

CONTACT POINTS

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Severe contact allergy to footwear in a young child

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Key words: allergic contact dermatitis; atopy; balsam of Peru (*Myroxylon Pereirae*), children; chromate; cobalt; colophony; footwear; plantar juvenile dermatitis; PTBPF resin.

Although previously considered rare, allergic contact dermatitis in children is a significant clinical problem (1–3). It becomes more frequent with increasing age (4). By the age of 5 years, children are just as susceptible to being sensitized to an allergen as an adult (3).

Case Report

A 5-year-old female patient, with plantar juvenile dermatitis and family and personal history of atopic dermatitis, presented with bilateral and symmetrical diffuse erythema, vesicles, bullae and exulcerations on the dorsum of her feet and toes as well as on the plantar surfaces, with severe itching (Figs 1 and 2). The lesions evolved for 1 year and aggravated whenever she wore shoes, especially in summer. The severity of the clinical picture kept her away from school causing a significant impact in her psychosocial development.

Patch tests with standard series of Portuguese Contact Dermatitis Group (GPEDC) and shoe series (Chemotechnique®) resulted in the reactions summarized in Table 1.

We advised the parents to use chromium-free tanned leather footwear over 2 pair of cotton socks. We also stressed the need of having 2 pairs of shoes to alternate day-by-day, allowing them to dry. Although



Fig. 1. Exsudative ulcerations of the dorsum of the feet and toes.

not sensitized, the use of rubber shoes was not recommended. Occlusion and moist environment would worsen juvenile plantar dermatitis and could promote new sensitizations. The use of topics containing Balsam of Peru was forbidden. With these strategies and topical corticosteroids, the lesions improved gradually and disappeared in 3 weeks with no recurrence in a 6-month follow-up.

Discussion

Foot eruptions in children are usually self-limiting, but occasionally symptoms may persist and be resistant to

treatment. Allergic contact dermatitis must be considered in such cases (5).

Contact dermatitis due to shoes has not much been described in children, accounting for its probably underestimated incidence and prevalence (1, 6).

Patch testing is usually required for a definitive diagnosis, although it has not yet been standardized in children (1). This should not present practical difficulties, because patch testing has been performed and shown to be of benefit even in children younger than 2 years of age. The concentrations used for testing in adults can safely be used when patch testing infants and children (4, 7).



Fig. 2. Erythema, exudation and bullae of the plantar surfaces of both feet.

Table 1. Results of patch tests with standard series of GPEDC and shoe series (Chemotechnique®)

	D3
Potassium dichromate (0.5% pet.)	++
Cobalt chloride (1.0% pet.)	++
Colophony (20.0% pet.)	++
Balsam of Peru (25.0% pet.)	+
p-tertiary-butylphenol-formaldehyde resin (1.0% pet.)	+++

pet. = petrolatum.

In the literature, in children as well in adults, the most common sensitizers are represented by rubber chemicals (1, 2, 5, 6, 8, 9), p-tertiary-butylphenol-formaldehyde resin in adhesives (1, 8, 9), chromium salts used as tanning agents (1, 5, 6, 8, 9), colophony (5, 6, 8), dyes (1, 6) and more rarely nickel (1). Patients with atopic eczema also tend to react to constituents of topical medicaments and topical antibiotics, the most frequent sensitizers being benzocaine, neomycin, gentamycin, balsam of Peru and parabens (1, 2, 5).

Avoiding the shoes or allergens that have been identified is often sufficient to improve the symptoms (1, 8).

With reference to atopic children having a lower capacity for sensitization than nonatopics, like several other authors, we agree that atopic children have a greater capacity for sensitization (10, 11).

Therefore, we recommend that all patients with foot dermatitis, which does not respond to treatment, should be patch tested to exclude shoe allergy, as this represents a potentially curable condition (8).

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Contact allergy to cinnamal in a patient with oral lichen planus

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Key words: allergic contact stomatitis; cinnamal; cinnamon; food flavourings; oral lichenoid dermatitis; oral lichen planus.

Case Report

A 44-year-old woman presented with a 6-month history of painful white plaques on her tongue, buccal mucosa and gums. She had been diagnosed clinically with persistent oral candidosis, but had failed to respond to treatment with nystatin suspension or oral fluconazole. Fungal cultures were negative, as were her human immunodeficiency virus, hepatitis and antinuclear antibody serologies. On examination, she had hyperkeratotic plaques covering the majority of her dorsal and lateral tongue and involving her buccal mucosa. Amalgam fillings and acrylic restorations were present, but there was no gold. A biopsy from the buccal mucosa showed oral lichen planus (OLP).

Patch testing with a standard series, a dental series, food dyes, a fragrance screen (including fragrance mix), spearmint, peppermint and chewing gum showed positive reactions to nickel (++) , cobalt (+), cinnamal 1% pet. [+ on day (D) 2, ?+ at D4], wood tars (+) and methylhydroquinone (+). There were also ?+ reactions to neomycin, Euxyl K 400 and Disperse Blue 124. She had diminished salivary production with and without flavour stimulation, and decreased tear production by the Schirmer I test.

The patient stated that she chewed cinnamon-flavoured gums and ate cinnamon-flavoured candies throughout each day. She discontinued cinnamon gums and candies, and avoided toothpaste containing cinnamal, and when seen 1 month later, her OLP had cleared completely, without other treatment.

Discussion

The term 'lichenoid' is sometimes used to describe lichen planus-like eruptions due to drugs, as well as allergic contact dermatitis and stomatitis (1). In many cases, the presentation is clinically and histologically indistinguishable from idiopathic lichen planus (1, 2). Such lesions have been attributed to a wide variety of possible causes (3), including contact allergy. A classic example is the lichenoid contact dermatitis from exposure to colour film developers (4). Oral lesions have been

associated with allergy to dental restorations containing acrylates (5) and various dental metals, including mercury (6), gold (7), chromate and cobalt (8), copper (9), zinc (10), palladium and platinum (11). Eugenol has been reported to exacerbate OLP (12), and sensitivity to colophonium has also been associated with oral lichenoid lesions (OLL) (13). Allergy to flavours, including menthol (14), peppermint (14) and spearmint (15) have been linked with OLL and OLP less frequently, although there are several reports of allergy to cinnamal with lichenoid dermatitis and stomatitis (16–19).

The present case is of particular interest because the patient, who had what seemed clinically and histologically to be severe OLP, experienced a dramatic clinical response following discontinuation of products containing cinnamal, despite her weak patch test reaction (+).

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A case of type IV hypersensitivity to topiramate and carbamazepine

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Key words: carbamazepine; delayed-type allergy; drug eruption; topiramate.

Case Report

Cutaneous adverse reactions during antiepileptic therapy are rather frequent. The most involved drugs are aromatic anticonvulsant such as carbamazepine, primidone, phenytoin and phenobarbital (1). These drugs are often responsible for adverse reactions which are grouped in the anticonvulsant hypersensitivity syndrome (AHS), which usually develops 2–8 weeks after the beginning of therapy; this syndrome is characterized by rash, fever, lymphadenopathy and rarely eosinophilia, elevation of liver enzymes and involvement of other organs (2, 3). Pathophysiologic mechanism of this syndrome is still not well known, but it has been proposed that arene oxides, the toxic metabolite of aromatic anticonvulsant (Fig. 1), could bind to cellular macromolecules causing cell aggression or a secondary immunological response (4).

Adverse reactions such as pruritic and erythematous rashes, photosensitivity, alterations in skin pigmentation, exfoliative dermatitis, Stevens–Johnson syndrome and AHS are described in 2–4% of patients on carbamazepine (5). Some authors (6, 7) have demonstrated a type IV cell-mediated allergy to carbamazepine or to its metabolite carbamazepine epoxide in patients with skin eruptions due to this antiepileptic therapy.

Topiramate is a sulfamate-substituted monosaccharide (Fig. 1), with a molecular structure different from the other antiepileptic drugs parasthesia is the most common side-effect. No cases of type I or type IV hypersensitivity to topiramate have been described. In a recent work, 5 cases of pruritus during antiepileptic therapy with topiramate were described (8).

We present the case of a 55-year-old woman with seizures, observed with erythema of the neck, nausea and vomiting after a 2-month treatment with topiramate (TopamaxTM) 100 mg a day. The drug was immediately discontinued and all symptoms disappeared in few days.

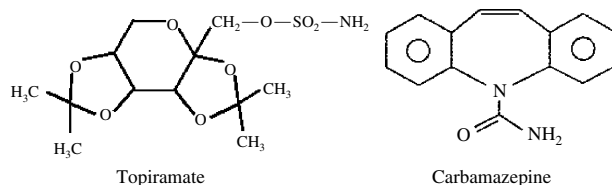


Fig. 1. Molecular structures of topiramate and carbamazepine.

Then the patient was treated with carbamazepine (TegretolTM) 200 mg a day, but after 2 weeks she presented erythema and oedema of the face and pruritus of the legs. Carbamazepine was immediately discontinued, and symptoms disappeared in some days.

So the patient was treated with clonazepam with no side-effects.

The patient underwent a complete allergological evaluation; skin prick and patch tests with topiramate and carbamazepine were performed. Skin prick tests were carried out on the volar surface of the forearm using the tablet powder dissolved in saline at a concentration of 90 mg/ml. Patch tests were performed using both drugs dissolved in petrolatum at a concentration of 10%.

Evaluation of skin prick test was assessed after 20 min and 48 hr, and all resulted negative. Patch tests evaluated after 72 hr were positive for both drugs [++ according to the NACDG recommendation (9)].

Patch tests with carbamazepine and topiramate carried out in 10 healthy subjects were negative.

The patient was also skin prick and patch tested with other anticonvulsant drugs (phenytoin, phenobarbital, primidone, lamotrigine, valproic acid, levetiracetam, vigabatrin, tiagabine and citicoline) with negative results (skin prick and patch tests were performed using the tablet powder, dissolved, respectively, in saline, at a concentration of 90 mg/ml, and in petrolatum, at a concentration of 10%).

The clinical findings and results of the allergological evaluation put in evidence the coexistence in the same patient of a Type IV, cell-mediated hypersensitivity to carbamazepine and to topiramate. An immunological cross-reactivity between carbamazepine and topiramate can be ruled out because the 2 drugs have a different chemical structure (Fig. 1) and belong to different classes of anticonvulsant drugs.

Moreover, this is the first report in literature of an allergic reaction to topiramate.

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Contact allergy to topical corticosteroids in children with atopic dermatitis

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Key words: atopic dermatitis; contact allergy; topical corticosteroids.

Since their introduction in the clinical practice in 1952, topical corticosteroids have been the mainstay of treatment for atopic dermatitis (AD) (1). Topical corticosteroids can induce side-effects, which may be local or systemic, including hypersensitivity reactions.

However, anti-inflammatory and immunosuppressive properties of corticosteroids can mask the sensitization. So, steroid hypersensitivity should be considered in any patient whose dermatitis fails to improve or worsens after systemic or topical administration of corticosteroids.

The aim of this study was to evaluate the prevalence of contact sensitization to topical corticosteroids in patients with AD.

Patients and Methods

We studied 71 children (35 males and 36 females) with AD, ranging from 5 to 12 years (mean 7.6 years), attending the paediatric ambulatory of our dermatological clinic over a period of 1 year (July 2003 to July 2004). All patients had used topical corticosteroids for a period longer than 6 months, during the last 2 years. The most used were hydrocortisone-17-butyrate, mometasone furoate, methylprednisolone aceponate and betamethasone-17-benzoate. Hydrocortisone-17-butyrate and methylprednisolone aceponate are known

as sensitizers. The SCORAD index was used to evaluate the severity of eczema (2). 30 children (42.2%) had mild AD (SCORAD lower than 25); 31 (43.6%) had moderate AD (SCORAD from 25 to 50); 10 (14.1%) had severe AD (SCORAD higher than 50).

Eighteen of the 71 patients (25.3%) with AD reported a history of aggravation or not improvement by topical corticosteroids. Within the sample of patients observed and relative to the improvement/aggravation of their symptoms during the treatment, the levels of the SCORAD index found were significantly different ($\chi^2 = 8.91$; $P = 0.012$).

All the kids were patch-tested with our children patch-test series (Table 1), with the markers of sensitization to topical corticosteroids (tixocortol pivalate 0.1% pet., budesonide 0.01% pet. and hydrocortisone-17-butyrate 1% ethanol) (3) and with topical preparations used by patients. Patch test were performed using Finn Chambers® (Epitest Ltd OY, Tuusula, Finland), and readings were made after 2, 4 and 7 days. Reactions were read and interpreted according to ICDRG guidelines.

Results

1 child (1.4%) (female, 6-year-old, SCORAD = 38.3) was positive to tixocortol pivalate, hydrocortisone-17-butyrate and Locoidon® cream

(+D2/+D4/+D7). She referred an aggravation of dermatitis after the use of the topical above mentioned. 4 of 71 patients (5.6%) showed positive patch test to nickel sulphate; 1 (1.4%) reacted to potassium dichromate and to *p*-tert-butylphenol formaldehyde; 2 (2.8%) were positive to mercaptobenzothiazole and 2 (2.8%) to lanoline alcohol. The remaining 61 patients (85.9%) were negative to tested allergens.

Discussion

In our study, the contact sensitization to topical corticosteroids resulted rare in AD children, despite the prolonged use of topical corticosteroids.

This might be explained by down-regulation of the Th1 cells in AD subjects (4).

To conclude, corticosteroid contact allergy does not seem to explain a significant number of patients with aggravation of AD during topical corticosteroid treatment.

However, although contact sensitization with topical corticosteroids seems to be rare in children with AD, it is useful to perform patch test with these drugs because it is clinically impossible to distinguish an exacerbation of AD from contact allergy to corticosteroids. On the other hand, chronic eczema may go on without exacerbation and still be corticosteroid allergy.

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Allergic contact dermatitis from triphenyl phosphite

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Key words: allergic contact dermatitis; triphenyl phosphate; triphenyl phosphite.

Triphenyl phosphite (TPP) is a clear liquid that slowly hydrolyses to liberate phenol. It is insoluble in water, but soluble in aromatic organic solvents. It is used as reactive diluent for epoxides and as antioxidant and stabilizer in phenolic, polyethylene, polyvinyl chloride, polyurethane and polyolefin resins. It confers increased heat resistance to the finished products, where it is used as a flame retardant. It is considered a neurotoxin as well as a cutaneous irritant and sensitizer (1). Adverse cutaneous reactions to TPP have been described only twice: 1 case of

Table 1. Allergens and vehicles used in our children patch test series

Allergens	% Vehicle
Nickel sulphate	5% pet.
Neomycin sulphate	20% pet.
Wool alcohols	40% pet.
Thiuram mix	1% pet.
Para-tertiarybutyl phenol formaldehyde resin	1% pet.
N-isopropyl-N-phenyl-paraphenylenediamine	0.1% pet.
Fragrance mix with sorbitan sesquioleate 5%	8% pet.
Potassium dichromate	0.5% pet.
Balsam of Peru	25% pet.
Disperse blue mix (124/106)	1% pet.
Mercaptobenzothiazole	0.25% pet.
Para-phenylenediamine	1% pet.
Colophony	20% pet.
Benzocaine	5% pet.
Euxyl K400 [methyltribromo glutaronitrile/phenoxyethanol (1 : 4)]	1% pet.
Carba mix	3% pet.
Ammoniated mercury	1% pet.
Ethylenediamine dihydrochloride	1% pet.
Methyl-chloro-isothiazolinone	0.01% aq.
Dimethylaminopropylamine	1% aq.

allergic contact dermatitis and 1 report of contact urticaria (2, 3). We have witnessed a case of allergic contact dermatitis to TPP that followed an initial irritant exposure.

Case Report

A 46-year-old man has been working for 6 years in a plastic pipe factory. He is regularly exposed to epoxy and phenolic resins and with amine catalysts. At times, he must work on a production line that makes fireproof pipes for electrical wiring, where he adds a solution of Doverphos-10[®] (100% TPP) to the resin mixture. In March 2004, he accidentally spilled undiluted Doverphos-10[®] on his forearms and abdomen, and within 4 days developed a painful dermatitis at those sites. With time, the lesions became pruritic and spread to the upper chest, neck and arms. With topical corticosteroid treatment, the eruption slowly resolved over 1 month. In May and June, the patient tried to return to work and within 4 hr, without obvious contact, developed what he described as an itchy, warm, sheet-like redness involving the previously affected areas. This eruption would disappear within 1 hr of leaving the workplace and has not been documented. The patient was withdrawn from work, pending the results of the investigation.

Patch testing was done in October 2004 with the NACDG standard series, with a glues and adhesives series that contain triphenyl phosphate (Chemotechnique, Malmö, Sweden), and with Doverphos-10[®] 2.5% and 1.25% in pet. 4 controls did not react to these concentrations of TPP. At D2 and D4, the patient showed a + reaction to Doverphos-10[®] 2.5% only.

Discussion

Recommended concentrations for patch testing with TPP range from 0.05% to 0.1% pet. (2, 4). We elected to test our patient with concentrations of 1.25% and 2.5% pet. because 4 controls did not react to these concentrations. The morphology of our patient's reaction was suggestive of a true allergic reaction. We believe that our patient's initial irritant contact dermatitis paved the way for subsequent sensitization with autoeczematization, a phenomenon already described (5). This is further corroborated by the fact that 4 of 4 controls developed an irritant reaction to TPP 5% pet. and that 1 became actively sensitized, developing after 14 days a long-lasting + reaction at the site of the previous irritant patch test reaction.

We cannot exclude the possibility that the sensitizer was not phenol, since it was not tested separately; however, we believe this unlikely, even though TPP is known to slowly release small amounts of phenol. We have difficulty in explaining the reactions that have occurred on 2 separate occasions at work after our patient's initial reaction with Doverphos-10[®], since he had no further contact with this product. However, he describes the workplace a hot and stressful environment. Although TPP has been described as a cause of contact urticaria (3), it is most likely that his reactions were triggered by heat in his work environment, thereby causing erythema at the site of his partly healed contact dermatitis.

Triphenyl phosphate is a well-known plasticizer in the plastic industry and, like TPP, is also used as flame retardant in phenolic resins, celluloid, nitrocellulose, and acetocellulose.

Similar to the case of O'Driscoll et al. (2), our patient showed no reaction when tested to triphenyl phosphite. Although triphenyl phosphite and TPP share a similarity of names and chemical structures (Fig. 1), they do not seem to cross-react.

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Erythema multiforme due to methotrexate reproduced with patch test

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Key words: methotrexate, erythema multiforme, patch test, drug eruption

Case Report

We present the case of a 74-year-old woman with seronegative poliartthritis diagnosed 3 months ago. The

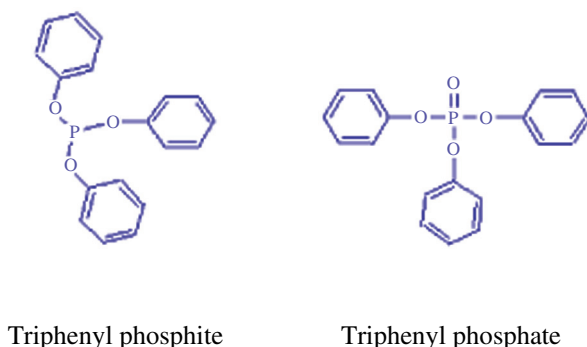


Fig. 1. Chemical structures of triphenyl phosphite and triphenyl phosphate.

patient had been treated during the last 2 months with oral ibuprofen, naproxen and omeprazol and subcutaneous methotrexate, 20 mg per week plus oral folic acid rescue (15 mg) 24 hr later. The patient was referred with a cutaneous rash affecting the trunk and the extremities, which had started 20 days ago. Initially, the lesions consisted in erythematous macules and papules that had become progressively confluent over the skin surface of the trunk, both arms and legs. During the last days, a diffuse tender erythema with extensive erosions developed over the left arm. A positive Nikolsky's sign was also present, but no blisters were observed. Palms, soles and mucosal surfaces were not affected. No fever was detected. Blood cell count and liver function test did not show abnormalities. A skin biopsy was taken from the left arm. The sections showed a lichenoid tissue reaction, with dermal oedema and a moderate perivascular infiltrate composed of lymphocytes and eosinophils. Based on these features, a diagnosis of erythema multiforme was therefore made. Oral and topical corticosteroids were prescribed, and all the medication that the patient was receiving was discontinued. With this treatment, the cutaneous lesions resolved within 14 days showing re-epithelialization without progression to extensive full thickness skin loss.

6 months later, a patch test study was performed. We tested the GEIDC standard series, the most usual antiseptics used in our country (chlorhexidine digluconate, etanol 70% and iodine povidone) and the patient's previous medication: ibuprofen 5% pet, naproxen 5% pet, omeprazol as is, Acofol[®] (folic acid) as is and Methotrexate Lederle[®] (1 vial, 25 mg/ml) as is. All tested materials were applied on Finn chambers and fixed with Scanpor[®] tape. The patient removed the patches after 2 days, and a first reading was performed on the 3rd day. The test results were graded according to the criteria of the International Contact Dermatitis group. On D3, only potassium dichromate 0.5% was positive (++). On a second reading on D7, papules, oedema, erythema and pruritus were detected in the area where methotrexate patch was placed (+). No lesions beyond the

patched area were observed. A punch biopsy from the patch test area was performed. Again, the sections showed a lichenoid tissue reaction with similar features to the previous biopsy, but in less intense grade, erythema multiforme-like. Patch testing with Methotrexate Lederle[®] as is was also performed in 10 healthy controls, with negative results.

Discussion

Many cutaneous adverse reactions to methotrexate have been reported in the literature including mucositis, urticaria, angioedema, photosensitivity, alopecia, maculopapular eruption, erythema, desquamation, erythema multiforme, Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), cutaneous vasculitis, radiation recall dermatitis and erosion of psoriatic plaques (1–3). In some of them, as urticaria or angioedema, an allergic mechanism is clearly involved. Others, like alopecia, are toxic-mediated reactions. But whether erythema multiforme, SJS and TEN are allergic or toxic-mediated reactions remains controversial (1). In the cases reported in the literature, frequently appears the association to non-steroidal anti-inflammatory drugs (NSAIDs) concomitant intake (as in our case) or the increasing in the methotrexate dosage (1, 2). Non-steroidal anti-inflammatory drugs, sulphonamides and salicylates may compete with methotrexate for albumin-binding sites, causing an increase in free active methotrexate in the serum (1). This would suggest a toxic dose-dependent mechanism for toxicity. But no patch test studies were performed in any case of SJS nor NET associated to methotrexate intake (1–3). In the literature, only appears patch test study performed with this drug in 2 cases of occupational dermatitis associated to methotrexate manufacture. In these cases, patch tests were able to demonstrate sensitization to methotrexate and precursors (4, 5).

In conclusion, we have reported a new case of erythema multiforme associated to methotrexate. An allergic mechanism explained this cutaneous reaction, and it could be demonstrated with patch test. The positive reaction to methotrexate

was detected late, in the 7th day, clinically and histopathologically.

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Garlic-fingered chefs

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Key words: allergic contact dermatitis; chef; garlic; non-dominant hand.

Case Report

Allergic contact dermatitis to garlic is described in caterers and can be an important occupational hazard. Our department provides dermatology care for an area in East London with a large immigrant population from Bangladesh. The catering trade is a major source of employment in the area. We commonly see curry

Table 1. Patients tested to diallyl disulphide, (n = 26)

Occupation	Curry chef	Housewife	Others
Patch tested to diallyl disulphide	13	11	2
Positive patch test to diallyl disulphide	4	0	0
Atopic	1	7	1
Type 1 symptoms	0	0	0

chefs with hand dermatitis, and we wanted to see whether garlic was an important allergen in this group.

We reviewed the notes of all patients who had been patch tested to diallyl disulphide during a 12-month period. With the aim of recruiting further chefs to our study, we also visited 32 local curry restaurants, and we wrote to local general practitioners asking them to refer chefs with hand dermatitis.

Of the patients tested to 5% diallyl disulphide, we noted which hand was involved and occupation. We enquired about atopy and the presence of type 1 symptoms after contact with garlic. We also recorded the treatment given and the subsequent response (Table 1).

All 4 chefs who had positive patch tests to diallyl disulphide had presented with dermatitis of the non-dominant hand, with hyperkeratosis and fissuring of the thumb, index and middle finger. We advised them to avoid contact with garlic and onion and prescribed topical emollients and potent topical corticosteroids. We reviewed all chefs at 3 months. 1 had managed to change job and had no further contact with garlic or onion. His dermatitis cleared. The other 3 continued to work as curry chefs and found it impossible to avoid chopping garlic. Garlic and onions have to be chopped by hand – garlic crushers are slow and electric processors are invariably being used for some other ingredient. It is impractical for chefs to wear gloves. 1 patient responded very well to Acitretin at a daily dose of 25 mg. 1 responded well to topical psoralen-ultraviolet A (PUVA) after 12 weeks. Both continue to work as curry chefs. The fourth chef also continued to work and has a persistent dermatitis but has declined further dermatology care.

Discussion

Garlic has long been recognized as an occupational hazard amongst chefs, housewives and those who practise herbal remedies. It is best known as a powerful irritant.

There are relatively few reports of allergic contact dermatitis to garlic in the literature (1) and rarely systemic contact dermatitis to garlic has been seen (2). This small study shows that it is a problem amongst curry chefs who find it difficult to avoid exposure to this allergen in the course of their work. Treatment may be difficult and require second line therapies.

As garlic is such a powerful irritant, its constituent diallyl disulphide at strength ranging from 1% to 5% is used to test for allergy. Type 1 reactions to garlic have been rarely reported.

In summary, we show that garlic is an important sensitizer in curry chefs. Avoidance is very difficult. We have demonstrated the benefit of using Acitretin or hand PUVA.

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Occupational allergic contact dermatitis to sodium lauroyl sarcosinate in the liquid soap

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Key words: cosmetics; occupational allergic contact dermatitis; soaps; sodium lauroyl sarcosinate; surfactant cleaning agents.

Case Report

A 41-year-old nurse enrolled in Graduate Degree Program developed acute severe eczematous reaction on her hands, face and neck. She was originally evaluated by an allergist who thought she might have a latex allergy. However, immunoglobulin E latex serology was negative and dermatitis persisted even though she started to wear and use latex-free gloves and products. Patient thought that her dermatitis always developed after required out-of-town hospital rotation and possibly related to soap used at that particular hospital. Open and unoccluded patch tests showed +3 bullous reaction to Acute Kare hand soap manufactured by Steris Company but not to any other ingredients of TROLAB European Standard Tray Patch Test Panel or other personal hygiene products including open unoccluded patch tests to two other soaps. After confidentiality agreement about ingredient disclosure with Steris Company was signed, the patient was patch tested with individual ingredients labelled by Steris Company as A to G. Repeated patch tests showed +3 bullous reaction to ingredient G which was disclosed to be 30% aqueous solution of sodium lauroyl sarcosinate in sterile water containing no preservatives. 2 volunteers were also patch tested to ingredients G and Acute Kare soap. The results of the patch testing were completely negative. Once the patient stopped using Acute Kare soap, her symptoms immediately resolved, and she has remained symptom-free for the past 10 months.

Discussion

Allergic contact dermatitis to wash off products such as soaps are uncommon but have been reported including a report by these authors (1). Sodium lauroyl sarcosinate is a surfactant-cleansing agent widely used in soaps, shampoos and body washes. According to the FDA data, sodium lauroyl sarcosinate has been used in at least 118 cleansing formulations (2). According to the Cosmetic Ingredient Review Panel, it is supposed to be totally non-irritating and non-sensitizing (3). We believe this is a first literature report of

allergic contact dermatitis to sodium lauroyl sarcosinate. However, Fisher listed sodium lauroyl sarcosinate as a potential allergen in his textbook of dermatology (3).

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Provocative use test of 1 euro coin in nickel-sensitized subjects

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Key words: contact dermatitis; euro coins; nickel.

Nickel sensitization represents the most common cause of contact allergy in industrialized countries (1). Sensitization is acquired by exposure to nickel containing objects like jewellery, while the role of other sources of sensitization like coins, tools, handles, and keys is difficult to establish. These objects briefly in contact with the skin are not covered by the nickel directive (2). Earlier studies have shown that the 1 and 2 euro coins release very high amount of nickel (3). Considering the wide prevalence of nickel contact allergy and everyone's daily contact with money, it is necessary to establish if handling euro coins may elicit contact dermatitis in nickel-allergic people especially in subject occupational exposed to euro coins. The purpose of this study was to evaluate skin reactivity to a prolonged contact with euro coins at the palmar site of the hands and at the volar site of forearm.

Materials and Methods

We studied 15 volunteers (10 with relevant nickel-sensitization and without clinical signs of dermatitis and 5 healthy subjects). Patch test were performed with serial dilutions (5, 1, 0.5, 0.1, 0.05, 0.01 and 0.005%)

of nickel sulphate hexahydrate (Sigma, St. Louis, MO, USA) in distilled water and with 1 euro coin, in a 'circulated' condition, not cleaned or pretreated. The serial dilutions of nickel sulphate were applied to the healthy skin of the forearm by means of Finn Chambers on Scanpor[®] tape (Epitest[®], Tuusula, Finland) containing a filter paper disk. The euro coins were applied contemporaneously to the healthy skin of the contralateral volar site of forearm, thenar eminence and thumb (palmar side), and fixed with tape (Fixomull[®], Beiersdorf, Germany). Patch test responses were evaluated at 48 and 72 h (D2 and D3) and scored as follows: erythema = 1, erythema, infiltration = 2, erythema, infiltration, some papules and/or vesicles = 3; erythema, infiltration, many papules and/or vesicles = 4; erythema, infiltration, spreading papules and/or vesicles = 5. Patch test responses graded ≥ 2 were considered positive.

Results

All nickel-sensitized subjects (100%) showed positive reactions to the provocative test with 1 euro coin at the volar site of the forearm with a good correlation between intensity of skin response and positive reactions to the lowest nickel sulphate concentrations (Table 1). Positive reactions at the thenar eminence and thumb were observed only in 1 patient (10%), who showed a low-sensitization threshold to nickel expressed by positive reactions to low-nickel concentrations (0.005%).

Table 1. Patch tests results in 10 nickel-sensitized volunteers

Number	Patch tests with serial dilutions of nickel (D3)							Patch tests with 1 euro coin (D3)		
	5%	1%	0.5%	0.1%	0.05%	0.01%	0.005%	Forearm	Thenar eminence	Thumb
1	2	2	1	—	—	—	—	2	—	—
2	2	—	—	—	—	—	—	2	—	—
3	2	2	1	—	—	—	—	2	—	—
4	2	2	—	—	—	—	—	2	—	—
5	5	5	3	3	2	2	2	3	2	2
6	2	—	—	—	—	—	—	2	—	—
7	2	—	—	—	—	—	—	2	—	—
8	3	2	1	—	—	—	—	2	—	—
9	2	—	—	—	—	—	—	1	—	—
10	2	2	—	—	—	—	—	2	—	—

1 = erythema; 2 = erythema, infiltration; 3 = erythema, infiltration, some papules and/or vesicles; 4 = erythema, infiltration, many papules and/or vesicles; 5 = erythema, infiltration, spreading papules and/or vesicles.

Discussion

The role of coined money as an elicitor of nickel-related hand eczema has been a matter of controversy since 1930 (4). In this study, we have demonstrated that skin reactivity to euro coins is low at the palmar site of the hands. This may be correlated to the protection of the thick horny layer and explains the low incidence of nickel hand dermatitis from normal handling of euro coins (5). These results indicate that hand eczema in nickel-sensitized subject is more probably associated to skin irritation from water, soap or food or to unknown endogenous factors rather than the release of nickel from coins (6). However, this study confirms the results of our previous research in which we demonstrated that skin reactivity to euro coins is high at the forearm (7). Thus, nickel transfer from the hands to other sites of the body (for example, eyelids) resulting from manipulation may induce dermatitis. Further studies are necessary to establish the role of euro coins in maintenance of hand eczema in nickel-sensitized patients, where the compromised skin barrier may facilitate penetration of nickel and hence greatly increase reactivity.

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Contact urticaria and respiratory symptoms induced by indirect contact with goat dander: a case report on vet's wife exposure

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Key words: allergy; asthma; contact urticaria; goat dander; indirect exposure.

Case Report

Contact with goats may sensitize such people as veterinary surgeons, laboratory workers and farmers (1, 2), but it should be stressed that this occupation may be an important risk factor for sensitization by passive transport also to the family members of the people working with animals.

A 45-year-old woman was referred to clinic because of acute urticaria and respiratory symptoms, such as chest discomfort and dyspnea, which had appeared when her husband who was a veterinary surgeon returned home after working at a goat farm. A detailed interview revealed that the symptoms usually appeared at about 1 hr after the man would return home and that he would not always change his clothes and had a bath after coming back from work. The vet's wife would often find goat dander on his clothes and shoes.

The patient did not notice any symptoms when the husband had been exposed to other farm animals, and she also had no symptoms while exposed to dogs and cats. She reported no other allergic diseases in the past.

The level of total immunoglobulin E (IgE) (Unicap; Pharmacia,

Uppsala, Sweden) was 89 kU/l. Prick tests to common allergens were negative, and those with animal epithelia (cats, dogs, rats, mice, horses, guinea-pigs, rabbits, hamsters and goats) have shown only a positive response to goat epithelium (Allergopharma, Reinbek, Germany). The testing for allergen-specific IgE (Allergopharma) yielded the following results: Class 2 for the goat epithelia (1.55 kU/l) and Class 0 for the following animal allergens: cat, dog, hamster, guinea-pig, rat, rabbit, mouse, cow and horse.

On admission to the clinic, she showed itchy blotches on her hands and presented respiratory symptoms, the pulmonary function test showed an airway obstruction.

After a few months, at the time when she was asymptomatic, she gave her written informed consent to take part in our investigation. A specific challenge test was performed on the goat farm in order to verify our hypothesis about the role of passive transport of allergens in the development of severe allergic symptoms.

30 min after allergen challenge, she showed itchy blotches on her hands (she was in contact with goat dander) that persisted up to 6 hr after the test. Following such exposure, clinical symptoms of asthma appeared, and these were observed up until 24 hr after the challenge. Additionally, a bronchial challenge test yielded an early peak expiratory flow fall by 30% (the measurement was performed at the goat farm). The patient was removed from the site of exposure with improvement in her symptomatology. The hair found on the patient's cloth and hands were identical to those of goats bred at the farm.

In conclusion, severe allergic reaction to goat dander was proved by both clinical and spirometric parameters during the period when her husband had occupational exposure to goat allergens as well as by the specific challenge test.

The observed increased sensitization to goat allergen in the vet's wife could be associated with either poor hygienic conditions at the husband's workplace or wearing the same clothes when working at the farm and at home. Therefore, when recording an allergic history, the profession of other family members

should be considered as an additional risk factor for allergic sensitization.

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Contact dermatitis by dipivefrine

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Key words: dipivefrine contact allergy

Glaucoma is a chronic, progressive, optic neuropathy for which there is a wide variety of effective, topical drugs. These agents include timolol,

befunolol, betaxolol, levobunolol, metipranolol, dorzolamide, pilocarpine, brimonidine, apraclonidine, latanaprost and dipivefrin.

In the Mediterranean region, adverse cutaneous reactions after topical administration of glaucoma agents are rarely observed. Recently, we have studied the first case of contact dermatitis to dipivefrin.

Dipivefrin chloride {4-[1-hydroxy-2-(methylamino) ethyl]-o-phenylene} is a prodrug synthesized by the addition of 2 pivalic acid groups to epinephrine which results in a more lipophilic compound with greater penetration of the corneal layer. Once within the eye, dipivefrin is de-esterified to its pharmacologically active form, epinephrine, which makes it a powerful sympathomimetic and glaucoma drug (1).

Local adverse reactions to dipivefrin include blurred vision, burning sensation, pruritus, blepharoconjunctivitis, reactive hyperemia, cystoid macular oedema and ciliary body oedema. Although less common, systemic side effects, such as tachyarrhythmia, extrasystoles and hypertension (2) may occur after topical epinephrine therapy.

Case Report

A 62-year-old man presented with a 3-year history of glaucoma, for which he was treated with several topical ophthalmic solutions. Treatment with Diopine® (one drop per eye twice daily) was prescribed in June 2003. 4 months later, the patient presented with pruritus, conjunctivitis and periorcular eczema, primarily in both lower eyelids (Figs 1 and 2). Neither his work in construction nor his

social history revealed exposure to other potential ocular allergens. Dipivefrine was withdrawn and therapy with timolol was initiated. 2 months later, he was patch-tested on the upper back with the European series (standard and medications) and the topical ophthalmic solution. Patch tests with European series were negative, whereas the patch test with Diopine® was positive (++) at D2 and D4, which was considered to be clinically relevant. 1 month later, he was then patch tested, using the same procedure, to all individual components of Diopine® and epinephrine 1% aq, to confirm the cross-reactivity between epinephrine and dipivefrine that was suggested by Parra et al. (3). The results of these patch tests are shown in Table 1. There was a strong reaction to dipivefrine chlorhydrate 1% aq at D2 (++) and D4 (+++) and there was a weak positive reaction to epinephrine 1% aq at D2 (+?) that was absent at D4.

Discussion

Dipivefrine is widely used in the topical treatment of glaucoma, and allergic contact dermatitis has rarely been documented. To date, there are only 3 communications of contact dermatitis to this drug (3–5). Taking this into consideration, low sensitivity and high tolerance (6) must be presupposed to the prescription of this drug.

Parra et al. suggested cross-reactivity between epinephrine and dipivefrine (3). Our results do not confirm this, as patch tests with epinephrine yielded only a weak-positive reaction at the 2-day-reading (D2)

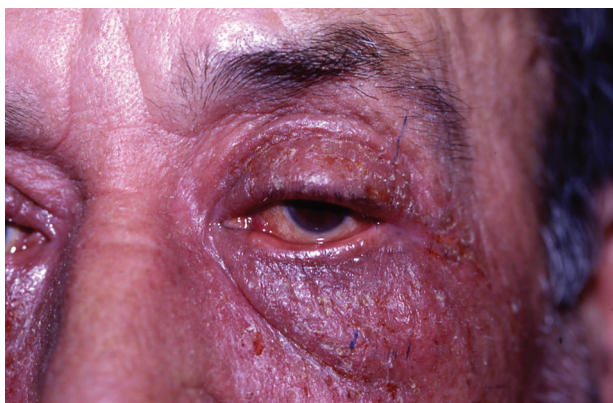


Fig. 1.

Table 1. Patch test results

Allergen	Concentration	Readings	
		D2	D4
Dipivefrine Chlorhydrate	1% aq	++	+++
Benzalkonium Chloride	0.1% aq	–	–
Sodium edetate	10% aq	–	–
Manitol	20% aq	–	–
Sodium Chloride	20% aq	–	–
Sodium metabisulfite	2% pet	–	–
Destillate water Aa		–	–
Epinephrine	1% aq	+?	–

aq., water; pet., petrolatum.



Fig. 2.

that evolved into a negative reaction at the 4-day-reading (D4). However, given their closely related structures, we do not rule out this risk and advise against its use in the future.

Systemic, ophthalmic and cutaneous reactions have been attributed to delivery vehicle components, like benzalconium chloride, disodium edetate, bisulfite etc (7). In this case, all components of ophthalmic solution were tested without reaction.

A variety of topical ophthalmic medications have been reported to cause allergic contact dermatitis and conjunctivitis. In consideration of the great number of individuals who receive these medications, we think that an 'ophthalmic tray' should be created and revised periodically. Several attempts to create patch tests for ophthalmic patients have been made but we still remain far from standardization. We think that the 'ophthalmic tray' proposed by Herbst and Maibach could be useful (8). We would include dipivefrine for the cases without cross-reactivity with epinephrine and Latanoprost as allergic contact dermatitis to this drug has been recently reported (9).

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Oxidative stress in mouse skin following application of contact allergenic 5-chloro-2-methyl-4-isothiazolin-3-one and oxazolone

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Key words: allergic contact dermatitis; 5-chloro-2-methyl-4-isothiazolin-3-one; 4-ethoxymethylene-2-phenyloxazolin-5-one; glutathione; glutathione disulfide; Kathon® CG; oxazolone.

It has been shown that contact sensitizers such as nitrohalobenzenes, sesquiterpene lactones and isothiocyanates perturbed glutathione status in mouse skin, whilst epicutaneous application of various non-allergenic analogues did not affect either glutathione or glutathione disulfide levels (1–3). Elevation of glutathione levels in mouse skin by 2-oxo-4-thiazolidine carboxylate administered subcutaneously could inhibit both irritancy and sensitizing activity of certain mono- and dihydric alkylbenzenes (4). These clearly suggest perturbation of glutathione status, and hence generation of oxidative stress in mouse skin is probably an inevitable event in the preimmunological phase of the contact sensitization process. We have now selected 2 further sensitizers from other classes of xenobiotics, 5-chloro-2-methyl-4-isothiazolin-3-one (an active ingredient of Kathon® CG) and 4-ethoxymethylene-2-phenyloxazolin-5-one (oxazolone-sensitizing agent), to examine their effects on glutathione status of mouse skin (5–10).

Materials and Methods

5-Chloro-2-methyl-4-isothiazolin-3-one was obtained from a commercial preparation of Kathon® CG supplied by Rohm and Haas Company, USA, using chromatographic techniques (5). Oxazolone-sensitizing agent (4-ethoxymethylene-2-phenyloxazolin-5-one) and other chemicals of the highest available quality were obtained from Sigma Chemicals (Poole, UK). The procedure adopted to examine the effects of sensitizers on glutathione status of mouse skin was essentially that of Schmidt and Chung (3). Briefly, the xenobiotics (5-chloro-2-methyl-4-isothiazolin-3-one and 4-ethoxymethylene-2-phenyloxazolin-5-one) under investigation were each dissolved in acetone and applied (5 µmol in 0.2 ml) to the shaved dorsal skin. After 12 and/or

Table 1. Changes in glutathione status of mouse skin 12 hr after application of contact sensitizers

Compounds	Sensitizers	Glutathione ($\mu\text{g GSH/g of skin}$)	Glutathione disulfide ($\mu\text{g GSSG/g of skin}$)	Total GSH ($\mu\text{g GSH} + \text{GSSG/g of skin}$)
5-chloro-2-methyl-4-isothiazolin-3-one	+	42.57 $\pm$ 13.09 (68.3)*	33.50 $\pm$ 2.56 (123.8)*	77.65 $\pm$ 14.26 (87.0)
Oxazolone†	+	70.23 $\pm$ 10.15 (112.8)	26.56 $\pm$ 13.26 (98.2)	95.93 $\pm$ 12.97 (107.5)
Oxazolone‡	+	87.18 $\pm$ 15.96 (140.0)	34.50 $\pm$ 4.86 (127.5)*	120.91 $\pm$ 17.89 (135.5)*
Control (acetone)		62.28 $\pm$ 8.37 (100.0)	27.05 $\pm$ 3.53 (100.0)	89.26 $\pm$ 8.59 (100.0)

+, allergenic; -, non-allergenic.

Each experimental data point was repeated 6 times and expressed as mean $\pm$ SD. Figures in parentheses represent percentage change relative to control (=100%).

* $P < 0.05$ compared to the control (Student's *t*-test).

†Oxazolone: 4-ethoxymethylene-2-phenyloxazolin-5-one.

‡24 hr after application of contact sensitizer.

24 hr, WSP mice were killed by cervical dislocation and the preshaved dorsal skin (about 9 cm²) removed quickly. The skins were processed, and glutathione and glutathione disulfide levels were determined according to the procedure described previously (3).

Results and Discussion

The results clearly show the sensitizers, 5-chloro-2-methyl-4-isothiazolin-3-one (an active ingredient of Kathon[®] CG) and 4-ethoxymethylene-2-phenyloxazolin-5-one (oxazolone-sensitizing agent) perturbed glutathione status of mouse skin relative to the untreated control at 12 or 24 hr. Glutathione and glutathione disulfide levels were elevated for 4-ethoxymethylene-2-phenyloxazolin-5-one suggesting oxidative stress had been generated leading to raised glutathione disulfide levels (Table 1). This in turn led to induction of glutathione synthesis and hence raised glutathione levels, and is consistent with previous findings on sesquiterpene lactones and isothiocyanates (3).

Epicutaneously applied 5-chloro-2-methyl-4-isothiazolin-3-one elevated glutathione disulfide levels whilst glutathione levels dropped at 12 hr relative to the control. This indicates oxidative stress had also been generated by 5-chloro-2-methyl-4-isothiazolin-3-one in mouse skin, probably involving events occurring in the preimmunological phase of contact sensitization. This finding is consistent with chemical inactivation of 5-chloro-2-methyl-4-isothiazolin-3-one/2-methyl-4-isothiazolin-3-one by glutathione-containing emollients (11).

In summary, the findings here and our previous studies on dinitrohalobenzenes, sesquiterpene lactones and

isothiocyanates indicate that only contact sensitizers perturbed glutathione status (1–3). This suggests perturbation of glutathione status could be developed as a rapid predictive test for potential allergenic chemical compounds and could be extended to cell culture systems.

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Diagnostic quality of the patch test preparation monoethanolamine 2% pet.

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Recently, we have reported monoethanolamine (MEA) to be one of the most frequent allergens in water-based metalworking fluids (wb

Table 1. Patch test reactions at D3 to MEA 2% pet.

Reaction	Study group (n = 370)	Control group (n = 452)
Negative	80.8	94.2
?	7.0	4.0
+	9.7	1.3
++	2.4	
+++		
ir		0.4

Values are expressed as per cent.

MWF) (1, 2). However, with a reaction index of 0.15 and a positivity ratio of 83% (1), the test preparation MEA 2% pet. cannot compete with the high diagnostic quality of other standard allergens (3). On several occasions, representatives of the lubricant industry have doubted the validity of these patch test results and suspected that, taking into consideration the alkalinity of MEA, positive reactions to this test preparation probably indicate irritation rather than contact allergy. If this should hold true, i.e. if MEA 2% pet. elicits a considerable number of irritant patch test reactions mimicking positive test reactions (like octyl gallate 0.3% pet. or phenyl mercuric acetate 0.05% pet.), this effect should be independent from occupational exposure to MEA. To test this hypothesis, we compared patch test results with MEA 2% pet. between metalworkers tested because of suspected MWF dermatitis and other patients, who most likely had had no contact with MEA.

We performed a retrospective analysis of data of the Information Network of Departments of Dermatology (IVDK) of the years 1999–2003. As the vast majority (95%) of the metalworkers tested due to suspected MWF dermatitis are men (2), the study group was restricted to male patients in order to exclude a potential confounding by a gender-

related difference in susceptibility or exposure to irritants or allergens. Hence, the study group consisted of 370 male metalworkers, aged 20–60 years, patch tested with MEA 2% pet. because of suspected MWF dermatitis. The control group, consisting of 452 patients without presumptive occupational exposure to MEA, was selected by matching for sex and age. As MEA may be found not only in wb MWF, but also in hair dyes (4), metalworkers and hairdressers were excluded from the control group. Differences between the study and the control group in proportions of positive test reactions or items of populations characteristics were tested for statistical significance using the two-sided Fisher's exact test.

Both groups did not differ significantly regarding the proportion of patients with past or present atopic dermatitis (study group: 17.8%; control group: 20.4%; $P=0.38$). Patch test reactions to MEA 2% pet. are listed in Table 1. Reaction index was 0.3 in the study group, and -0.5 in the control group. PR was 80% (study group) and 100% (control group). In Table 2, the proportions of positive test reactions to MEA, the 2 allergen preparations with well-known irritant properties mentioned above and to sodium lauryl sulfate (SLS) in the study group and the control group are

compared. The only significant difference between the 2 groups was noted with the proportion of positive test reactions to MEA, which was almost 10-fold higher in the study group (12.2% versus 1.3%; $P<0.0001$).

Patch tests with allergen preparations known for their irritant properties, i.e. octyl gallate 0.3% pet. and phenyl mercuric acetate 0.05% pet., rendered virtually the same proportions of positive reactions in patients with and without exposure to MEA, respectively. The same applies to the irritant reactions elicited by the irritant SLS. Against this background, similar results would be expected with MEA 2% pet., if positive reactions to this test preparation were also largely irritant, i.e. false-positive. However, the 10-fold higher proportion of positive reactions among patients tested for suspected MWF dermatitis strongly supports the interpretation of these reactions as true allergic.

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Table 2. Proportions of positive patch test reactions at D3 to monoethanolamine (MEA) 2% pet., 2 allergen preparations with known irritant properties and sodium lauryl sulfate (SLS)

Test preparation	Study group		Control group		P-value*
	Patients tested	% positive	Patients tested	% positive	
MEA 2% pet.	370	12.2	452	1.3	<0.0001
Octyl gallate 0.3% pet.	260	1.5	292	2.7	0.39
Phenyl mercuric acetate 0.05% pet.	148	8.1	247	7.7	1.0
SLS 0.25% aq.	121	32.2	96	26.0	0.37
SLS 0.5% aq.	135	43.0	105	32.4	0.11

*Fisher's exact test.

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Eyelid dermatitis with positive patch test to coconut diethanolamide

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Key words: allergic contact dermatitis;
 coconut diethanolamide; cosmetics; eyelid
 dermatitis.

Case Report

A 27-year-old non-atopic female presented with an eyelid dermatitis since 3 months. This dermatitis persisted despite the fact that she had stopped the use of make-up; she had acrylic artificial nails since 2 months and sometimes used hair dyes; patch tests were performed with Finn chamber tests with readings at D2 and D3, according ICDRG criteria, with standard European series, additional series (including toluene-sulfonamide formaldehyde resin), cosmetic, acrylates, hairdressing series, in 3 patch test sessions, using Chemotechnique Diagnostics allergens. The only positive patch test was coconut diethanolamide (0.5% pet.)++ at D2 and D3. After removal of the shampoo containing this allergen, the dermatitis cleared.

Discussion

Coconut diethanolamide, tensioactive synthesized with coconut oil is widely used in shampoos, soaps, shower gels, barrier creams, washing up liquids, metalworking fluids and hydraulic oils (1–6). Other names of coconut diethanolamide are: cocamide DEA, coconut fatty acid diethanolamide, cocoyl diethanolamide, coconut oil acid diethanolamide,

N,N-bis(2-hydroxyethyl) cocofatty acid diethanolamide (2).

Cocamide DEA has rarely caused allergic contact dermatitis; in a study during 1985–1992 about occupational allergic contact due to cocamide DEA (2), only 6 patients were allergic to this component; their dermatitis involved the hands. In these patients, no contact dermatitis to cocamidopropyl betaine was detected, as in our patient. Involvement of eyelids is not frequently reported in the literature with this allergen. Contact dermatitis to cocamide DEA and lauramide DEA in shampoos has already reported (1) in a 73-year-old man with worsening of his scalp psoriasis and itching and also eyelid dermatitis. Contact dermatitis to undecyleneamide diethanolamide in a liquid soap has also been described (7). Cocamide DEA is not cited as allergen in a study about 232 patients with eyelid dermatitis evaluated by patch tests (8). Coconut diethanolamide should be added in cosmetic series, and it should be useful to test this allergen in patients with eyelid dermatitis.

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Occupational airborne contact dermatitis from sporadic exposure to tetrazepam during machine maintenance

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Key words: airborne; allergic contact dermatitis; drug manufacture; maintenance; occupational; repairman; tetrazepam.

Case Report

A 58-year-old repair technician in a pharmaceutical factory was referred for evaluation of a 2-year history of a recurrent cutaneous eruption. The patient reported widespread pruritus every time he had to repair one of the machines manufacturing Myolastan[®] (tetrazepam) (Sanofi-Synthelabo, Riells, Barcelona, Spain). This machine compressed the powder into a tablet. When repairing this machine, the patient would open the glass shield and make contact with tetrazepam powder on the surface of the machine. Several minutes after repairing the machine, he consistently developed a widespread eczematous dermatitis involving both exposed and non-exposed areas. He used to carry out this procedure approximately $\times 1$ –3 per month. The patient claimed that he had always taken adequate protective measures (gloves, facemask and white coat) and that he needed to take oral antihistamine before coming into contact with tetrazepam machine in order to alleviate symptoms.

He was patch tested with a standard series, Myolastan[®] (crushed tablet) and tetrazepam (pure powder), both in pet. and diluted to 0.1%, 0.5%, 1%, 5%, 10%, 20% pet. and as is. The European standard series was negative, whereas Myolastan[®] and tetrazepam were clearly positive at 2 days at 0.5% and above. Tetrazepam (0.1%, 0.5% and 1%) patch tests in 20 control patients were negative. A biopsy specimen taken from a 0.5% tetrazepam-positive patch test reaction showed spongiotic dermatitis. On the basis of clinical history and patch testing, a diagnosis of an occupational airborne allergic contact dermatitis from tetrazepam was made.

Comment

Tetrazepam is a benzodiazepine containing a cyclohexene ring, currently used as a muscular relaxant. Cutaneous reactions to tetrazepam are not rare (1). Maculopapular exanthema, allergic contact dermatitis, photosensitivity, erythema multiforme, Stevens-Johnson syndrome and leukocytoclastic vasculitis have occasionally been reported and confirmed by positive patch test. In the majority of such cases, tetrazepam was orally administered and only in rare instances did topical contact with tetrazepam elicit the cutaneous adverse reaction (2-5).

Occupational environmental allergic contact dermatitis from tetrazepam has been reported in a nurse distributing medicines to her patients (3) and in workers in a pharmaceutical factory in close contact with tetrazepam powder (4). Lepp et al. (5) in 2003 reported a single case of occupational airborne contact allergy in a geriatric nurse. She was responsible for patients' medication, having to crush tablets to facilitate administration through nasogastric tubes, and developed a periorbital cutaneous reaction that progressed to involve the whole face. Patch testing with various drugs that she had dealt with showed positivity only to tetrazepam.

Allergic occupational dermatitis from drugs usually administered systemically is found most often in nurses, but occasionally physicians, veterinarians, dentists, hospital-cleaning staff and pharmaceutical manufacturing workers can be affected. In contrast to previously reported cases, our patient was exposed only sporadically to tetrazepam. This case illustrates that sensitization can develop after only minor, though recurrent, exposures to the responsible agent and highlights the importance of having accurate information regarding penetration rates through gloves, masks and protective clothes. Hence, education is necessary for employees, not only in those regularly exposed, but also in repair or maintenance technicians, who

come into contact with the agent occasionally, in order to increase awareness of potential sensitizing drugs. Once occupational contact dermatitis is confirmed, restriction from contact with the agent is recommended, including its oral intake.

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