

CONTACT POINTS

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Tolerance of fondaparinux in a patient allergic to heparins and other glycosaminoglycans

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Key words: adverse drug reaction; delayed-type hypersensitivity; fondaparinux; heparin; heparinoid.

Delayed-type hypersensitivity (DTH) reactions to subcutaneously injected heparins are fairly common, and cross-allergy with different types of heparins is frequently observed (1).

Case Report

We here report a 57-year-old Caucasian female patient with a history of DTH to several heparins, who was admitted as an inpatient for treatment of venous ulcers. In the light of her history, the glycosaminoglycan danaparoid (Orgaran[®]) was chosen for prophylactic anticoagulation, which was necessary because of immobility and obesity. Two days after the initial injections, the patient developed erythematous plaques and disseminating papulovesicles at the injection sites (Fig. 1). Assuming DTH to danaparoid, anticoagulation was switched to the low molecular weight selective factor-Xa-inhibitor fondaparinux (Arixtra[®], Sanofi-Synthelabo, Berlin, Germany; 2.5 mg subcutaneously per day), because recent reports document absence of *in vitro* cross-reactivity with antibodies to heparin-platelet factor 4; these may be associated

with allergic heparin-induced skin reactions (2, 3). Fondaparinux was well tolerated throughout the treatment period of 2 weeks.

A comprehensive series of skin allergy tests was initiated 6 weeks after clearance of the patient's skin lesions using undiluted original drugs. Several heparins yielded positive i.c. test results at days 4–8 after injection of 0.1 ml (undiluted drug, applied to the inner aspect of the lower left arm) with erythematous plaques developing at the injection sites (Table 1). A therapeutic dose of pentosan polysulfate was also injected subcutaneously, resulting in the formation of a similar lesion. In contrast, all skin tests with fondaparinux remained negative, and re-exposure 4 weeks after termination

of the treatment was tolerated by the patient.

Discussion

The patient described here shows DTH responses to a wide spectrum of heparins as well as other glycosaminoglycans, a constellation repeatedly reported (1, 4). Our observation documented here suggests that the synthetic pentasaccharide fondaparinux might provide a safe alternative in those patients. Tolerance to fondaparinux despite allergies to different heparins and other glycosaminoglycans can be explained by a current hypothesis suggesting that heparins act as protein-bound haptens when triggering DTH responses (3). Protein binding requires polysaccharide chains of a critical

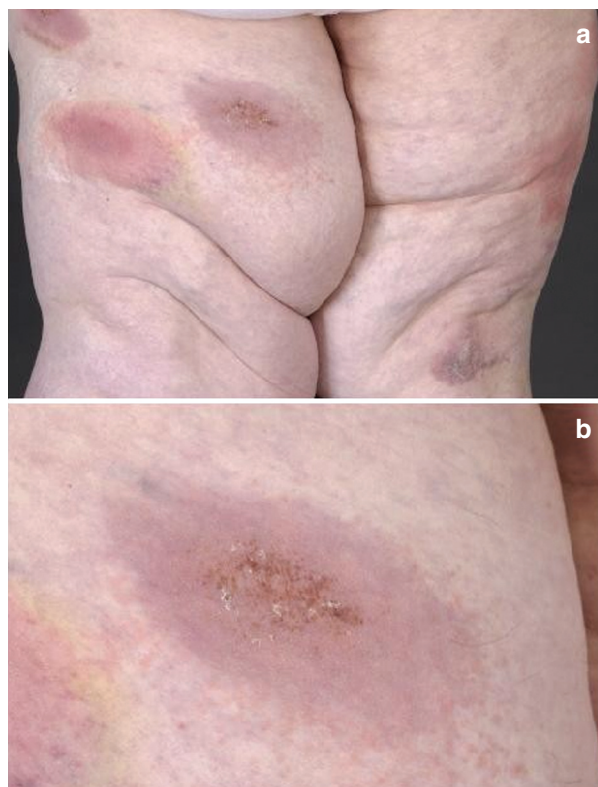


Fig. 1. Erythematous plaques with disseminating papulovesicles at the injection sites of danaparoid administered subcutaneously. (a) Injection sites of the right leg. (b) Detail of a lesion.

Table 1. Skin allergy tests performed to diagnose the contact allergies to heparins and other glycosaminoglycans (the prick tests performed initially with all substances remained negative at t = 20 min)

Substance	i.c. test			Subcutaneous challenge
	Day 1	Day 4	Day 8	
Unfractionated heparin Calciparin® Sanofi-Synthelabo	Negative	Positive	Positive	ND
Nadroparin Fraxiparin® Sanofi-Synthelabo	Negative	Positive	Positive	ND
Certoparin Mono-Embolex® Novartis	Negative	Positive	Positive	ND
Danaparoid Orgaran® Celltech	ND	ND	ND	Erythematous plaques after 2 days of treatment
Pentosan polysulphate Fibrezym® bene	Negative	Negative	Negative	Erythematous plaque after 6 days
Fondaparinux Arixtra® Sanofi-Synthelabo	Negative	Negative	Negative	No DTH reactions after 2 weeks of subcutaneously administration and upon re-exposition

DTH = delayed-type hypersensitivity; ND = not determined.

length (5). As fondaparinux is only a pentasaccharide, its polysaccharide chain may simply be too short to mediate protein binding.

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Application of protective creams: use of a fluorescence-based training system decreases unprotected areas on the hands

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Key words: Dermalux system®; fluorescence; occupational hand dermatitis; skin protection.

Occupational contact dermatitis is amongst the most frequent occupational diseases. The majority comprises irritant contact dermatitis of the hands (1, 2). The efficacy of protective creams in the prevention of hand dermatitis has been proven in *in vitro* and *in vivo* studies (1, 3, 5). Observed lack of protection might be caused by uneven or partial application of protective creams (4, 6). A fluorescence-based method has been developed to monitor the carefulness of self-application of protective cream (2). A fluorescence reference protective cream was formulated and applied at the workplace to train workers in high-risk occupational environments in the adequate use of protective creams (2). This fluorescence-based training system for skin protection (Dermalux system®, KBD GmbH, Weinheim, Germany) consists of a checkbox with 365 nm UV light and a fluorescence reference protective cream.

The acceptance of this training system was investigated using a self-administered questionnaire.

Subjects and Methods

A questionnaire was sent to users and customers of the Dermalux system® to collect the following information: occupation of the instructor, number of training locations, number of training sessions in 2001/2002, number of trained persons, characterization and skin status of the trainees, acceptance of the test preparation by the trainees, acceptance of the Dermalux system® by the instructors, subjective and objective evaluation of the fluorescence reference protective cream-covered area, quantity of the cream before and after application, unprotected areas of the hands at the first and second training sessions, increased consumption of protective cream and increased motivation to use protective products after starting the training.

Results

41 out of 104 (39.4%) questionnaires were returned and evaluated. Supervisors, trainees, nursing staff, employees, technical supervisors, physicians and patients were enrolled in this survey. 50% thought that they applied protective cream adequately before their first training session, but in fact, the application was incomplete, especially around the nails, between the fingers and on the dorsal aspect of the hands (Fig. 1). We found that application improved considerably after the second teaching session (Fig. 2).

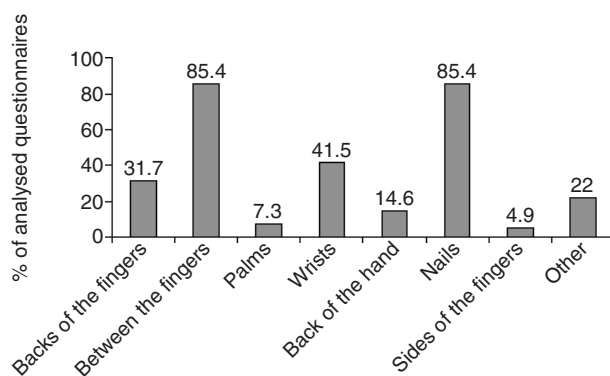


Fig. 1. Percentage of incompletely protected areas of the hands before first training session.

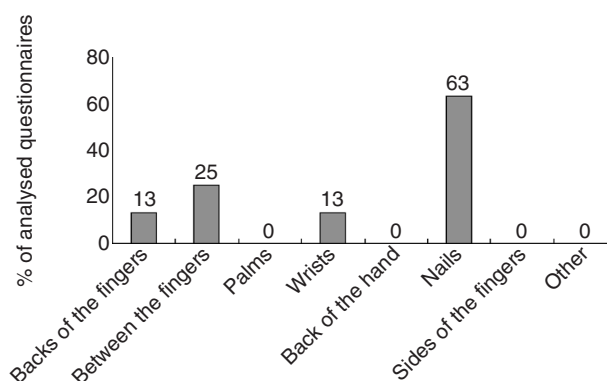


Fig. 2. Percentage of incompletely protected areas of the hands at second training session.

The fluorescence reference protective cream smelled reasonable ($n=24$) or bad ($n=11$). Its ease of application on the skin was assessed as good ($n=18$) or moderate ($n=17$). Its ability to sink in was assessed as good ($n=16$) or moderate ($n=19$), whereas its consistency was good ($n=16$) or moderate ($n=19$).

Conclusion

Our survey showed that the use of the Dermalux system[®] as a training tool in critical occupational working conditions improved the benefit of protective cream application. Repeated training improved this benefit further, as the trainees became more aware of the critical application method. However, cosmetic acceptance regarding odour, ease of application, absorption and consistency of the fluorescence reference protective cream was reported as suboptimal. The Dermalux system[®] can be considered as an effective tool to visualize and train in the proper use of

protective cream, giving direct feedback about the most commonly unprotected regions.

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Localized aquagenic urticaria: efficacy of a barrier cream

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Key words: aquagenic urticaria; barrier cream; prevention; treatment.

Case Report

A 43-year-old woman presented with a 20-year history of chronic urticaria. Her medical history included hypertension treated for the past 5 years (urapidil and zofenopril) and 3 episodes of facial angioedema (cause undiagnosed) 5 years previously, but no atopic signs. Both her mother and her sister had atopic dermatitis. The latter who could not be examined also had the same urticarial manifestations.

The urticaria, in the form of extremely pruriginous papules, appeared after contact with water of over 10 min duration (shower or bath in fresh or salt water, hot or cold water), which prevented bathing. Urticaria also occurred during episodes of profuse sweating (heat, effort) together with dermographism. All the 3 types of urticaria were strictly limited to the neck, V of the chest and upper shoulders. Oral cetirizine (10 mg/day) was effective on

the cholinergic urticaria but did not prevent the reaction to water.

Tests carried out by means of a 20-min contact with a damp compress at room temperature were positive on the V of the chest with tap water, distilled water and 10% NaCl, though negative on the forearm. These same tests remained positive after prior application of an emollient and a water-resistant block sun. Both rash and pruritus, however, were suppressed by a skin protection cream (Lipotop Protect® Spirig Laboratory, Nancy, France), an oil-in-water emulsion composed of aqua, paraffinum liquidum, behenyl alcohol, glycerin, aluminium chlorohydrate, ethylhexyl palmitate, Simmondsia chinensis, seed oil, cethet-10, steareth-20 and dimethicone, which permitted prolonged water contact.

Discussion

Water-induced urticaria is a rare, sometimes familial, form of physical urticaria: since its description in 1964, less than 40 cases have been reported. There are localized presentations, as with our patient, generally limited to the upper part of the body. The combination of dermographism and cholinergic urticaria is rare. In our case, the urticaria was moreover limited to the same areas, whatever the trigger factor. Heat-induced urticaria cannot be considered as a reaction to the water in the patient's own sweat, as it was prevented by oral antihistamines ineffective on water-induced urticaria.

The pathophysiology remains obscure: water may act as an epidermal antigen solvent permitting its diffusion in the dermis and the liberation of histamine by sensitized mast cells. 2 recent observations favour the role of saline concentration and osmolarity (1). Our observation does not confirm this hypothesis, as the reaction to all the tested solutions was identical.

The usual treatments recommended (2), emollients and oral antihistamines, are often ineffective, as in our case the patient merely avoided all prolonged contact with water, taking rapid showers and no baths. The inefficacy of emollients and water-resistant block sun was confirmed by our tests. Prior application of a protective cream, more generally used to protect from repeated washing, however, permitted prolonged

water contact and the renewal of aquatic activities. This is a simple and practical treatment, with no side effects as compared to phototherapy, an accepted alternative proposed for resistant cases.

Authors' note: We have no financial or other interest in the development or marketing of Lipotop Protect®, and we selected it ourselves from a range of similar products available on the market.

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Hand dermatitis in a student caused by Basic Red 46

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Key words: allergic contact dermatitis; Basic Red 46; lack of cross-sensitivity; occupational; textile dyes.

Case Report

A 17-year-old student presented with an 8-month history of bilateral hand dermatitis. This had started as dryness and chapping of the palmar and dorsal aspects of both hands, followed by the appearance of vesicles, pruritus and secondary infection, which had

required treatment with oral flucloxacillin. In the 2 months before presentation, there had been secondary spread to the forearms, trunk and face. There had been only a slight response to the application of aqueous cream and betamethasone valerate 0.1% cream.

9 months previously, she had begun a course in textiles and graphic design at a further education college. This involved regular contact with a variety of textile dyes, and she had previously had extensive contact with paints, dyes and textiles at school. She wore rubber gloves at college after the onset of her hand dermatitis. There was a past history of mild childhood atopic dermatitis, and she had both asthma and hay fever. There was also a strong family history of atopy.

She was patch tested to the European standard series, bases and preservatives, acrylates and textile colours and finishes series (all Chemotechnique Diagnostics, Malmö, Sweden). There was a + reaction to Basic Red 46 1% pet. on both days 2 and 4. Following restriction of her contact with coloured textiles at college, her hand dermatitis cleared completely and there has been no recurrence after a further 9 months.

Discussion

Basic Red 46 is a basic or cationic dye having a monoazoic structure and is used in the dyeing of acrylic and polyester textiles as well as wool, silk and nylon (1). Fousserau reported dermatitis of the trunk and arms due to Basic Red 46 in the black, blue and red threads of a wool/acrylic sweater (2). His patient also reacted to the azo dyes Disperse Orange 3 and Disperse Blue 106, which are relatively common allergens, and *p*-phenylenediamine. The author suggested that these might be cross-reactions. Basic Red 46 in Nomex® flame-retardant clothing has also been reported as causing an extensive occupational dermatitis (3). Most recently, Basic Red 46 in acrylic work socks has been described as the cause of a protracted occupational allergic contact dermatitis, complicated by septic arthritis (4).

The frequency of textile dye dermatitis is low, and allergy to basic dyes is rare. Doooms-Goossens (5) found only 28 cases of textile dye dermatitis in

3336 patch-tested patients, only 1 of these being a reaction to Basic Red 46; this patient also reacted to the Disperse Blues 106 and 124.

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Occupational contact dermatitis, with asthma and rhinitis, from camomile in a cosmetician also with contact urticaria from both camomile and lime flowers

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Key words: asthma; camomile; contact dermatitis; contact urticaria; cosmetician; lime; occupational; rhinitis.

Case Report

A 54-year-old woman had been working as a cosmetician for 34 years. She prepared herbal beauty masks (recipe: linseed 42.0%, camomile flower 24.0%, lime flower 13.0%, potato flour 19.0%, and borax 2.0%) and applied them to clients' faces. Her work caused worsening sneezing initially and, with time, orbital pruritus, dacryorhoea and rhinitis. 2 years ago, a paroxysmal cough, sometimes accompanied by dyspnoea, started making the patient leave the room she worked in. All the respiratory tract symptoms occurred only during contact with the herbal beauty mask. 6 months ago, the patient noticed dermatitis of both hands when working with the herbal beauty mask, with intermittent vesiculation. The patient had not noticed any wheals at work.

A dermatologist prescribed topical fluticasone propionate $\times 1$ a day and loratadine 10 mg oral $\times 1$ a day, which brought relief. During a 3-week holiday the skin changes regressed considerably, and the other symptoms did not occur. Soon after returning to work, the patient noted rapid worsening in both respiratory tract symptoms and dermatitis (bullae occurring). On examination, 3 months after she stopped working, the patient did not have any skin changes. Also, laryngological examination did not indicate any deviation from the norm.

On patch testing, she was positive to fragrance mix (Jaworski, Katowice, Poland). On open testing (1), immediate reactions read after 30 and 60 min were shown to the whole beauty mask, the herbal powder used in its preparation, lime flower and camomile flower, the diameter of wheal being approximately 1 cm. The beauty mask and herbal powder, diluted in water twice, also provoked wheals. Delayed reactions were looked for after 1 and 2 days and were positive to the whole beauty mask, the herbal powder used in its preparation and camomile flower, but negative to lime flower.

Prick testing was performed with a set of routine inhalatory allergens (Allergopharma, Reinbek, Germany), which includes lime and camomile allergens (*Matricaria chamomilla*). The results were positive with lime pollen (+) and camomile pollen (++)

A provocation test with allergen was carried out by means of acoustic rhinometry (2), each exposure to lime and camomile flower lasting 3 min. Following exposure to the flowers of both plants, sneezing (lasting 10–20 min), dyspnoea, nasal conchae swelling and hyperaemia occurred, which led to a decrease in the volume of the nasal cavities – a $\times 3$ decrease in the case of camomile and a more than $\times 2$ decrease in the case of lime. Provocation tests were thus assessed as strongly positive. The total immunoglobulin E (IgE) level was 607 kU/l.

Comment

The patient was diagnosed as having occupational contact dermatitis, with asthma and rhinitis, from camomile and contact urticaria from both camomile and lime flowers. Joint assessment by dermatologists, otolaryngologists and respiratory physicians is useful in such cases.

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Chromate: still an important occupational allergen for men in the UK

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Key words: allergic contact dermatitis; cabinetmaking; cement; chromate allergy; construction industry; metalworking; occupational dermatosis; shoes.

We have reviewed chromate allergic patients seen over a 3-year period, to ascertain whether occupation was still a current source of chromate exposure.

Patients and Methods

Retrospective analysis of the records of 1200 patients, patch tested over 3 years (1999–2002) at the Royal Hallamshire Hospital, Sheffield, identified 10 patients positive to chromate (+ and above). These cases were analysed for the clinical relevance of the reaction and the source of chromate exposure. There were 8 men and 2 women, with a mean age of 43 years (range 32–57). All had had hand dermatitis, 2 (both women) had also had foot dermatitis. A personal history of atopy (asthma, eczema and hay fever) was present in 4 patients.

Results

5 men were involved in the construction industry, 1 man was a metalworker, 1 a cabinetmaker and 1 a rotary grinder. One of the women was a nurse, the other an office worker. Co-allergens on patch testing, considered to be of potential relevance, were as follows: cobalt 4, thiuram mix 2, epoxy resin 2, fragrance mix 2, colophonium 1, paraphenylenediamine 1, tosylamide/formaldehyde resin 1 and Disperse Yellow 1.

Discussion

In all 8 men who were chromate allergic, chromate was considered to be both relevant and occupational. Possible sources of chromate included cement in the builders, metal fragments in the metalworker and rotary grinder, and paints and wood preservatives in the cabinetmaker. In the 2 women, both of whom also had foot dermatitis, chromate contact seemed most likely to be non-occupational and from tanned leather in shoes. Most of the patients had additional and potentially relevant contact allergies to other occupational chemicals that included rubber additives, epoxy resins and cobalt.

This small study suggests that chromate is still a major occupational allergen in the UK. All patients in the series had persistent hand dermatitis and 2 had foot dermatitis in addition. Technical developments in occupations, such as the addition of ferrous sulfate to cement (1), have already resulted in the reduction of chromium-

induced dermatitis in some countries (1, 2). Other countries should follow suit.

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Contact urticaria due to nitrile gloves

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Key words: 2, 2'-methylene-bis-(4-methyl-6-tert-butylphenol); antioxidants; contact urticaria; gloves; nitrile; Ralox LC; rubber chemicals.

Awareness of latex allergy amongst both healthcare workers and patients has prompted widespread use of a variety of alternative glove materials. Nitrile has proved popular for non-sterile procedures involving patient

contact. There have been very few reports of allergy to nitrile itself (1, 2) and only one report of contact allergy to an accelerator (morpholinyl mercaptobenzothiazole) in nitrile gloves (3).

Case Report

An experienced nurse with no previous history of glove-related symptoms developed urticaria of the hands and distant sites within minutes of donning a pair of nitrile gloves. Symptoms settled spontaneously after several hours.

Short contact tests were applied for 20 min to intact forearm skin using portions of a similar nitrile glove, a different brand of nitrile glove, a latex glove and a variety of commercially available rubber-processing chemicals. The only positive reaction was to the nitrile glove responsible for symptoms.

Samples of each chemical ingredient of the nitrile glove were kindly supplied by the manufacturer and applied, after suitable dilution, as short contact tests (Table 1).

15 min after application of the test materials, tingling was reported at the site of application of 2,2'-methylene-bis-(4-methyl-6-tert-butylphenol) (Ralox LC; Rashig AG, Ludwigshaven, Germany); after removal of the patch, a weal was visible at the test site. After a further 15 min, tingling had become more extensive, involving the test arm and hand and also the lips. Symptoms settled rapidly in response to intravenous chlorpheniramine.

Discussion

2,2'-methylene-bis-(4-methyl-6-tert-butylphenol) (Ralox LC) is an antioxidant added during the manufacturing of both natural and synthetic rubbers, including nitrile. It prevents age-

Table 1. Short contact tests to ingredients of nitrile glove

Test material	Concentration (%)	Vehicle	Test result
Liquakole green	0.01	aq.	–
Liquakole green	0.1	aq.	–
Acrylonitrile butadiene	0.1	pet.	–
Mercaptobenzothiazole	2.0	pet.	–
Dibutylthiocarbamate	1.0	pet.	–
2,2'-methylene-bis-(4-methyl-6-tert-butylphenol)	1.0	pet.	+

related brittleness and discolouration. Allergy to Ralox LC has not been recorded previously, but as nitrile gloves gain increasing popularity, further reports are to be expected. This patient's experience serves as a reminder that Type I natural rubber latex allergy is not the sole cause of glove-related urticaria.

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Allergic contact stomatitis from paraformaldehyde and copal in a dental root canal filling

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Key words: contact stomatitis; copal; dental filling; paraformaldehyde; patch test.

A 69-year-old woman was seen in April 2003 with pruritic erythema and swelling on her left side of the oral mucosa and cheek. She had received a root canal filling in the upper jaw on the morning of the day before and noticed her symptoms

12h later. She had previously received two such treatments. Her symptoms cleared with intravenous and oral corticosteroids. She had had no past history of drugs or metal allergies. The dental filling Hyper-band Kimura (Neo Pharmacy, Tokyo, Japan) contained 4 components, paraformaldehyde, copal, silicic anhydride and isoamyl acetate. We performed prick tests with 10, 1 and 0.1% aq. paraformaldehyde and patch tests with 10, 1 and 0.1% pet. paraformaldehyde, 1 and 0.1% pet. copal, 30% pet. silicic anhydride and 47.5% pet. isoamyl acetate. Only patch tests with Hyper-band Kimura (as is), 10% pet. paraformaldehyde and 1 and 0.1% pet. copal elicited oedematous erythema with pruritus at D2, D3 and D7 (Table 1). Patch tests with 10, 1 and 0.1% pet. paraformaldehyde and 1 and 0.1% pet. copal in 5 control subjects showed no reactions at D2, D3 and D7.

Discussion

Causes of allergic contact stomatitis are listed as foods, flavours, preservatives and components of dentifrices and dental materials. Paraformaldehyde, a formaldehyde-releasing substance, is used for root canal therapy. Formaldehyde is a well-known sensitizer and is therefore included in all standard series for patch testing (1). Formaldehyde used in dental therapy causes anaphylaxis (1–3) and contact urticaria (4) and rarely induces contact stomatitis (5). Copal, a natural resin from trees in South America, is used in varnish making (6), and its place in the spectrum of resins originating from trees of the Araucariaceae, Caesalpiniaceae, Dipterocarpaceae and Burseraceae families has been well delineated

(7). Contact sensitivity to copal is seen in workers during its production (6).

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Table 1. Patch test results

	D2	D3	D7
Hyper-band Kimura as is	++	++	++
Paraformaldehyde			
10% pet.	++	++	++
1% pet.	–	–	–
0.1% pet.	–	–	–
Other 2 components pet.	–	–	–
Copal			
1% pet.	+	++	++
0.1% pet.	–	++	++

Lymphadenosis benigna cutis induced by iatrogenic contact dermatitis from dinitrochlorobenzene

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Key words: allergic contact dermatitis; CD21; dinitrochlorobenzene; lymphoid follicle.

Case Report

A 38-year-old woman was referred to Kyushu University Hospital for evaluation of an itchy brownish patch on the right upper arm. She had a past medical history of alopecia areata and had been sensitized with 2% dinitrochlorobenzene (DNCB) in acetone on the right bicipital region and treated with topical immunotherapy 3 years ago. Because the patch was persistent and resistant to topical corticosteroid therapy, the region was surgically excised and immunohistochemical analysis performed. Histological examination of a specimen taken from the lesion showed a dense, diffuse infiltrate of lymphoid cells in the dermis. Follicular structures containing active germinal centres were also recognized (Fig.1). CD21-positive cells, which correspond to follicular dendritic cells, were detected in the light zones of germinal centres by immunohistochemical staining (Fig.2). Although CD4⁺ T cells and CD8⁺ T cells were loosely distributed in the extrafollicular area and germinal centres, the number of CD8⁺ cells were greater than those of CD4⁺ cells (data not shown). A diagnosis of lymphadenosis benigna cutis (LABC) was performed.

Discussion

LABC is a benign reactive lymphocyte proliferative disorder. Various

factors such as external injury, insect bite and other provocations have been reported to cause it (1). Clinically, LABC is characterized by reddish-brown, dome-shaped, elastic-hard papules and nodules. Histologically, dense cellular infiltration predominantly composed of lymphocytes in the dermis, with occasional formation of lymphoid follicles with germinal centres, has usually been observed (2).

The histological findings in the present case showed typical features of LABC induced by DNCB. Only 1 related case of iatrogenic benign lymphoplasia induced by squaric acid dibutyl ester (SADBE) has been reported (3). As far as we know, however, there are no reports of LABC at the site of primary sensitization with DNCB. Although the pathogenesis of formation of lymphoid follicles in the skin is not clear, the development of germinal centres is generally associated with the generation of memory B cells and antibody

production after antigenic stimulation in T cell-dependent immune responses.

The findings of our case indicate that a long-lasting allergic reaction caused by a potent contact allergen (DNCB) might be related to the mechanisms of lymphoid follicular formation.

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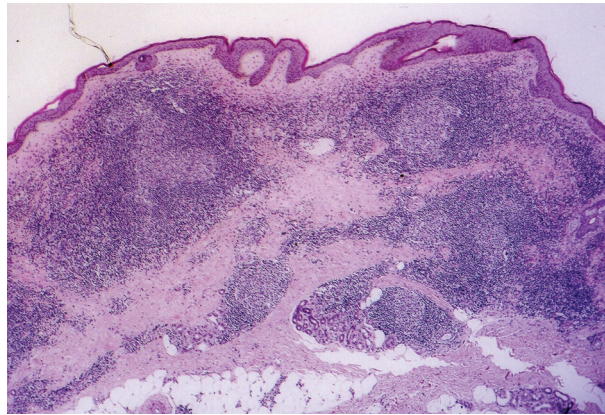


Fig. 1. Dense lymphoid cellular infiltration with germinal centres in the dermis.

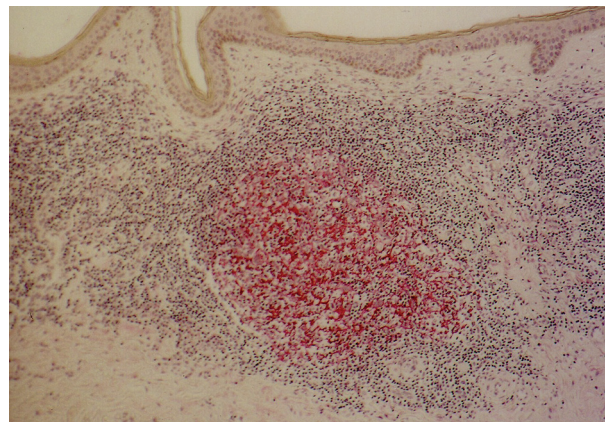


Fig. 2. CD21⁺ cells (follicular dendritic cells) detected in germinal centres.

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Occupational allergic contact urticaria and asthma from diphenylmethane-4,4'-diisocyanate

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Key words: adhesives; car industry; contact urticaria; diphenylmethane-4,4'-diisocyanate; occupational; polyurethane; respiratory effect

Case Report

A 28-year-old woman, who had a history of hay fever, presented with urticaria and breathing difficulties, which had developed during her work in a factory where plastic components were manufactured for the car industry. She folded and cut paper for an air filter and cleaned a robotic machine that glued the paper to the plastic ring of the air filter, using a 2-component polyurethane glue. According to its material safety data sheet, the glue contained diphenylmethane-4,4'-diisocyanate (MDI).

She used protective latex gloves only sporadically, and her hands came frequently into direct contact with the glue, although without any symptoms for a year. Then, suddenly one of the outlet pipes of the machine became obstructed, and she had to clean it out. During this, she had heavy and prolonged contact with the glue, inhaling its emitted vapour

for more than 6 h. During that day, she developed whealing on her face and acute dyspnoea, which required acute intervention in an emergency department with oxygen, intravenous corticosteroids and bronchodilators. Over the following 4 months, she developed during every working day dyspnoea, with wheezing and urticaria on the face, arms and trunk. She changed her machine twice during the next 12 months, avoiding direct contact with MDI, but continued to work in the same area, and after a few weeks, the urticaria and respiratory symptoms returned every working day, both of which starting 15–20 min after entering the workplace. The urticaria came up on the face, arms and trunk. During sick leave, she remained asymptomatic.

Patch tests with the European standard series and a diisocyanates series (Chemotechnique Diagnostics, Malmö, Sweden) showed positive reactions to thimerosal, nickel sulfate and cobalt chloride of past relevance. An open test on the back with her own MDI-containing hardener dispersed at 1% in pet. elicited a local urticarial reaction after 20 min, which lasted for several hours.

Testing with a CAP system immunoglobulin E (IgE) FEIA (fluoroenzymeimmunosassay) (Pharmacia Diagnostics, Uppsala, Sweden) to MDI (11.40 KU/l), toluene diisocyanate (TDI) (5.78 KU/l) and hexamethylene diisocyanate (HDI) (5.92 KU/l) indicated specific-IgE-mediated sensitization. Provocation tests involving the inhalation of MDI and TDI were also positive.

Results were consistent with occupational sensitization to MDI present in the polyurethane glue, causing both contact urticaria and asthma, simultaneously. The positive CAP assays to TDI and HDI probably indicated cross-sensitivity, as previously described, because no exposure to TDI and HDI had occurred (1).

Discussion

Isocyanates are increasingly used in the manufacture of various polyurethane products including adhesives (1- or 2-component glues) (4). Exposure to diisocyanates may cause systemic toxicity, asthma and allergic or irritant contact dermatitis (2, 6–8). Generalized urticaria has also rarely been reported, in which inhalation of

the isocyanate was believed to be the cause (3, 5). However, in these cases, measurements of specific IgE and an open test with the patient's own MDI were either not performed or negative. A case of urticaria and asthma from MDI has been described in which an IgE-mediated mechanism was believed to be involved (1). In this case, RASTs were positive for MDI, TDI and HDI, but a patch test with his own MDI-containing hardener was negative.

Our patient developed occupational contact urticaria and asthma from MDI. Testing with CAP IgE FEIA to MDI, TDI and HDI was positive, and she had a positive pulmonary provocation test to MDI and TDI, both of which confirmed an IgE-mediated mechanism. In addition, an open test with the MDI-containing hardener gave a positive urticarial reaction. Although non-allergic urticaria from MDI has to be considered (1), in our case, the patient had been in direct contact with an MDI-containing hardener for more than 1 year without developing symptoms and, only after heavy and prolonged contact had occurred, did she develop urticaria on direct contact with the MDI-containing adhesive. The results are consistent with IgE-mediated contact urticaria and asthma from MDI.

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Occupational contact dermatitis and contact urticaria in veterinarians

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Key words: contact allergy; contact urticaria; occupational contact dermatitis; veterinarians.

Reports abound with occupational contact dermatitis and contact urticaria of animal origin in northern European veterinarians (1–8). We undertook a study to obtain information on the frequency and causes of work-related dermatoses among veterinarians in the Bergamo district of southern Europe.

Patients and Methods

274 questionnaires were mailed to active members of the Bergamo Veterinary Medical Association.

Veterinarians identified by questionnaire as having a hand or forearm

skin problems from their job were invited to our Allergy Unit for physical examination and allergological investigation. Subjects were patch tested with the Italian standard series supplemented with the following occupational allergens: erythromycin 25% pet., streptomycin 2% pet., penicillin G 5% pet., spiramycin 5% pet., Tego G 1% pet., chloramphenicol 5% pet., eosin 5% pet., glutaraldehyde 0.2% aq., benzalkonium chloride 0.1% aq. and chloramine T 0.5% aq. They were also prick tested with a commercial standardized latex preparation from Stallergènes (Paris, France) and with a solution obtained by immersing 20 pieces of 1 × 1 cm high-protein (Gammex, Ampli-medical, Milan, Italy) latex glove in 5 ml of saline solution for 20 min and subsequently diluted 1:1000, 1:100 and 1:10 for testing, as well as a series of common inhalant allergens.

Results

Of the 274 questionnaires, only 54 (19.7%) were returned. Of those who did, 21 (38.8%) gave a history of skin problems, such as erythema, oedema, wheals, vesicles, dryness or irritation, localized to the hands and the forearms. All these 21 veterinarians were evaluated. There were 16 males ranging in age from 33 to 50 years, and 5 females aged from 31 to 40 years. 15 veterinarians described their practice as being exclusively or primarily based on small animals and 6 as being exclusively or primarily based on large animals. Of the 21 subjects investigated, 15 were shown to have occupational dermatoses: 4 cases of contact urticaria, 5 cases of allergic contact dermatitis and 6 cases of irritant contact dermatitis. Of the 4 with contact urticaria, 2 were positive to latex, 1 to cow dander and 1 to bovine obstetric fluids, this last case being diagnosed by direct observation only, as prick testing and radio-allergosorbent tests were both refused. Of the 5 with allergic contact dermatitis, we obtained relevant patch-test reactions to formaldehyde (1 case), glutaraldehyde (1 case), streptomycin (1 case), benzalkonium chloride (1 case) and Tego G (1 case). Atopy, defined as the presence of a positive skin reaction to at least 1 of the common inhalant allergens tested, was present in only 3 cases (2 males and 1 female).

Discussion

Although the current study is severely limited by the small number of veterinarians who responded to the questionnaire, it suggests that occupational dermatitis may be frequent among such workers in our area.

A questionnaire-based clinical study showed that in 189 Californian veterinarians, the most commonly reported contact factors were animals, protective gloves and specific medications (9). In a similar study from Kansas, the authors (10) showed that the most likely causes of contact dermatitis were repeated hand washing, obstetric-related factors and antiseptic agents. As yet, there is little agreement regarding the role of atopy as a predisposing factor for developing allergic or irritant contact dermatitis (11–14). The numbers with atopy in this study were too small to allow us to contribute further to this debate.

Past studies showed that the prevalence of hand eczema in the general population ranges from 2 to 10% (12). The current study agrees with previous investigations (1–3) showing that hand dermatoses are more common among veterinarians than in the general population. The specific causes of contact urticaria, allergic contact dermatitis and irritant contact dermatitis that we identified were the same as those previously reported from northern Europe and the USA (1–10).

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Very-low-voltage electrical injuries caused by cellular-phone chargers

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Key words: cellular-phone charger; contact burn; cutaneous ulcer; electrical injuries.

Case Reports

Case no. 1

A 20-year-old woman, who drank alcohol and fell asleep on a cellular-phone charger conducting electricity, developed a pair of small cutaneous ulcers on her right upper arm at the sites in contact with the charger's electrodes. The ulcer that had been in contact with the negative electrode was 8 mm in diameter and crusted; the other that had been in contact with the positive electrode was 5 mm in diameter and with yellowish necrosis. This charger had a capacity of 5.6 V/700 mA. As this patient had a history of contact dermatitis from a necklace, we conducted patch tests for metal allergy that showed a positive reaction to nickel. Although the electrode contact of the charger was made of nickel, we considered the cutaneous ulcers to be very-low-voltage electrical injuries.

Case no. 2

A 30-year-old woman, who was extremely tired when she went to bed, noticed in the morning that there had been a cellular-phone charger conducting electricity under her left buttock. The contact time was approximately 5 h, and she developed a pair of cutaneous ulcers with red haloes 5 mm in diameter at the sites in contact with the charger's electrodes. We biopsied the ulcers and found vascular necrosis at the site that had been in contact with the negative electrode and coagulation necrosis at the site that had been in contact with the positive electrode. Patch tests for metal allergy were negative. The charger was direct current 5.6 V/600 mA and made of nickel, phosphorus and magnesium. We diagnosed these cases also as electrical injuries due to very-low-voltage current.

Discussion

Electrical injuries, such as those caused by occupational accidents, storm and flood damage and suicide attempts, or those occurring in infants who accidentally touch electric outlets are common enough (1–3). Although many cases from high-voltage (>1000 V) to low-voltage (120–240 V) sources have been reported, cases like ours caused

by a voltage as low as 5.6 V are extremely rare. Our cases were considered to be caused by the long conducting period (more than 5 h).

Electrical injuries are classified into the following 3 categories: contact burn caused by current flowing within the body; arc burn caused by arc discharge; and flame burn caused by flame. Our cases are considered to be contact burn. The negative electrode site, which is the current entry point, sustained deeper necrosis and more severe skin damage than the positive electrode site. In general, the heat that is generated when electrical energy is converted into heat energy is determined by current, voltage, conducting time, contact resistance, etc., and described by $Q = I^2 R t$ [electric charge (Q), electric current (I), resistance (R) and time (t)] (4).

As the current and voltage of such chargers are very low, nothing would happen even if the skin were in contact with the charger for several minutes. When such a contact period becomes longer than 30 min, however, a tingling sensation occurs as the charger's small contact area has a large resistance. Skin ulcers, as in our cases, are considered to occur when this continues for several hours, alcohol intake or deep sleep making this more likely.

Cellular phones are now widely used in Japan. They have become one of the necessities of life, and most people from elementary school children to the elderly have one. People use them for other purposes besides phone conversation, including e-mail and Internet. Mainstream cellular-phone chargers have a compact and flat shape, and the body can easily come into contact with both electrodes. As people, in general, do not consider a charger to be dangerous, they often leave it switched on. We consider that the level of caution needs to be raised if cases like these are not to increase.

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Airborne occupational allergic contact dermatitis from *N,N*-bis[2-bromo-ethyl]aniline and *N,N*-bis[2-[(methylsulfonyl)-oxy]ethyl]aniline in a chemistry student

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Key words: airborne; aniline derivatives; chemist; contact dermatitis; cross-sensitivity; *N,N*-bis[2-bromo-ethyl]aniline; occupational; *N,N*-bis[2-[(methylsulfonyl)-oxy]ethyl]aniline.

Case Report

A 25-year-old male chemistry student with no previous dermatological history was synthesizing new molecules in an organic chemistry laboratory as part of his doctoral research. As he had contact with known irritants, he worked most of the time with latex gloves, without a mask but under a ventilation system.

He consulted our department in March 2003 with a 4-month history of recurrent eczema of both eyelids

(right more than left), around his mouth and nose and on his neck and the backs of both hands. When he stopped working, the lesions would gradually clear but would reappear in 2 days when he returned to work.

Patch tests with the European standard series, a rubber series and the ingredients of the topical pharmaceutical products he used were all negative, but patch tests with 3 of the products with which he came into contact in his laboratory gave positive reactions: *N,N*-bis[2-bromo-ethyl]aniline 0.5 and 1% pet., ++ and +++ at the D2 and the D4 readings, respectively. The patient was told to avoid this particular compound, but, when he returned to his laboratory, he again developed identical lesions on the face but now accompanied by urticarial lesions on the thighs, the left knee fold and the left ankle. 3 weeks later, patch tests were again administered with 1 pyridine and 2 aniline derivatives with which he had come into contact after he had returned to his laboratory. Now, he reacted to *N,N*-bis[2-[(methylsulfonyl)-oxy]ethyl]aniline 0.5% pet.: +++ at D2 and D4. The 2 aniline derivatives probably cross-react as their chemical structure is similar (Fig. 1). Both of these substances tested negatively in 1 control subject.

Comment

The patient was diagnosed as having an airborne contact allergy to the aniline derivatives that were being used as intermediates in chromophore synthesis (electronic non-linear optical application). He had developed this allergy even though he had worked most of the time with a ventilation system and worn latex gloves. However, because he recrystallized these molecules with the volatile solvents hexane and dichloromethane, outside the ventilation system, the solubilized chemicals had been released into the air and so came into contact with his exposed skin.

To the best of our knowledge, this is the first case report of airborne contact allergy to these aniline derivatives. Because of the severity of the eczematous reaction, we advised him to avoid absolutely all further contact with these intermediates. He has since been free of dermatitis.

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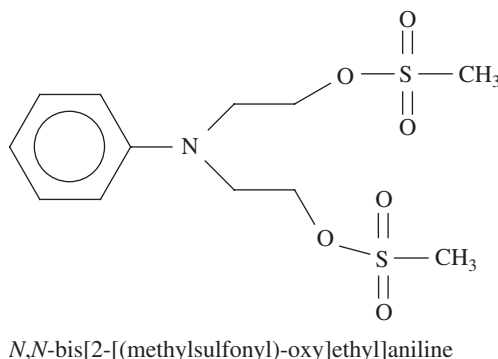
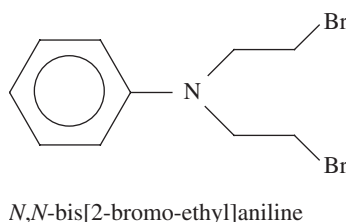


Fig. 1. The aniline derivatives to which the patient reacted.

Allergic contact dermatitis from polyethylene glycol monomethyl ether 350 in Solaraze[®] gel

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Key words: allergic contact dermatitis; medicaments; polyethylene glycol monomethyl ether 350; polyethylene glycols; Solaraze[®] gel.

Case report

A 74-year-old woman was referred after she developed eczema following the use of Solaraze[®] gel [diclofenac 3% w/w in 2.5% sodium hyaluronate (Shire Pharmaceuticals Ltd, Basingstoke, UK)] for actinic keratoses over the shins and dorsa of the feet. A use test on her forearm appeared to confirm a delayed reaction to Solaraze[®] gel. She was patch tested initially on her back to our extended standard series, cosmetics series and Solaraze[®] gel. All tests were negative at day 4. However, in view of the high clinical suspicion of allergic contact dermatitis, a repeat patch test with Solaraze[®] gel was applied to the left upper arm. This was positive (++) at day 4.

The manufacturers subsequently provided us with samples of the ingredients of Solaraze[®] gel: sodium hyaluronate, sodium diclofenac, polyethylene glycol monomethyl ether 350 (PEGMME 350) and benzyl alcohol. We patch tested on her back to the ingredients supplied, at the following concentrations: sodium hyaluronate 1, 5, 10% pet., sodium diclofenac 1, 3, 10% pet., PEGMME 350 5, 10% pet., and benzyl alcohol 5, 10% pet. All tests were negative. However, repeat patch testing on her left upper arm to the ingredients showed positive (++) reactions to PEGMME 350 at 5 and 10% pet. after 4 days. Patch testing to PEGMME 350 (5 and 10% pet.) was negative in 24 control subjects.

Discussion

Solaraze[®] gel is a relatively recent treatment for actinic keratoses (1–3). The summary of product characteristics (SPC) states that Solaraze[®] gel is contraindicated in patients with known hypersensitivity to its ingredients; diclofenac, sodium hyaluronate, benzyl alcohol and/or PEGMME 350, and in those with previous hypersensitivity reactions to other non-steroidal anti-inflammatory drugs. Also stated in the SPC under undesirable effects, 'Patch testing of previously treated patients indicates a 2.18% probability of allergic contact dermatitis sensitization (Type IV) to diclofenac with as yet unknown clinical relevance'. There is no mention of contact sensitivity to other ingredients of Solaraze[®] gel demonstrated by patch testing in these cases.

Contact sensitivity to diclofenac itself in eyedrops (4) and an ointment for musculoskeletal complaints (5) has previously been reported. To our knowledge, there are no previous reports of allergic contact dermatitis from PEGMME 350 as a vehicle in either diclofenac-containing or other medicaments.

Polyethylene glycols (PEGs) are the condensation polymers of various molecular weights (MWs) formed by reaction of ethylene oxide and water, in the presence of a catalyst. These are hydrophilic substances used as vehicles for many topical medicaments. There are previous reports of sensitization, both immediate-type contact urticaria and delayed-type eczematous reactions, to such medicaments, with confirmed sensitivity to their PEG excipients (6–9). Amongst 120 patients with topical medicament sensitivity, Bajaj et al. (10) showed positive patch-test results to PEGs in 8 (6.7%), most being to PEG 400, the lowest MW PEG tested. Stenveld et al. (11) also confirmed contact allergy to low MW, as opposed to high MW, PEGs in a nitrofurazone-containing topical preparation. Sensitization to PEGs may be underestimated because in one study, 9 out of 50 patients (18%) showed positive reactions to PEG 200 (12). However, reports of contact sensitivity to PEGs are infrequent, considering their widespread use, and they may have a relatively low sensitization potential (13, 14).

PEGMMEs differ from PEGs in that they are addition polymers of ethylene oxide and methyl alcohol, PEGMME 350 corresponding to the polymer with average MW 350. We have been unable to find previous reports of contact allergy to PEGMMEs, as opposed to PEGs, in either Solaraze[®] or other medicaments. The possibility of cross-sensitization to PEGs would seem chemically plausible, although we did not patch test our own patient to PEGs. The possibility of cross-sensitization of PEGs to propylene glycol has also been raised (11); in our patient, there was no reaction to propylene glycol in our extended standard series.

Patch testing to both Solaraze[®] gel and PEGMME 350 was negative on the back, but positive on the left upper arm. Such discordance is hard to explain but is, more generally, a well-recognized phenomenon. Bourke et al. (15) noted discordant results on opposite sides of the back in 30 of 383 patients (8%) patch tested.

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An isotopic response to patch testing

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Key words: eczema; fixed drug eruption; isomorphic; isotopic; Köbner.

Case Report

An 80-year-old woman with long-standing varicose eczema attended

for patch testing. She was tested with the British Contact Dermatitis Society standard series (excluding thiuram mix, formaldehyde, mercapto mix and mercaptobenzothiazole, to which she was already known to be allergic), medicaments and leg ulcer series and her own topical agents. On day 2 she had developed a circumscribed patch of microvesicular eczema over the site of her previous bacillus Calmette-Guérin (BCG) vaccination, which had been clear prior to patch testing (Fig. 1). Similar lesions had occurred at the site previously in association with flares of her eczema. Patch testing showed positive (++) results on day 4 to quaternium-15, methylchloroisothiazolione plus methylisothiazolinone and gentamycin.

Discussion

The isomorphic response of Köbner was first described by Heinrich Köb-

ner in 1876 and is defined as the development of isomorphic lesions in traumatized-uninvolved skin of patients who have cutaneous diseases (1). It occurs most frequently in psoriasis and is also commonly seen in lichen planus and vitiligo. Psoriasis vaccinalis has been described (2), where the disease preferentially affects old scar sites, including BCG vaccination, which may predate the disease by many years, as in our case. However, this does not strictly comply with Köbner's original definition of lesions that are precipitated by recent trauma in a patient with a pre-existing dermatosis.

The isotopic response is defined as the occurrence of a new unrelated skin disease at the same location as a previously resolved skin lesion (3). The most common primary lesion has been herpes zoster or simplex and a wide range of secondary conditions have been reported, including allergic contact dermatitis. Although



Fig. 1. Plaque of eczema at the site of previous bacillus Calmette-Guérin (BCG) vaccination.

a vaccination site has not previously been reported as the primary lesion, eczema does not usually exhibit the Köbner phenomenon, and our case seems more in keeping with the diagnosis of an isotopic, rather than an isomorphic, response.

Once a tissue has been inflamed, it appears to carry a memory of the event, such that future insults may localize to the same site. This may be due to localized changes in vascularity and vascular permeability or to the presence of a chronic inflammatory infiltrate including memory T cells. Comparisons may be drawn with a fixed drug eruption, where an increase in expression of intracellular adhesion molecule-1 on lesional keratinocytes, following first exposure to the drug, is thought to provide a localized-initiating stimulus for activation of disease-associated epidermal T cells on subsequent exposure (4). In our case, reactivation of eczema as the result of patch testing may have acted as the trigger.

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Occupational contact dermatitis caused by a personal-computer mouse mat

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Key words: 2, 6-di-*tert*-butyl-4-cresol; allergic contact dermatitis; computer; diphenylthiourea; mouse mat; neoprene rubber; occupational; office workers, polyvinyl chloride; zinc dibutylthiocarbamate.

Reports of allergic contact dermatitis caused by personal-computer use are gathering (1–7).

Case Report

A 57-year-old man presented with a sharply demarcated eruption on the palmar aspect of his right thumb, where there was erythema, scaling and vesiculation. This had been developing over 7 months. The remaining digits showed no changes.

He used a personal computer (PC) at work for up to 6 h every day. The lesions would clear when he was not working, and he associated relapses with continuous use of his computer and, specifically, with contact with the mouse mat.

Patch testing with the Spanish standard series, rubber additives series, acrylates series, epoxy series and plastics and glues series (Chemotechnique Diagnostics, Malmö, Sweden) was positive to fragrance mix (++), diphenylthiourea (+++), 2,6-di-*tert*-butyl-4-cresol (+++) and zinc dibutylthiocarbamate (++) at 2 and 4 days.

The manufacturers informed us that the basic composition of their mouse mats was neoprene rubber and polyvinyl chloride. We recommended that the patient use the PC mouse without the mouse mat, and the thumb dermatitis improved within 7 days.

Comment

Our patient was allergic to neoprene rubber, specifically to diphenylthiourea in it, and also he was allergic to zinc dibutylthiocarbamate in natural rubber. In addition, he was allergic to 2,6-di-*tert*-butyl-4-cresol, which is an antioxidant widely used in rubber, plastics and glues. The positive patch tests confirmed our clinical suspicion of allergic contact dermatitis caused by mouse mat, which improved once the patient stopped using it.

Previous reports (1–7) have implicated the keyboard, keyboard wrist-rest and the mouse itself, rather than, as in this case, the mouse mat.

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