phone 1 month and 18 months later that her skin remained clear as she retrained for clerical work.

Discussion

This patient had both Type I and Type IV sensitivity to GTG. In the only other report of Type I allergy to GTG of which we are aware (3), an 80% solution of GTG was sprayed on the face, arms, and chest of a hairdresser when a container burst. Chemical burns resulted and affected the patient's eyes. 4 days after the accident, generalized urticaria broke out; this condition recurred whenever the patient went to the beauty salon to work during the next 3 years. Repeated patch tests with GTG 1% pet. were negative, but a scratch test with a 1:12,500 saline solution of GTG was positive. These authors (3) hypothesized urticaria related to inhalation, instead of to skin contact as reported above.

Type I sensitization may be more common than reported. We were prompted to do an open test for urticaria only after the patient reported the brief episode of streaking erythema emanating from the GTG patch-test site.

Acknowledgement

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Results of patch testing with hydrocortisone butyrate in different vehicles

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Key words: hydrocortisone butyrate; vehicle; patch test method; corticosteroids; medicaments; false-positive reactions; methyl ethyl ketone; ethanol. © Munksgaard, 2000.

The most appropriate concentration and vehicle for patch testing corticosteroids remains debatable. Ethanol has been found to be more sensitive than pet. (1–3). With hydrocortisone butyrate, we found intradermal testing the most sensitive (4).

To increase further the sensitivity of the patch test, we compared ethanol (eth.) with other vehicles that are used in patch testing (5) or have been suggested as enhancing corticosteroid penetration (2, 6), and also recommended organic lipophilic bases (7).

Method and Results

Patients positive on patch testing to either tixocortol pivalate 1% pet. or budesonide 1% eth. were tested to hydrocortisone butyrate 1% in various vehicles. Of 39

patients, 21 had 1 or more reactions. The positive results are shown in Table 1.

Comment

Patient nos. 1–4 all produced reactions to vehicles A, B or both, indicating that the vehicles were irritant. These reactions cast doubt on the responses seen in patient nos. 3–8. It is probable that these are irritant rather than allergic and that vehicles A and B did not increase the sensitivity of the patch test. Patient nos. 9, 10 had reproducible reactions to hydrocortisone butyrate, with negative reactions when using eth. as vehicle. In these patients, no single vehicle gave consistently positive reactions. Methyl ethyl ketone (MEK) and Medilan oil were the only vehicles that consistently did not give reactions to vehicle control. Of the 3 vehicles, Medilan oil detected

Table 1. Positive results of testing hydrocortisone butyrate (HCB) 1% in various vehicles and controls at D 2 and D 4.

Patient no.	1	2	3	4	5	6	7	8	9*	10
HCB in eth.										
HCB in Medilan										++&NT
Medilan										
HCB in Medilan oil									+&-	
Medilan oil										
HCB in Acetadepts									?+&+	
Acetadepts									?+&-	
HCB in MEK									?+&+	
MEK										
HCB in vehicle A				?+&+	-&++	-&+	+&+	-&++	?+&?+	++&NT
vehicle A		?+&-		-&?+					?+&?+	
HCB in vehicle B			+&+	+&++				-&++	-&+	++&NT
vehicle B	?+&?+		-&+	?+&++					-&?+	++&NT
Patient no.	11	12	13	14	15	16	17	18	19	20
HCB in eth.	+&++	+&+	-&++	?+&++	+&+	-&+	++&++	-&++	-&++	+&++
HCB in Medilan	+&++	+&+	-&?+	?+&+	+&++	-&?+	+&NT	++&NT		++&NT
Medilan										+&NT
HCB in Medilan oil	-&++	-&+	-&+	++&+	+&++	-&?+		++&NT		++&NT
Medilan oil										
HCB in Acetadepts	++&++	+&+	-&+	?+&+	++&+	+&+	?+&NT	++&NT		++&NT
Acetadepts										
HCB in MEK	-&+	+&+	-&++	-&+	+&+	-&?+	+&NT	++&NT	?+&++	+&NT
MEK										
HCB in vehicle A	?+&++	+&+	-&++	++&++	+&+	-&?+	+&NT	++&NT	+&++	+&NT
vehicle A	?+&+					-&?+			+&++	
HCB in vehicle B	-&++	++&+	?+&++	?+&++	++&++		++&NT	++&NT	+&++	++&NT
vehicle B				?+&+	-&?+	-&?+			+&++	

* Good history of exacerbation with topical use; 1 patient excluded from analysis because of unreadable conjoined positive reactions. MEK=methyl ethyl ketone; vehicle A=ethanol 45%, propylene glycol 10%, isopropyl alcohol 45%; vehicle B=propylene glycol 70%, propylene carbonate 17%, water 13%.

9, ethanol 10 and MEK 11 of the 12 patients (9–20) considered to be allergic to hydrocortisone butyrate.

Ethanol has, till now, been our vehicle of choice when testing hydrocortisone butyrate. Irritant reactions to ethanol are very rare in our experience and we did not include ethanol as a control in the study. There has, nevertheless, been speculation that metabolic alteration in dehydrogenase function may predispose to corticosteroid contact allergy, through increased production of hapten, with parallel irritant reactions to ethanol from excess production of acetaldehyde (8). It has, furthermore, been suggested that true contact allergy to alcohol might be related to corticosteroid allergy (9). In our group of patients, we consider the reactions to vehicles A and B are better explained by irritancy. It should be noted that, where performed, patch tests to 20% aqueous propylene glycol were negative.

The results of this study suggest that the use of MEK for detecting delayed hypersensitivity to corticosteroid by patch testing may result in a more sensitive test with a low incidence of false-positive reactions. The high number of reactions seen to the vehicle A and B controls emphasizes the importance of being aware that an isolated reaction to corticosteroid in some recommended vehicles (2, 5) may be potentially irritant.

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Allergic contact dermatitis due to Icelandic poppy (*Papaver nudicaule*)

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Key words: phytodermatitis; poppies; *Papaver nudicaule*; Icelandic poppy; plants; allergic contact dermatitis; opium; morphine. © Munksgaard, 2000.

Case Report

An elderly lady presented with acute eczema of her palms and perioral skin, which developed after gardening. She had many flowering plants, including Icelandic poppies (*Papaver nudicaule*) that were treated as weeds. She had a long previous history of eczema and was already known to be fragrance and nickel sensitive. She had been avoiding these allergens conscientiously and had achieved good control of her eczema.

Patch testing was performed the following summer, using 8-mm Finn Chambers, to the Chemotechnique plant series, privet leaf, lawn grass, and poppy stem and leaf (bruised beforehand). Readings were made at D2 and D4. The patient developed ++ reactions to both poppy parts, most marked at D4, the other tests remaining negative. 5 control patients were tested to the same parts of the poppy: none developed a positive reaction.

We concluded that our patient had developed contact

allergy to poppies, avoidance of this plant having prevented further flares of acute dermatitis.

Discussion

A small number of plant families cause 95% of all reported cases of plant dermatitis confirmed by patch testing (1). In a patient with a history strongly suggestive of plant allergy and negative patch testing, it is, however, important to test to individual species within each group. 1 recent paper revealed that sesquiterpene lactone mix 0.1% pet. failed to detect 38% of Compositae-sensitive patients (2). A careful history and a visit to the patient's home may be required to identify the relevant plant. When patch testing with an unfamiliar plant, several different parts of the plant should be used, as allergy may be more concentrated in 1 part than another (1).

Contact allergy to poppies has not previously been reported, though there are reports of contact dermatitis from opium and morphine. In the past, these drugs were obtained by drying latex from the seedpod of *Papaver somniferum* (3) and contained a mixture of compounds; these days, synthetic opiates are used. A woman developed dermatitis of the eyelids following instillation of 2% ethylmorphine hydrochloride into her conjunctival sac as treatment for cataracts (4). A child developed dermatitis from wet dressings of lead and opium for cutaneous infection of the scrotum. Patch testing to the constituents of the dressing and to powdered opium confirmed contact allergy to opium. This child developed further dermatitis when given parenteral opium (5); to

our knowledge, our patient has never received a systemic opiate.

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Gold sensitivity in Israel – consecutive patch test results

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Key words: gold; gold sodium thiosulfate; contact allergy; relevance; children; nickel; cobalt; chromate. © Munksgaard, 2000.

Gold sensitivity remains controversial (1). Allergic contact dermatitis from gold has been described only rarely (2), though rates of patch test allergy from 1 to 23% have been reported (3–12).

Patients and Methods

406 consecutive patients, attending the contact dermatitis clinic of Rabin Medical Center, were patch tested with gold sodium thiosulfate (GST) 0.5% pet. (Chemotechnique), added to the European standard series, using Finn Chambers on Scanpor tape. Patch tests were removed after 2 days (D), and readings made at D2 and D3, as recommended by the ICDRG. All patients completed a questionnaire prior to patch testing.

Table 1. Details of the positive and negative groups derived from questionnaire

	Positive group	Negative group
mean age (years)	38.4	44.2
female:male ratio	33	1.54
direct skin contact with gold objects	73%	50%
pierced ears	79%	48%
gold dental restorations	21%	17%
history of gold therapy	3%	none
self-reported suspicion of gold allergy before testing	none	2%
history of resolution of eczema after gold avoidance	6%	2%

Results

Of the 406 patients tested for GST, 34 (8.4%) had a positive reaction: follicular in 2 patients, ?+ in 2, + in 24, ++ in 6, and +++ in 4. The mean age of the positive and negative groups was 38.4 years (range 9–70 years) and 44.2 years (range 4–90 years), respectively. The positive group contained 3 children aged 9–14 years. The female:male ratio was 33:1 (33) in the positive group and 212:138 (1.54) in the negative group.

The questionnaire responses are shown in Table 1. Only 1 patient (3%) had a history of gold therapy. None of the patients who were positive to GST had suspected gold allergy before testing. Only 2 such patients had a history of eczema that resolved after gold avoidance.

23 of the GST-sensitive patients also had positive reactions to the European standard series: 16 to nickel, 9 to chromate, 6 to cobalt, 5 to fragrance mix, 2 to 4-para-phenylenediamine (PPD), 2 to MCI/MI and 1 each to neomycin, benzocaine, N-isopropyl-N'-phenyl-4-phenylenediamine, epoxy resin, 4-tert-butylphenol-formaldehyde resin, formaldehyde and sesquiterpene lactone mix.

Discussion

Recent studies using GST have reported gold allergy in 3.2% (8) to 13% (5) of consecutively patch tested patients, compatibly with our study (8.4%). Also in keeping with previous reports, almost all the patients were female (4, 5). All 3 of the GST-sensitive children wore gold jewellery and 1 was also positive to nickel. A high

proportion of the positive patients (68%) had other positive reactions to the European standard series, many to other metals (nickel, chromate and cobalt).

The clinical relevance of a positive patch test to GST remains difficult to evaluate, there being no overall difference between positive and negative groups with respect to attributability of symptoms to gold.

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Polyhexamethylenebiguanide: a relevant contact allergen?

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Key words: polyhexamethylenebiguanide; polyaminopropyl biguanide; CAS 28 757–47–3; hexamidine isethionate; CAS 659–40–5; cosmetics; preservative; biocide; contact allergy; surveillance; relevance; occupational; hospital cleaner. © Munksgaard, 2000.

Polyhexamethylenebiguanide (PHMB) (Fig. 1) has long been used as a biocide and more recently as a preservative in cosmetics. As PHMB is biocidal (1–3) and particularly because it is structurally related to hexamidine (Fig. 1), to which Type-IV sensitization has been reported (4), we added it to the cosmetics and medicaments series of the German Contact Dermatitis Group (DKG).

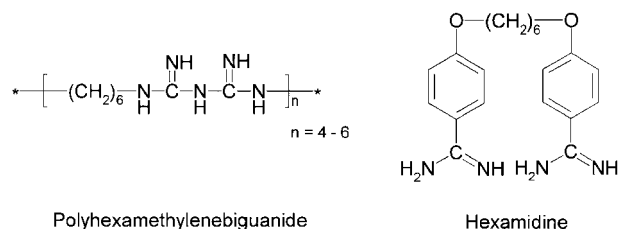


Fig. 1. Chemical structures of the diamidine biocides polyhexamethylenebiguanide and hexamidine.

Patients and Methods

10 of the 33 departments of the IVDK (1) participated in the study conducted in 1998. Patients included were those suspected as having contact allergies to cosmetics and medicaments. The patch test population ($n=1554$) is described by the MOAHLFA index (1) as follows: M: 35%, O: 15.4%, A: 18.6%, H: 30.6%, L: 14.5%, F(ace): 18.7%, A (age >40 years): 62.5%. PHMB was supplied by Unilever Research and tested at 2.5% aq. Exposure to the patch was 1D in 389 (25%), and 2D in 1165 (75%). Reading was carried out at D3.

Results

6 patients (3 men, 3 women, 1 with atopic dermatitis, all age >40 years) had a + reaction, none had ++ or +++ reactions. 3 others had IR or ?+ reactions. In 2 patients with a + reaction, there was definitely no relevance (other allergens being unequivocally causal), in 3 relevance was unknown, and in 1 it was current: the patient

worked as a hospital cleaner with a PHMB-containing disinfectant. In the atopic dermatitis patient, an 'angry back' reaction cannot be excluded as the total number of reactions was 15.

Discussion

In a previous series of 374 patients tested to 2.5% PHMB, 2 positive reactions were found, 1 being possibly relevant (5). Our 6 + reactions (=0.4%) represented a similarly low sensitization rate (5). 1 of our reactions may have been false-positive, and only 1 relevant, and that not due to cosmetics. The absence of any ++ or +++ reactions may imply that there were other false-positives.

There are 3 possible explanations of the results of our study.

(1) Too low a patch test concentration (2.5%). Biocides, in general, are known for their irritant potential (3). However, the number of ?+/IR reactions ($n=3$) to PHMB was surprisingly low. Furthermore, the same concentration had previously been tested at St John's (5).

(2) PHMB not yet being used very frequently in cosmetics or in other products with significant skin exposure.

(3) The sensitizing potency of PHMB being low, as suggested by predictive tests (6, Basketter, personal communication).

In summary, our study shows PHMB sensitization to be extremely rare, which is in line with expert assessment (7). Nevertheless, consideration should be given to testing with PHMB, together with other preservatives, in individual cases.

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Localized aquagenic urticaria

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Key words: localized urticaria; aquagenic urticaria; hands; plastic gloves; occupational; sweating; p-phenylenediamine.
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A 30-year old non-atopic woman had a 4-year history of pruritic 2–3 mm wheals surrounded by erythema localized on her hands with sparing of palms. No other areas of the skin were affected. This happened within 5 min of contact with water, regardless of its temperature. Sweating, provoked by plastic gloves worn at work, provoked the same lesions. The urticaria spontaneously cleared without residua in 20 min. She never wore rubber gloves because these had caused dermatitis some years ago. Previous treatment with oral antihistamines, cetirizine and hydroxyzine had been ineffective. Full blood count, differential leukocyte count, erythrocyte sedimentation rate, thyroid function tests and immunoglobulin levels were normal.

Patch testing to the European standard series showed a positive reaction to p-phenylenediamine (PPD) at D2

and D4. An ice-cube test was negative. Water challenge tests were performed by immersing 1 hand in water for 5 min at 20°C and 37°C on different days. This elicited small punctate wheals on the hand tested, resolving spontaneously after 20 min. The same tests were negative on the arm and foot. No urticarial reaction occurred when acetone was applied locally for 5 min.

Comment

Approximately 25 cases of aquagenic urticaria have been reported (1), but to our knowledge, only 1 other case of localized aquagenic urticaria (2). It has been suggested that an epidermal water-soluble antigen diffuses into the dermis and causes histamine release from sensitized mast

cells (3). Localized cold urticaria has been connected with antigenic stimulus or tissue injuries (4–6).

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Recurrent rejection of a spinal cord stimulation system

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Key words: spinal cord stimulation; foreign body reaction; low-virulence infection; contact sensitivity, complication.
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Spinal cord stimulation (SCS) consists of positioning an electrode in the epidural space on the dorsal aspect of the spinal cord at the level of the nerve roots innervating a painful area, electric current from the electrode bringing about paraesthesia, a sensation that suppresses the pain. Current from the electrode is supplied by a pulse generator in the lower anterior abdominal wall. The complication rate related to SCS systems has been reported to vary between 20 and 75% (1). In 5 to 15% of cases, complications of various kinds necessitate removal of the system (2, 3). The main cause for system removal is infection.

Case Report

A 52-year-old male reflex sympathetic dystrophy patient was being successfully treated by SCS. 2 months after implantation, he presented with signs of an infected SCS system. The skin overlying the pulse generator and the extension lead was diffusely touch-sensitive, though there was no erythema or swelling. Body temperature was 37.8°C, ESR 22 mm/h, C-reactive protein 8 mg/l and leucocytes 16.9* 10⁵/l. All symptoms remained for a period of 10 days, after which time it was decided to remove the complete system.

After opening the skin, the system was found to be surrounded by a clear exudate. The tissue displayed no signs of infection and there was no pus present. Bacteriological cultures of wound fluid and system material grew no pathogens. Over the course of the following month, after a 14-day course of 2000 mg flucloxacillin oral daily, clinical signs of infection faded and blood counts returned to within the normal range.

2 months after removal, the SCS system was re-implanted. 9 months later, signs of infection recurred, exactly repeating those observed during the 1st episode. As the symptoms did not subside, we were forced to remove the complete system once again. The results of the

operation and bacteriological culture were similar to the previous findings. To investigate the possibility of an allergic contact hypersensitivity to parts of the SCS system, patch testing was performed. The tests included rubber and metal screening series, as well as silicone rubber and metal parts obtained from the pulse generator. None of the materials tested proved to be a sensitizer. The unknown cause of the recurrent clinical picture of infection has excluded this patient from further treatment with SCS.

Comment

Because of the position of the SCS electrode in the epidural space, all consequences of infection may be dramatic; 1 patient, e.g., developed paraplegia following infection (2). Therefore, signs of infection should always lead to immediate removal of the complete SCS system. Once signs and symptoms of infection with negative bacteriological cultures had occurred for the 2nd time, we suspected contact hypersensitivity to materials of the SCS system to be the cause of rejection.

Although a very rare condition, allergic reactions to cardiac pacemakers have previously been reported. Allergic reactions, however, are regularly characterized by responses of the skin overlying the pacemaker, e.g., an erythematous rash (4), local swelling and pruritus (5), or vesicular lesions (6). A striking feature in the present case was the *lack* of any such visible skin reactions.

The contact eczema in cases reported previously developed after a period varying from 2 days to 24 months, and consequently the 2 periods of, respectively, 2 and 9 months between SCS system implantation and the start of rejection symptoms does not rule out the possibility of contact hypersensitivity. The negative patch tests, on the other hand, indicate that an allergic reaction is unlikely, although false negativity is a well-known problem of such tests (7).

In summary, the present case report describes a patient who responded to SCS positively, but who could not continue to undergo this treatment because of inflammatory-type reactions of unknown pathophysiology.

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Allergic contact dermatitis due to clobetasone butyrate

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Key words: allergic contact dermatitis; clobetasone butyrate; corticosteroids; medicaments; D7 reading. © Munksgaard, 2000.

Case Report

A 36-year-old man, with a long history of atopic dermatitis of the neck, chest and arms, complained of an exacerbation on his neck after applying 0.05% clobetasone butyrate ointment (Kindavate®) and 0.3% prednisolone valerate acetate ointment (Lidomex®). Patch testing with these agents revealed a positive reaction only to the 0.05% clobetasone butyrate ointment on D7. Further patch testing with individual ingredients, including pure 0.05%, 0.01% and 0.005% clobetasone butyrate, disclosed a positive reaction only to this ingredient (Table 1). The patient did not agree to further patch testing with other corticosteroids which might induce cross-sensitivity.

Comment

Tixocortol pivalate, hydrocortisone butyrate and budesonide are important markers of corticosteroid contact allergy (1). In contrast, allergic contact dermatitis due to clobetasone butyrate is rare. Only 1 case has been previously reported in the English literature (2), in which a reaction to clobetasol propionate was also shown. Review of the Japanese literature revealed a further 2 cases (3, 4). It is essential to read reactions on D 7 when patch testing with corticosteroids, because positive reactions may be slow to appear.

Contact Dermatitis 2000; 40: Table 1. Patch test results

Allergen	%/veh	D2	D3	D7
Lidomex® ointment	as is	—	—	—
Lidomex® cream	as is	—	—	—
Kindavate® ointment	as is	—	—	+
clobetasone butyrate	0.05% pet.	—	?+	+
clobetasone butyrate	0.01% pet.	—	?+	+
clobetasone butyrate	0.005% pet.	—	?+	+
white petrolatum	as is	—	—	—
paraffin oil	as is	—	—	—

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Epoxy-by-proxy dermatitis

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Key words: epoxy resin; 2-part paint; contamination work clothing; domestic clothes washing; allergic contact dermatitis; airborne. © Munksgaard, 2000.

Case Report

A 54-year-old woman presented with a 4-day history of dermatitis of her neck and face, particularly the eyelids. 2 years previously, she had presented with similar facial dermatitis, and had been patch tested to our standard series, face series and her own cosmetics. The following positive reactions had been seen at 2 and 4 days: epoxy resin ++; imidazolidinyl urea ++; benzophenone-4 +; moisturizer containing benzophenone-4 +. No relevance was found for the epoxy resin reaction at that time.

Since patch testing, she had assiduously avoided all topicals containing benzophenone-4 or imidazolidinyl urea. 24 h before the present recurrence, she had visited her son who worked at a paint factory preparing 2-part epoxy paints. Because his washing machine had broken down, she had washed all his work-soiled clothes for him by hand, wearing protective gloves.

Comment

We believe that our patient developed facial allergic contact dermatitis following contact with unhardened epoxy resin in components of 2-part paint. The non-working (1) as well as the working environment (2) can be a source of epoxy resin. It is worth enquiring about the occupations of other members of the family circle when faced with an unexplained patch test reaction to epoxy resin. ('Proxy' is a legal term for one person acting on behalf of another.)

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Allergic contact dermatitis from benzalkonium chloride in an antifungal solution

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Key words: allergic contact dermatitis; antifungals; benzalkonium chloride; medicaments; patch testing technique. © Munksgaard, 2000.

Case Report

A 35-year-old woman presented with an 8-month history of intensely pruritic eczema, beginning on the feet and spreading to the lower legs. The lesions were erythematous to dark-brownish, edematous, lichenified, and exudative. There were no systemic symptoms and no personal or family history of atopy. She had been treated intermittently with Triaxin® (NDC Laboratories, USA), an antifungal solution, for tinea pedis.

Patch tests with the European standard series and a shoes series (Chemotechnique Diagnostics, Malmö, Sweden) were all negative, but Triaxin® as is was strongly positive. On patch testing with the ingredients of Triaxin®, benzalkonium chloride (0.1% aq. and 0.01% aq.) elicited ++ reactions and all other ingredients were negative (Table 1). Patch tests with benzalkonium chloride (0.1% aq. and 0.01% aq.) in 5 control subjects were negative. We observed a focal flare of her skin lesions during patch testing. The patient was recommended to

stop using this medicament, and her condition soon improved thereafter.

Discussion

Benzalkonium chloride is widely used for disinfection and preservation (1–3). A well-known irritant, but a rare sensitizer, recent reports have described it as causing allergic contact dermatitis, stomatitis and conjunctivitis (2–5). Systemic reactions from chemically-related drugs, such as cholinergics, antihypertensives, neuromuscular blockers, or heparin antagonists, have also occurred (2, 4).

Although the standard patch test concentration of benzalkonium chloride is 0.1% aq., this may still elicit false-positive irritant reactions (1). To confirm the positive reaction to benzalkonium chloride (0.1% aq.), we performed a patch test with benzalkonium chloride (0.01% aq.), as recommended by Andersen & Rycroft (6), as well as a control study with benzalkonium chlor-

Table 1. Patch test results

	D2	D4
European standard series	—	—
shoes series	—	—
Triaxin [®] as is	++	++
ingredients of Triaxin [®]		
benzalkonium chloride		
0.1% aq.	++	++
0.01% aq.	++	++
propylene glycol 5% aq.	—	—
triethanolamine 2% pet.	—	—
citric acid 1% aq.	—	—
quaternium-15 1% pet.	—	—
distilled water	—	—

ide (0.1% aq. and 0.01% aq.). This, together with the focal flare that was provoked, provides sufficient evidence for the diagnosis of allergic contact dermatitis from benzalkonium chloride.

This is the 1st report of allergic contact dermatitis from benzalkonium chloride in antimycotics.

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Dihydrocodeine: a drug allergy diagnosed by patch testing

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Key words: co-dydramol; dihydrocodeine; codeine; opioids; medicaments; cutaneous adverse drug reactions; positive patch test; lack of cross-sensitivity. © Munksgaard, 2000.

Case Report

A 49-year-old woman developed a widespread maculopapular eruption 24 h after taking 2 co-dydramol tablets for toothache. She had presented on several previous occasions with rashes presumed, at the time, to be due to antibiotics. It became apparent, on reviewing her case notes, that on each occasion that she had been thought to have had a cutaneous reaction to an antibiotic, she had also received dihydrocodeine for analgesia.

She was patch tested with the European standard series, antibiotics and analgesics (Table 1), the largest dose tablets being ground up and dispersed at 20% pet. Intradermal tests to penicillin and cefuroxime were negative. RASTs to penicillin G, penicillin V and ery-

thromycin were negative (class 0), and cefuroxime class 1.

Comment

Dihydrocodeine is a widely-prescribed semi-synthetic opioid (1). A positive patch test to dihydrocodeine has previously been reported as a cross-reaction with codeine phosphate (2). Codeine phosphate has been reported as causing fixed drug eruption (3) and erythema multiforme (4), and elicit a positive patch test in a generalized dermatitis (5), an occupational dermatitis (6) and an urticarial (2).

It seems likely that all our patient's drug eruptions are explained by her allergy to dihydrocodeine. She had taken either co-dydramol (10 mg dihydrocodeine tartrate and 500 mg paracetamol per tablet), or DF 118[®] (dihydrocodeine tartrate 30 mg) on each such occasion.

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Table 1. Patch test results

Allergen	% w/v	D2	D4
codeine phosphate	20% pet.	—	—
dihydrocodeine tartrate	20% pet.	++	++
erythromycin	20% pet.	—	—
benzylpenicillin	20% pet.	—	—
cefuroxime	20% pet.	—	—
paracetamol	20% pet.	—	—
metronidazole (Metrotop [®] gel)	as is	+	+

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An unusual cause of post-auricular dermatitis

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Key words: allergic contact dermatitis; thiuram mix; rubberized spectacles retainer; armed forces. © Munksgaard, 2000.

Case Reports

Case no. 1

A 19-year-old Chinese national serviceman presented with a 2-month history of itchy post-auricular rash in August 1993. There was no personal history of atopy, but his sister had allergic rhinitis. Bands of eczema were detected in the retro-auricular crease and on the posterior aspect of the pinna.

Case no. 2

A 20-year-old Chinese national serviceman presented with a 1-month history of pruritic rash behind the ears in November 1996. He had a past history of asthma and atopic dermatitis. Symmetrical erythematous scaly patches were present behind both ears.

Case no. 3

Another 20-year-old Chinese national serviceman presented with a 2-week history of rash behind the ears in June 1998. There was no personal or family history of atopy. Symmetrical brown patches were seen behind both ears.

All 3 patients reported prior use of rubberized spectacles retainers as a curved pliable extension to the posterior ends of the earpieces of their spectacles, to stabilize them while undergoing vigorous military physical training.

They were patch tested to the National Skin Centre standard series, additional rubber series and their own spectacle retainers, in the manner recommended by the ICDRG (1). All 3 patients were positive to thiuram mix and the rubberized spectacles retainers. Patient no. 3 also reacted to carba mix.

They were treated with topical corticosteroid and were advised to stop wearing their rubberized spectacles retainers. Patient no. 1 continued to wear the retainer, but avoided direct skin contact by applying a plaster over it.

Upon review in 4 to 6 weeks, there was complete clearance of the post-auricular dermatitis in all 3 patients.

Discussion

Nakada & Maibach (2) included metals, plastics, plasticizers, solvents, UV stabilizers, antioxidants, dyes and waxes among causes of allergic contact dermatitis from spectacles. Rubber was not one of the reported contact allergens. Hearing aids can also lead to symmetrical post-auricular dermatitis, as well as to dermatitis in the external auditory meatus, reported allergens including acrylates, plastics, UV stabilizers and para-tertiary-butylphenol-formaldehyde resin (3–6). Rubber is again not one of the reported contact allergens. Thiurams (7) have not previously been reported as contact allergens in rubberized spectacles retainers.

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Combined contact allergy to tea tree oil and lavender oil complicating chronic vulvovaginitis*

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Key words: allergic contact dermatitis; medicaments; herbal remedies; tea tree oil; lavender oil; essential oils.
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Tea tree oil is used in cosmetic, "over-the-counter" and dermatological preparations (1). Its antiseptic (2) and antimicrobial (3) properties are well accepted and it has been demonstrated to be efficacious in acne (4).

Case Report

A 28-year-old woman was referred to the Department of Genilo-Urinary (GU) Medicine with a 4-year history of vulval and perianal soreness and irritation, which had been unsuccessfully treated by her general practitioner with oral and topical antifungals. She was noted to have eczema of her right hand and gave a 6-month history of a rash on her right hand, legs, forearms, periorbital area and axillae. She had used tea tree oil products extensively and had also used creams containing lavender oil.

Examination revealed marked erythema and lichenification of the groin, suprapubic area and perianal and vulval mucosa. Her right (dominant) hand showed eczema while the left hand was unaffected. She also had an eczema of the periorbital area and axillae. A curdy vaginal discharge and a large ectropion was noted. Microscopy of the vaginal secretions revealed candida. Tests for gonorrhoeae, chlamydia and trichomonas infection were negative. The patient was advised to stop using tea tree and lavender oil products and prescribed miconazole nitrate cream vaginally, and clobetasone butyrate, nystatin and oxytetracycline cream, and an emollient, for her skin lesions. The rash cleared completely in 1 month.

Patch testing, using Finn Chambers on Scanpor Tape (Epitest, Finland), with the European standard series, tea tree oil (Thursday Plantation), and aromatherapy lavender gel (Boots, Nottingham), showed positive reactions at day (D) 2 and D 4 to quaternium-15 (+), tea tree oil (++), and lavender gel (++). Further patch testing to the constituents of the lavender gel confirmed allergy to lavender absolute (++ D 2 and D 4 at 10% pet. and 50% pet., – at 2% pet.) Subsequently, patch testing 50 controls with lavender oil absolute 10% pet. produced no positive reactions.

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Discussion

Tea tree oil is an essential oil in which gas chromatography has revealed approximately 100 different plant terpenes, the principal being terpinen-4-ol and 1,8-cineole (5). Australia is the only country producing tea tree oil commercially (6). The first report of allergic contact dermatitis was by Apted (7) in 1991. Subsequently, De Groot & Weyland (8) reported generalized contact dermatitis due to tea tree oil ingestion. Use in the genital and perianal area may mimic chronic fungal vulvovaginitis. Our patient undoubtedly had had several attacks of candidal vaginitis and had used tea tree oil products with subsequent exacerbation.

Lavender oil is an essential oil obtained from *Lavendula officinalis* and is widely used in perfumery, typically in aromatherapy (9). Lavender oil contains geraniol, linalool and linalyl acetate (10). Allergic contact dermatitis has been reported in those using it medically (11), in aromatherapy and occupationally (12). Lavender oil can also cause photosensitization (13) and induce pigmentation (14). Patch testing is usually carried out to 2% lavender oil absolute. We suggest that this concentration may be too low to identify all cases of lavender oil sensitivity and that 10% may be more appropriate.

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Possible allergy to complex titanium salt

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Key words: titanium; axillary dermatitis; allergic contact dermatitis; irritant contact dermatitis; cosmetics; patch testing technique. © Munksgaard, 2000.

Case Report

We report the results of an investigation of axillary dermatitis arising during a routine human skin irritancy study. 23 volunteers participated in a study which involved normal use of a marketed antiperspirant deodorant in one axilla, whilst a novel formulation was assessed in the other. The novel formulation contained 10% ammonium titanium lactate (ATL) as an alternative to the common aluminium chlorhydrate active.

Following approximately 2 weeks of 1× or 2× daily use, a number of panellists developed mild/moderate axillary irritation to the prototype formulation. This was generally seen as localized mild to moderate erythema, in some cases with follicular involvement; upon appearance of this reaction, axillary exposure was stopped. In 2 cases, the reaction intensified for a few days after cessation of exposure and was slow to resolve. Although minor skin irritation is often seen during axillary studies, the development of such reactions led to the suspicion that, at least in certain individuals, the mechanism might be allergic.

Patch testing was carried out on 30 individuals (9 male, 21 female; age range 25–54 years, mean age 40 years) divided into 3 groups: group A ($n=11$) were panellists with an adverse skin reaction to the ATL-containing formulation; group B ($n=10$) were panellists who

been exposed to the ATL-containing formulation, but who had had no skin reaction; while group C ($n=9$) were matched individuals who had never knowingly been exposed to ATL. 8 mm Finn Chambers on Scanpor (Epitest, Finland) were applied for 2 days (D) and reactions read 1 h after removal and at D3. The patch test substances applied were 5% nickel sulfate, 1% cobalt chloride, 10% titanium dioxide (all in pet.), together with 10% ATL in base formulation and the base formulation alone. The reactions in the 3 groups are shown in Table 1.

Positive reactions (one +++, one ++ and one +, all tending to be stronger at the later reading) were seen to ATL in group A; there were no reactions to ATL in either groups B or C. A small number of reactions were also seen in each group to common metal allergens, but there was no pattern relating these reactions to any other, including the response to ATL. No reactions were seen to the base formulation or to any other allergens tested.

Discussion

Titanium allergy is very rarely reported/discussed in the literature, to the point where the impression is that this metal may not be associated with allergy (1, 2). Nevertheless, the results of patch testing clearly indicate that

Table 1. Patch test results

Grade of reaction	Group ² →	ATL-containing product			Non-ATL-containing product			Cobalt chloride			Titanium dioxide			Nickel sulfate ¹		
		A	B	C	A	B	C	A	B	C	A	B	C	A	B	C
–		8	9	10	11	9	10	9	8	10	11	9	10	6	8	7
+		1	0	0	0	0	0	2	0	0	0	0	0	0	0	0
++		1	0	0	0	0	0	0	1	0	0	0	0	3	1	2
+++		1	0	0	0	0	0	0	0	0	0	0	0	0	0	0

¹3 panellists (2 in group A, 1 in group C) not tested with this material due to known allergy.

²Group A comprised individuals with an apparent skin reaction to the ATL-containing product; group B were individuals treated with an ATL-containing product but with no adverse reaction; group C were individuals not exposed to ATL-containing products.

3 individuals appear to have developed contact allergy to a complex titanium salt, ATL. Since there were no reactions in groups B and C, we were convinced that the reactions seen must be allergic.

Given that ammonium lactate/lactic acid are not sensitizing, at the least not significantly so, we suspected that titanium might be the important element driving these allergic responses. Some scattered reactions also occurred to cobalt and to nickel, but these did not correlate with the responses to ATL, ruling out cross-reactivity as an explanation. As mentioned above, titanium is widely used without generating any real evidence to date of skin sensitization. No responses were seen to the titanium dioxide patch tests. As a consequence, we conclude that it may be the complex ammonium titanium lactate salt that may actually be responsible.

However, it might be interesting to investigate the use of ATL as a patch test agent in cases of suspected titanium allergy. Recently, workers in Japan (3) have sug-

gested that titanium chloride or sulfate at 0.1% or 0.2% in pet. may be a useful indicator of titanium allergy. At this early stage, however, it is not possible to comment on the relationship between positive patch test reactions to these simple salts, compared with the reactions to the more complex salt described herein.

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Contact dermatitis from tosylamide/formaldehyde resin with photosensitivity

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Key words: allergic contact dermatitis; photosensitivity; tosylamide/formaldehyde resin; nail varnish; cosmetics.
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Case Report

A 55-year-old housewife, with a history of allergy to penicillin, had used many cosmetics since the age of 35 years without problems. In June 1999, she noted pruritus on the neck, which in a few days increased to erythema and papules. Her dermatologist recommended avoidance of inexpensive jewelry, and treated her with a topical corticosteroid. 15 days later, after a domestic accident, she was hospitalized with a fracture of the right leg and pelvis. During 30 days of hospitalization, she had no further symptoms on the neck. Once discharged, she returned home and felt pruritus on the neck again. Within a few days, erythema and papules had reappeared in this area, with symptoms clearly worsening with solar exposure. At patch testing, there were excoriations, papules and erythema on both sides of the neck.

On patch testing (D2 and D4 readings): TestTM allergens were negative:

1. the standard TRUE;
2. the Chemotechnique perfumes series was negative;
3. the Chemotechnique cosmetics series was negative.

2 months later, as the patient continued to insist on her worsening in the sun, we phototested her, with a normal result, and then photopatch tested her with the Scandinavian photopatch test series, with the addition

of tosylamide/formaldehyde resin, with the following positive reactions:

	Irradiated		Non-irradiated	
	D2	D4	D2	D4
tosylamide/ formaldehyde resin 10% pet.	+	++	?+	+

After this, the patient stopped using nail varnish and, with topical corticosteroids, the whole condition disappeared within 20 days.

Discussion

Contact dermatitis due to nail varnish is commonly caused by tosylamide/formaldehyde resin (1–5), which had therefore been replaced by alternatives in some products (6). Onycholysis has also been described from it (7), as well as bladder cancer induction in mice (8, 9). Some have claimed that it is present as an impurity in saccharin (10, 11), though our patient had been using such a sweetener for more than 10 years with impunity.

We have never observed photosensitivity associated with tosylamide/formaldehyde resin allergy before. This

resin should surely be included in any cosmetics series, though it is *not* in the current Chemotechnique one.

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Flare-up reaction of pseudoephedrine baboon syndrome after positive patch test

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Key words: flare-up reaction; baboon syndrome; pseudoephedrine; ephedrine; sympathomimetic drugs; cutaneous adverse drug reactions; positive patch test; cross-sensitivity. © Munksgaard, 2000.

Pseudoephedrine and ephedrine are both based on a phenylpropanolamine skeleton, and the only difference between them being the configuration of the asymmetric carbon bearing the hydroxyl group, which is S in the former and R in the latter (1). Allergic reactions from sympathomimetic drugs are rare despite extensive use as vasoconstrictors (2). Pseudoephedrine may produce a non-pigmenting fixed drug eruption, its most frequent cutaneous adverse reaction (2–4), pustular eruption (5, 6), eczematous eruption (1), generalized red itchy dermatitis (7), generalized erythematous rash with facial angioedema (8) and scarlatiniform rash (9).

Case Report

A 73-year-old woman consulted us about pruritic symmetric erythema on her buttocks, abdomen, back, groins, inner thighs, ankles and palms, proceeding to papules and pustules over these regions, 6 h after taking 1 capsule of Logradin® (loratadine, pseudoephedrine, titanium dioxide, talc, saccharin, Avicel ph 10.5, lactic acid sulfate, calcium sulfate hydroxide, gum arabic). Biopsy showed subcorneal and suprabasal pustules, edema in the papillary dermis and an inflammatory infiltrate, with eosinophils, in the papillary and reticular dermis. The lesions cleared 15 days after stopping the drugs, and treatment with oral and topical corticosteroids. The patient's medical history revealed a similar erythematous

eruption 20 years ago, after taking a drug that contained ephedrine.

Patch testing was performed with the GEIDC standard series, components of Logradin® and ephedrine. The patient showed positive reactions to nickel sulfate 5% pet. (++) , pseudoephedrine 1% pet. (++) and ephedrine 1% pet. (++) at D2 which persisted to D4. The pseudoephedrine and ephedrine reactions were pustular. Biopsy of the patch test reaction to pseudoephedrine showed subcorneal pustules, some of them in follicles, spongiosis in the Malpighian layer, severe edema and a perivascular mixed-cell infiltrate, with eosinophils, in the papillary dermis. We observed 2 erythematous plaques, away from the patch tests and at sites where she had previously developed the eruption, one on upper left scapular region, 1 cm in diameter, and another in the middle of the back, 3 cm in diameter, at D4. Biopsy of these plaques showed vesicles, spongiosis (without pustules), slight edema, and a lymphocytic infiltrate. Patch testing with pseudoephedrine 1% pet. was negative in 42 controls.

Discussion

The appearance of cutaneous lesions similar to baboon syndrome after Logradin® ingestion, positive patch test with pseudoephedrine, flare-up reaction after patch test with pseudoephedrine, and negative controls confirm a drug eruption from pseudoephedrine, via (at least) a

Type IV hypersensitivity reaction. Positive patch test to ephedrine and an eruption 20 years ago after taking oral ephedrine suggest a cross-reaction between pseudoephedrine and ephedrine (1, 3). Histopathologic findings of positive pseudoephedrine patch test and flare-up reaction have not been reported previously. None of these features are specific for a drug eruption, but the presence of eosinophils in the inflammatory infiltrate favors this diagnosis.

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