

CONTACT POINTS

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Intolerance to rubber presenting as suspected but not confirmed natural rubber latex allergy

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Key words: methyl tertiary butyl ether; natural rubber latex; patch testing; prick test; rubber tyre; rubber; aqueous extracts; scratch test; Type I allergy.

Case Report

A 28-year-old woman, with no previous skin disease but with Type I allergy to nuts, had not eaten banana since childhood or kiwi since the age of 13 because of tingling of the lips and tongue when eating them. She had been working in a sports shop for 8 years when she started to get tingling sensations on the lips and oral mucosa when near rubber objects. She noticed this for the first time when she was in a room where 60 rubber car tyres were stocked.

During this period, she had had to be anaesthetized at her local hospital and, when a black rubber mask was placed over her mouth, she had immediately felt tightness of breath and was given systemic corticosteroids. At other times, she felt tingling sensations on the lips and oral mucosa when she had to go down to the basement of the shop where the proprietor kept new bicycles, when she accidentally bought a latex pacifier for her baby and when blowing up a balloon. At home, she had never worn rubber gloves.

After 1.5 years of parental leave, she was due to return to work. By this time, the sports shop owner had stored all the new bicycles on the ground floor, the room in which the

patient was to work. Because she feared anaphylaxis on return to work, she underwent medical investigation at the local hospital with latex prick tests, using a commercial allergen (Soluprick[®], ALK Abelló, Hørsholm, Denmark), radioallergo-sorbent test (RAST) (Pharmacia Diagnostics, Uppsala, Sweden) for latex, and patch testing with the Swedish standard series supplemented with a piece of latex glove, without latex Type I or IV allergy being detected. There was, however, erythema with pruritus, the size of a palm, on the back under the piece of latex glove when this was removed after 2 days.

She was referred to us for further investigation, when patch testing with our standard series and a rubber additives series including several accelerators, and a series of immediate tests including prick tests (Stallergènes S.A., Antony, France) and scratch tests with latex and extracts of rubber products were performed. Tests were performed on 2 occasions within a month. Patch tests were all negative and the results of the immediate tests are summarized in Tables 1 and 2.

Despite several negative prick tests to commercial latex allergens, the patient gave an immediate reaction to a prick test with an aqueous extract of a rubber tyre from the sports shop. Surrounding erythema was 10 cm in diameter and infringed on the other tests, making us repeat testing on another part of the arm, but even then the erythematous macules around the aqueous extract were close to the ethanol test. 45 min after an oral antihistamine, cetirizine 10 mg (Zyrlex[®], UCB, Malmö, Sweden), a 4th prick test with the aqueous extract of the rubber tyre gave a negative reaction where the prick was placed, though to the left of this area erythema was seen (Fig. 1).

Throughout testing, the patient was symptomless from the lips, oral mucosa and respiratory system. 22 controls were prick tested with the aqueous extract from the rubber

tyre with negative results. 3 patients previously shown to be Type I allergic to latex by prick tests with commercial allergen went through the same procedure with negative results. Serum from the patient and a piece of the rubber tyre to which the patient had reacted were sent to the Allergen Laboratory, Skin and Allergy Hospital, Helsinki, Finland, for immunospot analysis and latex RAST inhibition test. Results were negative for both.

The patient declined to return to the shop and found other work in an office, where she remained well. 2 years after her 1st visit to us, she returned for additional immediate tests, including closed, scratch chamber and prick tests to some rubber additives, viz. black rubber mix, thiuram mix, tetramethylthiuram disulfide, tetramethylthiuram monosulfide, zinc diethyldithiocarbamate, zinc dibutyldithiocarbamate, diphenylguanidine and mercaptobenzothiazole. All these tests were negative. A prick test with banana on the arm was also negative after 20 min, as was a provocation test with banana held inside the lower lip for 20 min. The patient told us that she had been symptomless since her last visit to us.

Discussion

This patient's history was suggestive of Type I natural rubber latex hypersensitivity (1), even though prick tests and RAST for latex were consistently negative. Prick tests to commercial latex allergens are not 100% sensitive and a negative latex RAST does not exclude latex allergy (2). Latex glove eluates may also give false-negative reactions because the glove eluted may be of low-allergenic content (2). The 4 mm reaction to the aqueous extract of the rubber tyre is consistent with a positive reaction (3) and the erythema with a 10 cm diameter surrounding the wheal was specific to the patient, as 22 controls were negative as well as the 3 latex Type I allergic positive controls. An

Table 1. First test session, closed and prick testing with latex

Closed test	15 min reading	Comments on additional signs
Stallergènes extract	—	
Latex glove eluate*	—	
Prick test		
Stallergènes extract	—	
Latex glove eluate*	—	Pruritus
Soluprick positive control†	+	
Soluprick negative control‡	—	

*Mölnlycke latex glove, >100 AU/ml of latex.

†Histamine positive control.

‡Saline negative control.

Table 2. Second test session, open, prick and scratch testing of different rubber articles as is and as extracts

Test method	Object	Extraction medium	15 min reading	Comments on additional signs
First test, volar forearm				
Closed test	Rubber tyre	Methyl tertiary butyl ether	—	
	Rubber tyre	Acetone	—	
	Rubber tyre	Ethanol	—	
	Rubber tyre	Water	—	
	Latex condom	Water	—	
	Latex pacifier	Water	—	
Second test, volar forearm				
Prick test	Rubber tyre	Methyl tertiary butyl ether	?	Erythema, test is too close to aqueous extract test
	Rubber tyre	Acetone	—	
	Rubber tyre	Ethanol	?	Erythema, test is too close to aqueous extract test
	Rubber tyre	Water	+	4 mm wheal, surrounding erythema 10 cm diameter with distant red flares outside, stinging, increased heat
	Latex condom	Water	—	
	Latex pacifier	Water	—	
	Soluprick positive control*		+	5 mm wheal
	Soluprick negative control‡		—	
Scratch test	Rubber tyre		?	
	Latex condom		?	
	Latex pacifier		?	
Third test, inner upper arm				
Prick test	Rubber tyre	Methyl tertiary butyl ether	—	
	Rubber tyre	Acetone	—	
	Rubber tyre	Ethanol	—	Similar macular erythema as to the aqueous extract, test is too close to aqueous extract test
	Rubber tyre	Water	?	Several erythematous macules with diameter >3 cm around prick, increased heat and smarting pain
Fourth test, outer right shoulder				
Prick test	Rubber tyre	Ethanol	—	
Fifth test, dorsal right shoulder, after 10 mg cetirizine				
Prick test	Rubber tyre	Water	?	Erythema and increased heat to left side of prick

*Histamine positive control.

‡Saline negative control.

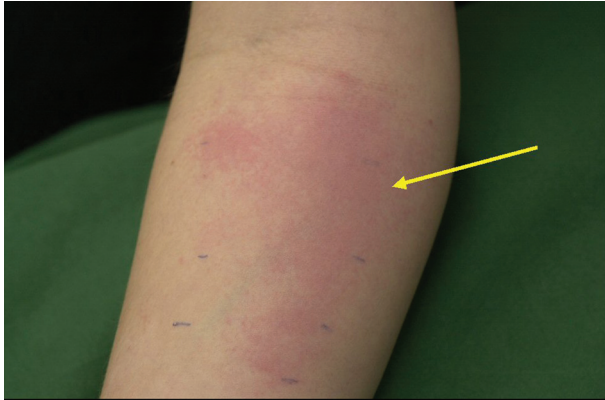


Fig. 1. Prick test with rubber tyre in water extract (yellow arrow) on volar forearm: surrounding erythema (10 cm diameter) around test site with distant red flares outside.

immunospot was performed to detect whether the patient's serum had immunoglobulin E (IgE) to rubber tyre extract. However, no IgE binding could be demonstrated from the patient's serum to rubber tyre extract or to latex samples. Furthermore, there was no binding from the pooled serum of latex-allergic patients, i.e. no IgE binding or allergenic activity could be demonstrated in the tyre sample.

The exact nature of this patient's reactions thus remains obscure. The patient's repeated reactions to the aqueous extract of the rubber tyre are suggestive of a water-soluble allergen that was not latex. Even though IgE binding was not found, another type of immunological non-IgE-mediated reaction might be present, presenting as an immediate skin reaction on skin testing. A histamine/leucotriene release test or a lymphocyte stimulation test against the tyre extract may have given further information but could not be performed. Immediate-type allergic reactions to rubber additives have been reported (4–6), but their significance may be uncertain. The test method in some studies was scratch testing, which is claimed to give a high rate of false positives (2). Controlled provocation tests with the rubber tyre, condoms and the latex pacifier, such as rubbing these objects against the lips and oral mucosa with the patient blindfolded and wearing a nose-clip, might also have been done but, even if positive, the precise cause would still have remained unknown.

Acknowledgement

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Contact dermatitis from Diazald

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Key words: allergic contact dermatitis; chemical industry; Diazald; occupational.

Case Report

A 39-year-old chemical process worker presented with an 18-month history of an intermittent itchy rash temporally related to exposure to Diazald – an organic intermediate. His 1st episode occurred 2 weeks after starting Diazald manufacture and affected the skin between the fingers and over the wrists. Subsequently, he developed infected, open sores over the hands requiring absence from work for 6 weeks before his symptoms settled. 12 months later, he had a 2nd episode of a similar rash, which involved the skin patchily over the arms, face, wrists and feet. His symptoms settled slowly over several weeks.

The industrial manufacture of Diazald results in the production of Diazald cake or powder. Our patient was required to pack Diazald cake into 50 kg containers by digging it out of the reactor with a shovel. For this work, he was provided with, and used, personal protective equipment: gloves, spectacles, face shield and overalls. After his 2nd episode of dermatitis, he was moved from this job to an office-based position in the maintenance department. On occasions, he was still required to go into the factory processing area and, after these site visits, he would develop an itchy erythematous rash over his face, arms, legs and groins, which would settle over a few days.

He had a past history of a skin reaction to diphenylmethane-4,4' diisocyanate some years ago, but otherwise no history of skin disease and was on no regular medications. He had a family history of atopy.

Examination showed residual eczema over the upper thighs, with some scrotal lichenification.

He was patch tested to a standard series, an isocyanates series, a textile dye and resins series, the fragrance mix breakdown, his own medications and Diazald at 0.01% in pet. He had a ++ reaction to Diazald at 2 and 4 days. 30 control subjects patch tested to Diazald were negative.

Discussion

Diazald is an organic intermediate whose chemical name is *p*-tolylsulfonylmethylnitrosamine or *N*-methyl-*N*-nitroso-*p*-toluenesulfonamide (1). Diazald is known to have antimicrobial activity against yeasts, fungi and bacteria (2). It is a methylating agent and its major use is in the laboratory preparation of diazomethane, another methylating agent, and the synthesis of other biologically active compounds (3). In this particular circumstance, it was used as an intermediate in the manufacture of solid rocket propellant. As far as we are aware, contact allergy to Diazald has not been reported previously.

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Allergic contact dermatitis from benzyl alcohol in multiple medicaments

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Key words: allergic contact dermatitis; benzyl alcohol; lichen scleroses; medicaments, *Myroxylon pereirae* resin.

Benzyl alcohol (BA) is an aromatic preservative with anaesthetic and antipruritic actions. Despite its widespread use in topical medicaments and cosmetics (and also in some industrial products), sensitization to this allergen is considered rare. BA has been reported as responsible for allergic contact dermatitis from antibacterial and antimycotic creams, topical corticosteroids, sunscreen, analgesic spray, sclerosing agent, epoxy adhesive and cutting oil (1–6).

Case Report

A 46-year-old woman presented with a 2-year history of itching of the vulva and perianal area and recurrent erythema and oedema following the application of various topical antibiotics and antimycotics prescribed by her physician for suspected infectious vulvovaginitis. A punch biopsy of the vulva, carried out 1 year later in the dermatological department of her city, showed the histological features of lichen scleroses, confirming the clinical diagnosis. Topical therapy with methylprednisolone aceponate cream (Advantan[®] cream, Schering SpA, Milan, Italy) caused firstly moderate improvement, but some days later, it was stopped because the patient developed local erythema and oedema. Thereafter, the patient came to our department for allergological investigations. Patch tests were performed, in different steps, according to the guidelines of the ICDRG (readings at days 2, 4 and 7) and gave the following positive reactions:

- (1) Italian (SIDAPA) standard series (extended) to *Myroxylon pereirae* resin, fragrance mix, *p*-phenylenediamine, benzocaine and paraben mix;
- (2) components (tested separately) of fragrance mix to cinnamic alcohol, oak moss absolute, geraniol and of paraben mix to benzyl paraben;

- (3) 10 topical preparations used by the patient (patch tested as is) to Bactroban[®] cream (Glaxo-smithkline SpA, Verona, Italy) and Gyno Canesten[®] cream (Bayer SpA, Milan, Italy);
- (4) 14 components of these topical preparations to BA (5% in pet.).

BA proved to be the common preservative in Bactroban[®] cream, Gyno Canesten[®] cream and Advantan[®] cream. Negative patch test reaction to the last product was attributed to the presence in the cream of methylprednisolone aceponate.

Discussion

Concomitant reactions to *M. pereirae* resin and BA, according to Hausen (7), should not be considered a true cross-reaction, because BA is present in *M. pereirae* resin at 1–2% concentration. We are going to start a study concerning the relevance of sensitization to BA in patients allergic to *M. pereirae* resin.

Sensitization to paraben mix in our case is probably not relevant, because it was caused only by benzyl paraben, a no-longer-allowed preservative. This positive reaction could be related to contact allergy to BA, produced in the skin as a result of the hydrolytic decomposition of benzyl paraben (8).

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Allergic contact dermatitis caused by parabens in a compress

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Key words: allergic contact dermatitis; compress; cosmetics; medicaments; methyl paraben; paraben paradox; propyl paraben.

Case Report

A 68-year-old Japanese woman suffered an eruption, a rectangular-shaped, pruritic erythematous macular area on the right knee, following the use of a compress, Seltouch[®] (Wyeth Japan, Tokyo, Japan) containing methyl and propyl parabens as preservatives. The compress was discontinued, and we treated the patient with betamethasone valerate ointment containing butyl paraben 0.18% and propyl paraben 0.02%. The eruption subsided 7 days later. During the same period, the patient used a variety of cosmetics that also contained parabens, but these did not cause skin problems in the areas to which they were applied.

The manufacturer generously provided us with all of the ingredients contained in the compress. Patch testing of the patient showed positive reactions to both methyl and propyl paraben at 5% pet. on D2 (+), D4 (+) and D9 (+). The concentration used did not result in a false negative (1–4).

Discussion

Parabens are the most commonly used preservatives in both medicaments and cosmetics. As far as we know, this is the first case of allergic contact dermatitis due to parabens in a compress.

The 'paraben paradox' is the situation in which an individual can safely use cosmetics containing parabens but will develop allergic contact dermatitis and inflamed skin from using medications containing parabens (4–6). The reason for this is that therapeutic agents easily penetrate and sensitize skin that is inflamed, eczematous, excoriated or damaged, while cosmetics are usually applied to normal skin which is hard to penetrate (4–6).

This case is another example of the puzzling paraben paradox. In this case, the occlusive conditions might have promoted the absorption of parabens. Because of the occlusive environment, parabens in a compress are more likely to cause allergic contact dermatitis than parabens in cosmetics or other medicaments.

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Metamizol as a cause of postoperative erythroderma

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Key words: cutaneous adverse reactions; erythroderma; metamizol; patch testing technique; positive patch test; pyrazolone; surgery.

Metamizol is one of the most frequently prescribed analgesics. It is involved in immediate IgE-mediated reactions (urticaria/angioedema), non-allergic non-steroidal anti-inflammatory drug (NSAID) intolerance, severe skin reactions such as Steven's–Johnson syndrome or toxic epidermal necrolysis (1), and other delayed reactions such as fixed drug eruption (2) and contact dermatitis.

Case Reports

Case 1

A 72-year-old woman, with a previous history of contact dermatitis from metals and diagnosed as allergic to muscular relaxants, developed, 48 h after surgery, an erythematous widespread skin reaction. The lesions resolved in 4 weeks without desquamation.

She had been operated on under local anaesthesia and had been treated with paracetamol, metamizol and omeprazol.

Table 1. Prick, intradermal, patch and oral provocation test results

Case	Drug	Prick (mg/ml)	Intradermal (mg/ml)	Patch	Oral
1	Novocaine	20 –	0.05 –	–	Well tolerated
	Lidocaine	50 –	2 –	–	Well tolerated
	Mepivacaine	20 –	0.2 –	–	Well tolerated
	Metamizol	400 –	1,10 –	48 h ++ 96 h ++	
	Proeffergan® (Paracetamol)	100 –	1 –	–	
	Omeprazol	40 –	0.1,1 –	–	
	Clorhexidine 20%	–	–	–	
	Hibimax® 5%	–	–	–	
2	Diclofenac				Well tolerated
	Metamizol	400	1,10 –	96 h +	
	Piroxicam				Well tolerated
3	Vancomycin	0.05 –	0.005 –	–	Not tested
	Teicoplanin	100 –	1 –	–	Not tested
	Metamizol	400 –	1,10 –	48 h + 96 h +	

Oral provocation tests with other NSAIDs, such as diclofenac (case 1) and piroxicam (case 2), were well tolerated.

Case 2

A 55-year-old man, with no history of atopy, developed a pruritic erythematous eruption on the arms and in the perianal region. The lesions began 24 h after urological surgery and resolved in 10 days with residual desquamation. He had been treated with a quinolone (ciprofloxacin), and suspecting that this could be the causative drug, prick testing and oral challenge were carried out with negative results. The patient insisted that, every time he had an operation, the same skin reaction appeared thereafter. Investigation was widened to other drugs involved in previous operations and metamizol found to be the common factor.

Comment

In the cases presented, a patch test with metamizol (50% pet.) proved useful in diagnosis. The correct metamizol patch test concentration is not clear, some authors suggesting it be tested as is (3), whereas others recommend 10% pet. (4,5). Although we have used a higher concentration (50% pet.), control tests performed in 40 patients gave negative results and we therefore do not consider this higher concentration to be irritant. Previous reports (6) of late reactions to metamizol showed positive intradermal test readings, but in our patients these were negative.

To conclude, metamizol must be considered a potential causative drug of delayed skin reactions in the context of postoperative and polymedicated patients.

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Case 3

A 66-year-old woman, with no history of atopy, developed, 2 days following urologic surgery, a widespread pruritic exanthema that resolved in 8 days with mild desquamation. She had received treatment with teicoplanin and metamizol.

Prick, intradermal, patch and oral provocation test results are shown in Table 1. Readings of prick and intradermal tests were done at 15 min and 24 h. Patch tests were read at 48 h and 96 h. Metamizol was patch tested at 50% pet. Patch tests were also performed in 40 control patients with negative results.

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Seminal fluid as a missed allergen in vulvar allergic contact dermatitis

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Key words: allergic contact dermatitis; consort dermatitis; post-coital vulvitis; seminal fluid.

The aetiological diagnosis of vulvitis is often difficult, given that this type of dermatitis may be secondarily aggravated by topical treatments or locally applied hygiene products. History taking concerning the periodicity of inflammation may be an important guiding factor to diagnosis. We report 2 cases of vulvar eczema which disappeared during the menstrual period and thus led us to consider the diagnosis of delayed hypersensitivity to seminal fluid.

Case Reports

Case 1

A 32-year-old woman with no atopy had experienced for the last 2 years a recurrent vulvo-vaginitis, which would completely regress during menstruation. Pruritus vulvae and slightly scaly erythema was to be found on the labia majora and minora. Several topical antifungal treatments had previously been applied without any benefit. Patch tests with vulvar hygiene products and the European standard series had all been negative.

The fact that symptoms would disappear in parallel with protective intercourse using condoms, as well as during menstruation, remained suggestive of postcoital vulvitis. A further patch test with the husband's semen applied in a Finn Chamber gave a positive (++) reaction after 2 days. This ++ reaction still persisted after 3 days without any diminution. A patch test with the husband's saliva was negative. For practical as well as ethical reasons, no control tests were performed with seminal fluid not originating from the husband. A blood test for antiseminal protein-specific immunoglobulin E (IgE) was negative.

Case 2

A 42-year-old woman with no atopy presented with vulvar itching. A diagnosis of vulvar seborrheic dermatitis had previously been considered, although imidazole treatment had provided no relief. Topical corticosteroids brought about only mild and transitory improvement. Careful review of the history disclosed the exact chronology of symptoms, with onset at the end of menstruation, 1 or 2 days after resumption of intercourse.

The diagnosis of postcoital vulvitis was put to the test with a patch test

with semen from the husband: the patch test was positive (++) after 2 days, thus allowing a diagnosis of contact allergy to seminal fluid to be made. A blood test for antiseminal protein-specific IgE did not demonstrate any associated Type I hypersensitivity. Symptoms disappeared with the use of condoms.

Discussion

The vulva may be the site of both irritant reactions and allergic contact dermatitis (1), but there is no mention in the literature of the possibility of contact allergy to semen. The most commonly reported contact allergens are perfumes and antiseptics, such as chlorhexidine and benzalkonium chloride, which are often to be found in women's hygiene products (2, 3). Preservatives are also to be found in tampons and sanitary napkins (4). Medicinal ovules and antimicrobial creams (5, 6) may worsen a pre-existing dermatosis, dermatitis from topical neomycin being a familiar example. Even tosylamide/formaldehyde resin in nail varnish may be the allergen responsible.

In persistent lichenified vulvitis, the results of patch testing have been found to be positive in as many as 27% of cases, which justifies a more exhaustive exploration of vulvitis by patch testing (7, 8), provided that the clinical importance of any positive tests be assessed (9). In such cases, the diagnosis of contact allergy to seminal fluid is quite simple to propose, given that symptoms recur only after intercourse.

Allergy to seminal fluid was first reported by Halpern et al. (10) in 1967, but only as a Type I hypersensitivity, clinically manifesting itself as a localized contact urticaria. In 1995, Poskitt et al. added dyspareunia to the other previously known symptoms of allergy to semen (11). The diagnosis in our cases was prompted by review of the history and supported by exclusion of all other known causes of vulvar allergy and pruritus (12).

The fact that allergenicity is not modified following vasectomy has been used as an argument confirming the direct responsibility of seminal protein (13). Several desensitization attempts at using different protein fractions (14, 15) have led to the finding that the Hu Se 1 fraction is involved in immediate allergy and that its molecular weight ranges from 12 000 to 75 000 Da. Mathias

et al. (16) underlined that semen antigen apparently reappears and is detectable in semen within 12 h following ejaculation. Desensitization using this protein fraction induces a decrease in specific IgE followed by an increase in the corresponding IgG (17, 18). Degranulation tests on sensitized cells of female patients, performed *in vitro*, suggested that the semen antigen is not male sexual partner specific.

In contrast to vulvar urticaria caused by immediate hypersensitivity, with concomitant risks of asthma or anaphylaxis (19), allergic contact vulvitis presents as a chronic local dermatosis with a benign prognosis. However, the possibility of later complication by immediate allergy and diffuse symptoms cannot be excluded, given the report of a case of exacerbation of atopic dermatitis in a woman presenting with Type I allergy to seminal fluid. This fact should encourage greater prudence when evaluating the prognosis in a patient presenting with antecedents of atopy (16). Nevertheless, anaphylactic reactions to semen may be severe, even in absence of atopy (13).

Along with natural rubber latex allergy, semen allergy must be considered in postcoital vulvar dermatitis (20).

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Direct and airborne contact dermatitis from propolis in beekeepers

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Key words: airborne; allergic contact dermatitis; beekeepers; occupational; propolis.

Propolis is a lipophilic substance used by bees to seal hive walls, repair defects and preserve aseptic conditions within. Propolis is a recognized cause of occupational contact dermatitis in beekeepers, mainly from collecting honey and cleaning hives (1). Nevertheless, beekeepers now constitute less than 25% of patients with sensitization to propolis, due to its increasing use in medicinal and cosmetic preparations (2).

Case Reports

Case no. 1

A 50-year-old woman, a beekeeper for 20 years, developed erythema, micropapules and itching on her fingers while collecting honey. Moreover, she had a previous history of a toxic reaction after receiving more than 50 bee stings. Later on, she tolerated bee stings without any reaction.

Case no. 2

A 54-year-old man, a beekeeper for 8 years, presented with scaly eczema on his hands when cleaning the hives over the last 5 years. He had had widespread dermatitis when working as a forester some years before.

Case no. 3

A 57-year-old man, a beekeeper for the last 10 years, presented with repeated episodes of erythema and facial itching 6 h after collecting honey from hives, evolving into facial swelling within 1 D. Corticosteroid

treatment became necessary to control his symptoms. Sometimes he wore a facial mask and protective spectacles but unsuccessfully. He handled honey without adverse effects.

In all 3 cases, patch tests with the European standard series and with propolis 10% pet., beeswax (as is), honey (as is), cinnamic alcohol 1%, vanillin 10% and benzyl cinnamate 5%, as well as a group of 13 contact allergens from plant extracts in case no. 2, were carried out, showing a positive reaction to propolis 10% pet. in all cases (case no. 1 and case no. 2: ++, case no. 3: +++). Sesquiterpene lactones (++) in case no. 2, wax (+) and nickel (++) in case no. 1 and honey (++) and wax (++) in case no. 3 were also positive. Specific immunoglobulin E against bee venom was positive only in case no. 1.

Discussion

Poplar bud secretion is the bee's major source of propolis and hence the origin of LB-1 (a mixture of 3 caffeic acid pentenyl esters), the major sensitizer of both propolis and poplar bud secretion. Chemical separation of various propolis samples and poplar bud extracts shows that LB-1 is always present (2); likewise, various other compounds are common to both (3).

We describe 3 cases of occupational contact sensitization to propolis, with varied features. Case no. 1 was typical of such contact dermatitis in beekeepers. Shared allergens between propolis and poplar buds explain propolis sensitization in the 2nd patient (2), who had previously had contact with poplar bud secretion while working as a forester. Contact dermatitis is well recognized in foresters, though few cases related to propolis have been described (4). The 3rd patient shows an atypical form of sensitization, airborne. In the literature, only 1 case (5) of airborne contact dermatitis due to propolis has been published, within it quoted another possible similar case.

In conclusion, we should consider propolis as both a direct and an airborne contact allergen in beekeepers. Likewise, in occupations with poplar contact, propolis should be considered as an allergen if dermatitis is present.

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Allergic contact stomatitis due to therapeutic propolis

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Key words: allergic contact stomatitis; lozenge; medicaments; mouthwash; propolis.

Case Reports

Case no. 1

A 64-year-old woman consulted her general physician about the manage-

ment of recurrent oral ulceration. The patient was given an alcoholic solution of propolis 25% as a mouthwash, 2× daily. 2 days after beginning the treatment, she reported progressive labial oedema, oral pain and swollen feeling, dysphonia and mild upper dyspnoea, aggravated each time that she rinsed her mouth. Corticosteroid and antihistamine treatment became necessary, with symptoms disappearing slowly in 3 D.

Case no. 2

A 65-year-old woman was prescribed propolis lozenges as a nutritional supplement and immune-system stimulant by a naturopath. She reported heat, pain and tongue swelling, with progressive upper dyspnoea, 8 h after taking the first lozenge. Emergency treatment with corticosteroid and antihistamine was necessary, after which symptoms disappeared within 3 D. She reported eating honey and handling wax without adverse effects, but she experienced localized pruritus with topical medicaments containing wax for leg ulcer treatment.

In both cases, patch tests with propolis 10% pet., cinnamic alcohol 1% pet., vanillin 10% pet., benzyl cinnamate 5% pet. and balsam of Peru (Myroxylon pereirae resin) were performed. Case no. 1 was also tested with the propolis 25% solution (as is) supplied by the patient, and case no. 2 with honey (as is) and wax (as is). A positive reaction (++) was observed to propolis 10% pet. in both patients, to propolis 25% (+++) in case no. 1 and to wax (++) and balsam of Peru (++) in case no. 2. Case no. 2 was also weakly positive to honey (+) and benzyl cinnamate 5% pet. (+).

Prick-by-prick tests with propolis 25% solution and with propolis lozenges were negative in both cases.

Discussion

Propolis is made by bees to build, protect and repair hives. Its major source is the resinous exudates of poplar buds. Propolis is used in cosmetic and medicinal preparations because of its antiseptic, anti-inflammatory and anaesthetic properties, among others. Its therapeutic qualities have been well documented for intraoral treatment (1). A warning is

indicated, however, that propolis should not be used in topical products because of its strong sensitizing properties (2), due mainly to 3-methyl-2-butenyl caffeate and phenylethyl caffeate, both major allergens, with benzyl salicylate and benzyl cinnamate playing a supporting role as sensitizers (3). Positive reactions to balsam of Peru in propolis-sensitive individuals are explicable because many compounds are common to both materials (3).

A few cases of cheilitis (4) and intraoral (5, 6) conditions due to propolis have been described, though an increase is to be expected now that toothpastes, lozenges, powders, chewing gum, mouthwashes and various remedies for intraoral uses containing propolis have become widely used. Because of this, propolis should be patch tested as a possible cause of allergic oral symptoms in users of such remedies or treatments.

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Contact dermatitis from a fishing rod

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Key words: carbon fibre; contact dermatitis; fishing rod; *N*-isopropyl-*N'*-phenyl-*p*-phenylenediamine.

Carbon fibre is a polymer which is a form of graphite. These fibres are used to reinforce epoxy resins and other thermosetting materials. Such reinforced materials are called composites because they have more than one component. Carbon fibre-reinforced composites are very strong for their weight. Because of this, they can be used to replace metals in many applications, from parts for aeroplanes and the space shuttle to tennis rackets, golf clubs and fishing rods. Carbon fibre is made from another polymer, polyacrylonitrile by a complicated heating process. Carbon fibres are known to cause airborne irritant contact dermatitis (1).

Case Report

A 28-year-old man was referred with eczema of the right palm, which had appeared 2 days before. The patient recalled the same lesions the previous month, treated with topical corticosteroid and oral antihistamine with rapid remission. Both episodes had occurred after prolonged contact (4 h approximately) with a carbon-fibre fishing rod.

After improvement in the skin lesions, the patient underwent patch testing with the European standard series, acrylates series, metals series and dyes series, with Finn Chambers on Scanpor® (Epitest, Tuusula, Finland) applied on the upper back. Reading was performed for 2 days with positivity, evaluated according with the International Contact Dermatitis Research Group criteria, for *N*-isopropyl-*N'*-phenyl-*p*-phenylenediamine (IPPD) (+++) and *p*-aminoazobenzene (+). We contacted the manufacturer of the fishing rod, who could not confirm the presence of either of these substances in the manufacture of its products. Nevertheless,

the patient seemed not to have had any contact with either substance in his hobbies or at work.

The history from the patient included anaphylactic shock after penicillin intake, when he was young. The history was otherwise negative for systemic diseases, respiratory allergy and food allergy; prick testing was negative for common inhalant and food allergens.

The patient, suspecting involvement of the fishing rod, covered the handle with insulating tape before further use. This practice allowed him to prevent any relapse.

Discussion

Little seems to be known about contact dermatitis from carbon fibre and products involved in its manufacture. To our knowledge, there are no similar reports of contact dermatitis from a fishing rod. A temporal relationship between the use of the fishing rod and the appearance of eczema, the absence of other identifiable causative factors or other explanations for the skin reactions and the recurrence of lesions after prolonged fishing rod contact, all prompted us to diagnose allergic contact dermatitis from an unconfirmed chemical used in manufacturing the fishing rod, possibly IPPD or a closely related substance.

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Allergic contact cheilitis induced by repeated contact with propolis-enriched honey

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Key words: allergic contact cheilitis; honey; patch tests; propolis.

Case Report

A 50-year-old housewife, with no personal or family history of atopy or allergic contact dermatitis, presented with a chronic pruritic cheilitis of 1-year duration. Avoidance of use of cosmetics, lipsticks and toothpaste, as well as the topical application of antibiotics and corticosteroids, failed to improve the cutaneous lesions. Dermatological examination showed erythema, scaling and crusting of the lips and perioral area, with complete sparing of the oral mucosa.

Patch tests with a standard and a cosmetics series (Chemotechnique Diagnostics, Malmö, Sweden) were performed according to the guidelines of Società Italiana di Dermatologia Allergologica Professionale e Ambientale (1) and a strong positive reaction (+++) to propolis 10% in pet. was shown. The patient denied the application of cosmetics containing propolis but reported the daily intake of homemade honey for breakfast. Patch tests performed with honey samples, provided by the patient herself, again showed a strong positive reaction (++).

The cessation of oral intake of honey resulted in complete remission of the cheilitis, while the ingestion of pills made with that same honey was not followed by recrudescence of eczematous lesions.

Discussion

We report what we believe to be the first case of allergic contact cheilitis caused by repeated contact with propolis contained in homemade honey. Cheilitis correlated with labial and perioral contact with honey, and, moreover, its avoidance led to a complete remission of the cheilitis. Mucosal lesions were not observed, and the oral ingestion of propolis-containing pills did not produce any effects. The patient had a strong positive reaction to patch tests with both propolis and honey.

Although no traces of propolis can usually be found in honey (2), it may happen, as in the present case, that some beekeepers intentionally add propolis to honey for 'therapeutic' purposes. Propolis has been widely used since ancient times in herbal remedies, because of its antiseptic, anti-inflammatory and antioxidant properties.

In recent years, herbal remedies of plant origin have gained increasing popularity and, accordingly, eczematous allergic reactions to them are on the rise (3). Contact dermatitis from propolis-based varnish in violin-makers and musicians has also been described (4). In addition, chronic stomatitis and throat complaints have rarely been caused by contact allergy to propolis contained in toothpaste, candies, tablets and chewing gums (5).

In conclusion, contact sensitization to propolis in the form of propolis-enriched honey has been shown to induce an allergic contact cheilitis of considerable chronicity.

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Contact allergy to 1-bromo-3-chloro-5,5-dimethylhydantoin in spa water

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Key words: 1-bromo-3-chloro-5,5-dimethylhydantoin; allergic contact dermatitis; bromine; chlorine; hypochlorite; spa; swimming pool.

Chlorinated and brominated products are used to sanitize pools and spas. They frequently irritate mucous membranes and skin and occasionally cause an allergic sensitization. Immediate or delayed reaction to sodium hypochlorite seems to be the common denominator in most cases. The following observation is an exception to the rule.

Case Report

A 41-year-old man had been using a spa since the fall of 2002. The water was filtered, circulated, maintained at neutral pH and periodically sanitized. In May 2003, the patient noted the appearance of eczematous lesions on immersed body areas, 2–3 days after bathing in his spa. With time, the eruption became more persistent and symptomatic.

The patient was using a disinfectant sold under the name Pro Guard[®]. This brominated pellet is composed of 1 ingredient, 1-bromo-3-chloro-5,5-dimethylhydantoin. The patient underwent patch testing with the NACDG standard series, sodium hypochlorite 1% aq. and 2%, 1% and 0.5% aq. solutions of Pro Guard[®] pellets. Readings at day 4 showed positive reactions to 2% and 1% Pro Guard[®] solutions. 6 controls tested negative to all Pro Guard[®] solutions.

Following this investigation, the patient replaced Pro Guard[®] by lithium hypochlorite pellets and has since been symptom free.

Discussion

We report contact allergy to 1-bromo-3-chloro-5,5-dimethylhydantoin alone.

Our patient did not react to sodium hypochlorite or DMDM hydantoin from the standard series. This observation is interesting for more than one reason. First, 1-bromo-3-chloro-5,5-dimethylhydantoin is commercialized in many countries under various names such as Di-Halo[®], Halobrome[®], Aquabrome[®], etc. The molecule releases both chlorine and bromine, even though retailers market it as a 'chlorine substitute' or as a 'brominating agent'.

20 years ago, this product caused an epidemic of dermatitis in British public pools (7). The investigators diagnosed irritant contact dermatitis on the basis of negative patch tests. In a more recent publication, we have reported a positive patch test to Di-Halo[®] in a patient sensitized to sodium hypochlorite (8). The positive reaction to 1-bromo-3-chloro-5,5-dimethylhydantoin was likely due to the generation of sodium hypochlorite in the solution. This reaction cannot be invoked in the present case, as the patient was not allergic to sodium hypochlorite. Fitzgerald et al. (9) have reported positive patch tests to Halobrome[®] in 3 patients without other sensitization. Our case shows clear similarity to those of Fitzgerald et al.

Second, substitution of 1-bromo-3-chloro-5,5-dimethylhydantoin by a hypochlorite compound was curative for our patient. In the presence of allergy to hypochlorites, the substitution becomes very difficult, as most of the effective disinfectants release some chlorine (10). The patient described in our previous publication has been able to use her pool with polyhexamethylene biguanide (Bacquacil[®] or Softswim[®]), a product available in the USA but not in Canada.

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Allergic contact dermatitis from Autan[®] spray: methyl glucose dioleate as sensitizing ingredient

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Key words: allergic contact dermatitis; Autan[®]; insect repellents; Isolan DO; methyl glucose dioleate.

Case Report

A 27-year-old woman presented during February 2003 for allergological

evaluation of a past episode of widespread eczema (July 2002) that involved the legs, arms and face and started approximately 8 h after direct application of Autan[®] Family Pump spray on these sites. The patient denied any previous use of this insect repellent product. The dermatitis reached maximum intensity approximately 1 day after the application of Autan[®], requiring hospitalization and treatment with systemic corticosteroids and antihistamines. The allergological history was negative, except for allergic contact dermatitis from certain metals.

Patch tests to the European standard series (performed in March 2003) showed a positive reaction only to nickel sulfate (++D2/++D3). Patch testing with Autan[®] spray (as is) showed a positive reaction after 3 days (?+D2/++D3). Further patch testing with the individual ingredients of Autan[®] Family Pump spray, kindly supplied by the manufacturer, showed a positive reaction only to the Isolan DO preparation (3% in paraffin oil), the main component of which is methyl glucose dioleate (MGD) (++D2/+++D3). All other ingredients (including the active ingredient KBR 3023) tested negative. The same preparation of Isolan DO was negative on patch testing in 10 controls.

Discussion

Autan[®] is an insect repellent widely used throughout the world. To our knowledge, there is no previous report in the medical literature of allergic reaction to this product, particularly for the active ingredient (KBR 3023; *Bayrepele*; hydroxyethyl isobutyl piperidine carboxylate). We describe a case of allergic contact dermatitis due to Autan[®] Family Pump spray, in which the patient reacted to Isolan DO containing MGD (the di-ester of methyl glucoside and oleic acid), a water-in-oil emollient and emulsifier used in cosmetic and topical products.

Although this substance is considered neither sensitizing nor irritating according to material safety data sheet, allergic contact dermatitis due to MGD has been reported in at least

4 previous cases: it was present in 1 case involving antimycotic paste (1), in 2 cases involving topical medicaments for leg ulcers (2, 3) and in 1 case involving cosmetics (4). Given the widespread use in skin care products and in topical products like repellents, clearly such reactions are relatively rare.

Additional studies are needed to evaluate whether MGD *per se* has a sensitizing capacity or whether co-formulants, contaminants or allergenic breakdown products in the Isolan DO preparation are responsible for the reaction. We tested technical MGD at the concentration present in Autan[®] Family Pump spray. Further testing with analytical grade MGD at different concentrations will have to be done in order to verify the sensitizing capacity of this compound. In the meantime, we have learned that the producer has been informed about 2 further cases of allergic skin reactions and suggests substituting Isolan DO with a suitable alternative in formulations. Finally, we underscore that the allergic reaction associated with Autan[®] use in the present case was not due to KBR 3023, the active ingredient.

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Is photopatch testing useful in the investigation of photosensitivity due to flutamide?

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Key words: flutamide; photoallergy; photopatch test; photosensitivity.

Flutamide is a steroidal anti-androgenic hormonal antineoplastic drug, administered orally, that inhibits the recapture and binding of testosterone and dihydrotestosterone to their specific receptors, obstructing the stimulating effects of androgens on neoplastic prostatic cells.

Various side-effects have been described, including toxic hepatitis, gynaecomastia, mastodynia, hot flushes and gastrointestinal alterations. To date, few cases of cutaneous photosensitivity reactions in patients treated with flutamide (1–8) have been published, with varying results of photoallergic investigation. There are also some published cases of pseudoporphyria and lupus-like reactions (8–11) after oral intake of flutamide, in which light is a relevant pathogenic mechanism.

Case Report

A 60-year-old patient was diagnosed as having advanced prostatic carcinoma, with possible lumbar vertebral metastasis, and treated by transurethral resection and bilateral orchiectomy. 7 days after starting oral treatment with flutamide (500 mg

every 12 h), he presented with a pruriginous cutaneous eruption that was erythematous and slightly oedematous on the face, neck and dorsa of the hands, restricted to photoexposed areas.

Suspecting flutamide, the patient stopped taking the drug, but the erythema progressed to eczematization of the lesions, some blisters even appearing. The symptoms disappeared partially with systemic corticosteroids and antihistamines prescribed by his physician.

He was referred to our department, where he was prescribed oral corticosteroids for a month, improving the lesions but giving rise to a fine desquamation and residual dry skin. Lichenification persisted in some areas for 2 months. He was not on any other treatment and had no history of other allergies.

We performed patch and photopatch testing with a photoallergen series (Chemotechnique Diagnostics, Malmö, Sweden) and flutamide at 5%, 10% and 20% in pet. (kindly provided by Schering-Plough Laboratories, Madrid, Spain), using Leukotest (BSN Medical, GmbH, Hamburg, Germany) and Mefix (Mölnycke Health Care AB, Göteborg, Sweden) as support. Allergens were duplicated on the patient's back and arms. After 1 D, one side was removed and irradiated with ultraviolet A (UVA) at a 5 J/cm² dose. At 24 h (D1), we took the 1st reading and the 2nd was taken 48 h later (D3), following ICDRG criteria. Results are summarized in Table 1. 8 healthy controls were negative on patch and photopatch testing to the same materials. A minimal erythema dose (MED) on flutamide was determined with a solar simulator (Solar-Light Company) and was clearly diminished, whereas the MED without flutamide was normal.

The patient has not taken flutamide again, and the reaction has not recurred. He was prescribed an alter-

native treatment for his prostate carcinoma.

Discussion

Flutamide, 2-methyl-*N*-4-nitro-3-(trifluoromethyl)-phenyl propamide, is an androgen-activity inhibitor. Its principal metabolite is 2-hydroxyflutamide. It is quickly and completely absorbed when taken orally, and it is metabolized in the liver, being eliminated by the kidneys (12). As a consequence of its anti-androgenic effect, it causes a reduction of androgen-dependent organs, such as the prostate gland and seminal vesicles, inhibiting spermatogenesis, decreasing libido and sometimes producing gynaecomastia. Its effectiveness in the treatment of prostate cancer has been demonstrated (13).

We consider our case to be a photosensitivity reaction induced by flutamide, based on the following criteria: lesions appearing after oral intake of flutamide and sun exposure; typical clinical picture (erythema, oedema, blisters and intense pruritus); distribution (exclusively on photoexposed areas such as the face, neck, V-neck and dorsa of the hands); and resolution of lesions via persistent desquamation and lichenification in some areas.

Patch- and photopatch-test results are difficult to interpret. A positive reaction in the non-irradiated area should be interpreted as irritant according to some authors (2, 4), but a more positive reaction in the irradiated area led us to suspect a photoallergic mechanism. We did not consider it to be a photoaggravated allergic contact dermatitis, because lesions appeared only in photoexposed areas.

To date, there seemed to have been a general agreement that patch and photopatch testing is unhelpful in the investigation of photosensitivity induced by flutamide. Some cases have been published with negative results (3, 4), others without such testing even having been published (6–8).

Finally, there is no consensus on the concentrations and vehicles to be used for patch and photopatch testing. Some have used pet. or water as vehicle (1, 4), others 50% propylene glycol and 50% ethanol (2) and still others acetone (5). Based on the present study and comparing it with previously published ones, we consider flutamide

Table 1. Photoallergic study

Allergens	Concentration and vehicle	Patch test		Photopatch test	
		D2	D4	D1	D3
Flutamide	5% pet.	+	+	++	++
Flutamide	10% pet.	+	+	++	++
Flutamide	20% pet.	+	+	++	++
Standard photoallergens		–	–	–	–

at 5% and 10% in pet. to be the ideal concentration and vehicle, though, at present, the diagnosis must be based more on the clinical history than on the results of such testing.

In conclusion, we report a new case of photosensitivity induced by flutamide, on which there are few publications. We underline that flutamide is a drug that can produce photosensitivity and probably more often than is published.

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