

CONTACT POINTS

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Dermatological problems in dental health personnel

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Key words: dental health personnel; epidemiology; hand eczema; respiratory effect; NRL gloves; questionnaire; skin changes.

Occupational skin diseases among dental health personnel, particularly involving the hands, have been an issue in recent years. Dental personnel come into contact with (meth)acrylate, which can cause skin irritation as well as contact allergy. In addition, they frequently wash their hands and use natural rubber latex (NRL) gloves, increasing their susceptibility to hand dermatitis. We surveyed the staff members of a university dental college and hospital.

Materials and Methods

52 dental staff members were interviewed using a standard questionnaire covering the duration of occupation, nature of work, various contactants encountered, past or present skin symptoms, history of hand dermatitis, history of atopy (asthma, eczema or allergic rhinitis) and nasal complaints. Hand examination was made in all cases.

Results

Of the 52 dental staff examined, 27 were dentists (18 male and 9 female), 18 were staff nurses (all female) and 7 were dental technicians (all male). The average age of the study group was 33 years (range 26–53 years). Average duration of employment in the study group was 11 years and in those with skin changes on the hands was 8 years. All except the 7 dental technicians wore gloves.

Out of 52, 9 (17%) had work-related skin symptoms. Itching of the hands with glove use was complained of by 7 (13%), dryness of the hands by 3 (6%) and pricking sensation of the hands by 2 (4%).

Skin changes such as fingertip scaling, dry chapped hands and prominent palmar markings were seen in 10 (19%). The commonest change was fingertip scaling in 4 (8%), followed by prominent palmar markings in 3 (6%) and dry chapped hands in 2 (4%). Eczematous plaques were seen in 3 (6%), 2 of them attributing this to glove use.

Of the 10 with skin changes on the hands, only 1 was atopic. A history of hand dermatitis was present in 7 (13%); 2 attributed this to gloves or glove powder; 1 each to (meth)acrylates and soaps, respectively; and 3 could not ascertain the cause.

Work-related allergic rhinitis was present in 2 (4%); 1 attributed this to inhalation of materials during sand-blasting of aluminium oxide and 1 to (meth)acrylates. Significant improvement of skin changes was noted during vacation by 3 (6%).

Discussion

The point prevalence of hand changes in the present study was 19%. Estlander et al. reported a closely similar prevalence rate (1), though other studies have recorded a higher point prevalence of around 35% (2). In the present study, many believed that their skin problem was due to prolonged contact with gloves or glove powder. NRL gloves can cause contact urticaria, allergic contact dermatitis and irritant contact dermatitis. Glove powder increases skin roughness and irritation, probably by mechanical rubbing of the skin surface leading to loss of barrier function of the skin (3).

None of the 7 dental technicians wore gloves while working, for fear of losing firm grip and tactile sensitivity which could diminish the quality of the end product. Only 1 reported hand dermatitis a year ago.

To conclude, the prevalence of work-related skin disease among our dental personnel was low and seldom affected their professional career. As powdered NRL gloves were frequently implicated, the use of non-powdered non-NRL gloves may be indicated (4).

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Allergic contact dermatitis from cosmetics applied by the patient's girlfriend

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Key words: allergic contact dermatitis; Compositae; consort dermatitis; helenin; plant extracts; sesquiterpene lactones.

Case Report

A 25-year-old metal worker presented with a 12-month history of recurrent facial dermatitis, favouring the eyelids, cheeks and perioral region. The patient reported worsening on Mondays and related the outbreaks to iron and cutting fluids used in the workplace.

Suspecting occupational contact dermatitis, patch tests with cutting fluids and other products used in his work were made, with negative results. The patient was then tested with the standard TRUE testTM standard series, including primin and sesquiterpene lactone (SL) mix 0.1% pet., and a positive (+) reaction to SL mix was obtained at D4. As he was SL positive, a patch test with Helenin Sigma[®] (commercialized preparation containing alantolactone and isolactolactone) was made, with positive results at D2 (+), D4 (+) and an eczematous reaction at D10.

SLs are present in the Compositae family of plants and are known to be important contact sensitizers. Many cosmetic products contain Compositae plant extracts, and hence the patient having denied using any cosmetics himself, we decided to patch test with his girlfriend's cosmetics and other Compositae plants. Readings taken at D4 showed +++ reactions to a make-up (containing *Matricaria parthenium*), a deodorant (containing *Laurus nobilis* and *Anthemis nobilis*), *M. parthenium* and *Frullania tamarisci*.

The patient was diagnosed as having allergic contact dermatitis due to SLs present in his girlfriend's cosmetics. Avoiding contact with these products and others containing Compositae plant extracts, the patient has remained free of symptoms.

Discussion

SLs are known to be important contact sensitizers and can be found in the plant families Compositae and Frullaniaceae (1, 2).

Cases of occupational contact dermatitis (often from airborne dust exposure) caused by Compositae plants have been

reported in gardeners and florists (3, 4). The use of these plants as extracts in perfumes and cosmetics can make them relevant in cases of recurrent facial contact dermatitis (5), even when the product is being used by the partner of the patient, as occurred in this case. Such contact should also be suspected with other allergens such as fragrances or topical medicaments (6, 7). Recently, a case of concurrent occupational and connubial dermatitis from hops has been reported in a female farmer with face and neck dermatitis (8).

Although many cases of allergic contact dermatitis from SL have been described, to our knowledge this is the first report of consort dermatitis from SL. In this case, patch tests with SL mix (0.1%) and Helenin Sigma[®] seemed to be good screening tests for diagnosis of allergic contact dermatitis caused by Compositae plants (2, 4, 9).

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Allergic contact dermatitis from cinnamon as an odour-neutralizing agent in shoe insoles

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Key words: allergic contact dermatitis; cinnamal; cinnamic alcohol; cinnamic aldehyde; cinnamon; fragrance mix; insoles.

Case Report

A 47-year-old man presented with a 1-week history of vesicular dermatitis on both soles consistent with a clinical diagnosis of podopompholyx. 2 days prior to its onset, he had started to use new commercially available insoles containing cinnamon powder as an odour-neutralizing agent in his shoes (Spinnrad[®], Norderstedt, Germany). There was no past history of plantar eczema. Treatment with topical corticosteroids initially failed to clear the skin lesions. He had developed erysipelas on the left foot 5 days after the onset of the eczema and was therefore hospitalized and treated with intravenous antibiotics in addition to topical corticosteroids. Within 2 weeks of this treatment, marked improvement of the eczema and clearance of the erysipelas were achieved.

Patch testing with the European standard series showed positive reactions to fragrance mix (+++ at D2, further testing stopped), balsam of Peru (*Myroxylon pereirae* resin) (+ at D2 and D3) and thimerosal (+ at D2 and D3). Testing with the components of the fragrance mix showed reactions to cinnamic aldehyde (cinnamal) (++) at D2 and (+++) at D3) and cinnamic alcohol (+ at D2 and +++ at D3). A strongly positive reaction was also obtained with both the inside and the outside of

the cinnamon insole (each +++ at D2, further testing stopped).

Discussion

Cinnamon is derived from the bark of *Cinnamomum* trees (1–3). Besides other components, cinnamon contains about 1–3% ethereal oils with cinnamic aldehyde as main constituent and about 35 other constituents such as eugenol and cinnamic alcohol. The constituents of oil of cinnamon are common allergens or irritants, and occupational allergic contact dermatitis from oil of cinnamon has frequently been reported in bakers, confectioners and cooks (4, 5). We describe for the first time contact with insoles containing cinnamon as a cause of allergic contact dermatitis.

Our patient showed positive patch tests to 2 constituents of oil of cinnamon, cinnamic aldehyde and cinnamic alcohol, but not to eugenol. As cinnamic aldehyde is also a component of fragrance mix and balsam of Peru, it may be the primary allergen. Cinnamon powder, as used in the patient's insoles, however, in contrast to oil of cinnamon, is known only rarely to cause sensitization or irritation, most likely due to the fact that it contains smaller amounts of cinnamic aldehyde than does oil of cinnamon (1). On request, the manufacturer confirmed that only cinnamon powder, and no additional oil of cinnamon or cinnamic aldehyde, had been used to produce the insoles.

Interestingly, the patient described that he often ate food flavoured with cinnamon. Thus, one could speculate that he had been sensitized to cinnamic aldehyde and cinnamic alcohol as the result of frequent oral contact. On the other hand, patients with contact dermatitis from cinnamon are known usually to tolerate cinnamon-containing food very well, and avoidance of cinnamon-flavoured food is not routinely recommended in patients with contact dermatitis from cinnamon (1). In accordance, there was no history of stomatitis or gastrointestinal symptoms after eating cinnamon in our patient.

Our report shows that the use of cinnamon in insoles runs the risk of inducing contact dermatitis in people who are not occupationally exposed to cinnamon. We therefore recommend reconsidering the use of cinnamon as an odour-neutralizing agent in insoles.

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A medicolegal controversy due to a hidden allergen in cutting oils

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Key words: abietic acid; colophony; contact allergy; cutting oils; occupational; thin-layer chromatography.

Case Report

A 54-year-old non-atopic man, working as a turner, was admitted with a diagnosis of eczema of the face and arms. The dermatitis healed with oral antihistamines and topical and systemic corticosteroids.

Patch testing with the Italian (SIDAPA) standard series showed sensitization to colophonium (+ D2/++

D3). A use test [repeated open application test (ROAT)] and further patch testing with the patient's own cosmetic products, suspected of having induced dermatitis, were negative. Both a ROAT with the cutting oil used at work by the patient and a patch test performed with the same oil (10% aq.) (+ D2/+ D3) were positive.

Further patch testing with a preservatives series and other allergens in cutting oils (abietic acid, triethanolamine, bisphenol A, resorcinol, zinc dithiocarbamate, methyl methacrylate and benzoyl peroxide) was negative, except for abietic acid (+ D2/+ D3). Allergic contact dermatitis due to colophonium and its constituent abietic acid, probably contained in the cutting oil, was diagnosed.

A medicolegal controversy ensued, as the 2 allergens were not declared in the material safety data sheet and the employer denied the presence of either abietic acid or colophonium in the oil. The patient was not allowed to change his usual job and was thus re-exposed to his normal activities, causing an immediate relapse of the dermatitis, which assumed the clinical features of airborne contact dermatitis.

In order to confirm the suspected occupational origin of his dermatitis, a sample of the oil was examined. The standardized allergen (colophonium 20% pet.) commonly used in patch testing and the cutting oil were comparatively submitted to the same chemical-analytical procedure. The acid components of both colophonium and cutting oil were separated and then compared using thin-layer chromatography (TLC) on silica gel. A similar distribution of the spots was clearly demonstrated in both the subdivided colophonium and the cutting oil. Mass spectrometry was performed on the products extracted from the silica gel. It demonstrated abietic acid as a constituent of the cutting oil.

Discussion

In conditions of heavy exposure to cutting fluids, the prevalence of dermatitis can vary from 30–50% (1, 2), while a prospective study showed a cumulative incidence of 77% among machinists within 6 weeks of exposure (2). Soluble cutting oil dermatitis is generally irritant, though contact

allergy can also occur (1), the most frequent allergens being additives, such as preservatives and anti-rust agents, or metals (nickel, cobalt and chromate) contaminating the fluid (3). Cases of cutting oil dermatitis due to colophonium allergy have also been reported (4), the usual source being tall oil-derived emulsifiers.

Colophonium (rosin) has countless applications at home and work (5, 6). It is used in solder flux, soaps, cutting fluids, insulation material, adhesives, glues, papers, printing inks, cosmetics, medicaments and in the manufacture of modified rosins. As a consequence, exposure to colophonium and modified colophonium is universal and, due to its well-known contact allergenic properties, much colophonium dermatitis has been reported in the literature. An unselected general population study of 793 Danish adults showed a prevalence of colophonium allergy of 0.4% in men and 1.0% in women, and higher prevalence rates are found in studies from patch test clinics or by selecting exposed workers (5, 7). Contact urticaria from colophonium has also been described (8).

Colophonium is composed of approximately 90% resin acids and 10% corresponding neutrals. Of the resin acids, 90% are isomeric with abietic acid. In spite of a previous claim that purified abietic acid is non-allergenic (9), recent studies have found that this substance is an important contact allergen and is a major allergen in unmodified rosin used for routine patch testing (10). Experimental results have shown that not only the resin acids themselves but also their oxidation products may cause allergic contact dermatitis (10, 11).

In the case reported, the patient's clinical features, history and patch test results were highly suggestive of airborne contact dermatitis from colophonium, or from some colophonium components, contained in the cutting oil used at work. Chromatographic detection of colophonium constituents in the cutting oil was essential to the firm diagnosis of occupational contact dermatitis.

We emphasize the role of analytical-chemical investigations, unusual in everyday clinical practice, in resolving diagnostic and medicolegal controversies.

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Phototoxic and photoallergic dermatitis caused by hydroxychloroquine

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Key words: hydroxychloroquine, photoallergic dermatitis, phototoxic dermatitis, positive photopatch test.

Hydroxychloroquine (HCQ) is a lysosomotropic amine used in rheumatology and dermatology for its immunosuppressive and photoprotective properties (1). The side effects of synthetic antimalarials are well known, although not frequent, and they can involve the gastrointestinal, ocular, haematopoietic, cardiovascular, auditory and central nervous systems (2). Among adverse cutaneous reactions, bluish-grey to black discoloration is the most common, while bleaching of the hair roots, lichenoid reactions, maculopapular eruptions, pruritus, exacerbation of psoriasis and porphyria cutanea tarda are less common (2). Exanthematous pustulosis (3), allergic contact dermatitis (4) and photosensitivity (5) are rare.

Case Report

A 74-year-old man with skin phototype IV, treated with HCQ sulfate (200 mg/day) for 1 year for rheumatoid arthritis, presented with a 4-month history of itchy erythematopapulo-squamous hyperpigmented dermatitis, involving only the light-exposed areas of the face and hands. The skin eruption began in the summer and spared the upper eyelids, retroauricular and submental areas.

Phototesting was performed using a Waldmann UV 800K lamp (Schwenningen, Germany), which is a bank of 6 fluorescent lamps Philips TLK 40 W/09 (UVA: 315–395 nm) and 4 Philips TL 20 W/12 (UVB: 285–350 nm) (Eindhoven, Holland). A significant decrease of minimal

erythema dose (MED) both in the UVA (5 J/cm²; normal value for skin type IV: 40–60) and UVB range (30 mJ/cm²; normal value for skin type IV: 45–60) was demonstrated. Photopatch testing with our light standard series, HCQ sulfate 5% in water and UVA-irradiation (2.5 J/cm²) was negative. However, a slight positive reaction to HCQ was observed after UVB irradiation (20 mJ/cm²).

The withdrawal of HCQ therapy allowed a slow resolution of skin lesions and partial increase of MED-A and MED-B (20 and 40, respectively). Photodermatitis relapsed the following summer, but brief therapy with topical and systemic corticosteroids procured a rapid recovery. However, sunlight exposure continued to cause itching on photoexposed areas for a further 3 months, despite constant sunscreen. After this, the patient became asymptomatic during a 2-year follow-up, and both MED-A and MED-B returned within the normal range. The positive test reaction to HCQ sulfate, in contrast, was confirmed by a photopatch test carried out at the end of follow-up.

Discussion

A more or less persistent photosensitivity may be an unusual side effect of antimalarial therapy. It was present in 1 of the 12 chronic actinic dermatitis cases reported by Lim *et al.* (6) and in 11 of 544 patients treated by Singh *et al.* (5) with HCQ for rheumatoid arthritis. More recently, Métayer *et al.* (7) described 4 subjects with photolocalized eruptions which developed from 6 days to 10 weeks after starting HCQ and associated with a decrease of MED. A positive photopatch test reaction to HCQ after exposure to UVA was seen in a 51-year-old black man investigated for vesicles, papules and depigmentation of light-exposed areas (8).

Generally, HCQ is included among systemic phototoxic substances (9), but in our case both phototoxic and photoallergic mechanisms may be proposed, as for certain other substances. Hyperpigmentation of involved skin, localization of lesions strictly to light-exposed skin, slow resolution after stopping HCQ and persistence of photosensitivity for some months are suggestive of a phototoxic reaction. The positive

photopatch test reaction to HCQ and its persistence with time, however, allow the advance of a photoallergic mechanism. We conclude that this positive reaction was seen only after exposure to UVB radiation.

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Allergic contact dermatitis from isohexadecane and isopropyl myristate

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Key words: allergic contact dermatitis; isohexadecane; isopropyl myristate; sunscreen.

Case Report

A 64-year-old woman presented to our department with a history of an eczematous rash after the application of a commercially available sunscreen with a sun protection factor of 50. The rash had appeared after 3 days of application of the sunscreen over the face, neck and limbs and had been very pruritic.

Patch tests with the European standard series gave positive reactions to formaldehyde, quaternium-15, imidazolidinyl urea and diazolidinyl urea. The ingredients of the sunscreen that she had used were obtained from the manufacturers, and patch tests were performed using them. There were positive reactions to isohexadecane 10% alcohol + at D2 and D4 and isopropyl myristate 10% alcohol + at D4. Both of these substances tested negatively in 20 controls.

Discussion

Isohexadecane is a mixture containing more than 99% C₁₆ isoparaffins. It is found in cosmetics, surface coatings, floor polishes, shoe creams, car polishes and protective waxes and insecticide solutions (1). Isopropyl myristate is used as a basis for relatively non-greasy emollient ointments and creams. It is also a solvent for

many substances applied externally. Other isopropyl fatty acid esters, including di-isopropyl adipate, isopropyl laurate, isopropyl linoleate and isopropyl palmitate have similar properties and are used for similar purposes to those of isopropyl myristate (2).

To the best of our knowledge, this is the first case report of allergic contact dermatitis from both isohexadecane and isopropyl myristate. We have advised our patient to avoid contact with products containing these chemicals.

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Widespread eczema from triflusal confirmed by patch testing

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Key words: cutaneous adverse drug reactions; platelet anti-aggregants; positive patch test; triflusal.

Triflusal is structurally related to, though not derived from, aspirin and is reported to inhibit platelet aggregation (1). It is generally well tolerated, though photoallergic reactions have been reported (2–5).

Case Report

A 64-year-old man, with non-insulin-dependent diabetes, hypertension and hypercholesterolemia, was admitted after myocardial infarction. Following discharge, he was treated with oral triflusal, metformin, simvastatin, amlodipine and atenolol. 3–4 weeks later, he presented with itching, erythema and vesicles on the lower legs, and over the next 2 weeks, confluent maculopapular lesions spread to the rest of the skin. He improved on oral corticosteroids and antihistamines, but the intense pruritus and disseminated eczematide lesions persisted.

2 months later, the patient was referred to the allergy unit. After consulting with his cardiologist, all treatment was suspended, except atenolol, platelet aggregation being inhibited instead with aspirin. The exanthem improved quickly though via severe scaling.

Patch testing with the European standard series, supplemented with triflusal, metformin, simvastatin and amlodipine (20% in pet.) was carried out 1 month later. Readings were taken at 2, 3 and 4 days (D). The only positive shown was to triflusal at D4 (++). 10 healthy control subjects were negative.

Oral challenge tests were performed on the rest of the medication taken, and all were well tolerated. Triflusal was prohibited, but 2 weeks later, when at home, the patient mixed up his metformin and triflusal by mistake and took a triflusal tablet. 3 days later, eczematide lesions and pruritus reappeared on the legs. He was again treated with oral corticosteroids and antihistamines.

Discussion

This is a case of widespread triflusal eczema, unrelated to sun exposure, in which sensitization was demonstrated by a positive patch test as well as a positive challenge test. A patch test is a diagnostic test with few risks, which on occasion can be useful in identifying non-immediate drug reactions.

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Black rubber tyre-maker's tattoo

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Key words: black rubber; carbon; occupational; tattoo; tyre-maker.

Traumatic tattoos result from the accidental deposition of pigment particles in the dermis (1). Frequently, they follow an abrasive injury that is contaminated by dirt, or a penetrating injury such as a pencil wound.

Case Report

A 54-year-old man presented with a 2-year history of multiple asymptomatic black macules on the dorsum of the hands and fingers (Fig. 1), palms and wrists, 1–2 mm in diameter. He was otherwise healthy and not taking any medications. Although a trained plumber, he was working in a black rubber tyre



Fig. 1. Black macules on dorsum of right index finger.

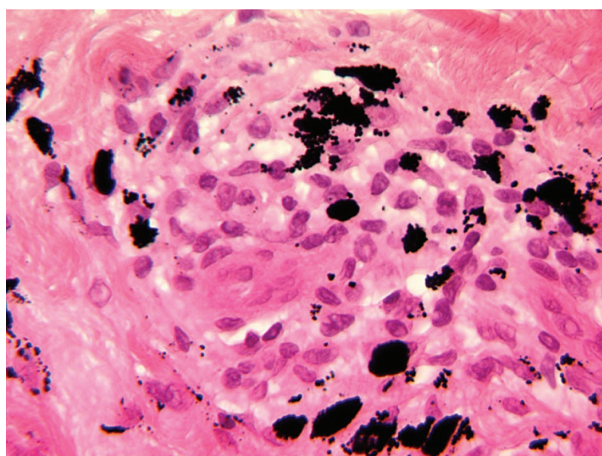


Fig. 2. Photomicrograph showing black pigment in macrophages, consistent with carbon (haematoxylin and eosin; original magnification $\times 250$).

factory at the time of presentation. He had developed his first lesion whilst cleaning the inside of pipes with steel wool when working as a plumber. However, it was not until he started work at the tyre factory that several more lesions developed.

His work involved using a machine called a steel breaker, which forms a 'steel band' layer in car tyres. The 'steel band' consists of a piece of black rubber with criss-crossing metal strips to increase strength and prevent nails penetrating the tyre. He did not wear gloves at work and tended inadvertently to traumatize his hands. Histopathological examination of a macule, excised from the left wrist, showed black pigment in macrophages, which was consistent with carbon (Fig. 2).

Discussion

Carbon is a black, odourless solid in the form of powder, pellets or paste.

Its main use is as a reinforcing agent in abrasion-resistant rubber products such as tyres, tubes, cables and other mechanical rubber goods. It is also used as a pigment in inks and paints.

Lucker et al. (2) reported the case of a 68-year-old miller with pinhead-sized greyish-blue pigmented macules on the fingers and dorsum of the hands. A biopsy revealed that these tattoos were due to the deposition of iron particles in the reticular dermis. Such 'millstone tattoos' were a fairly common finding amongst millers who worked between 1920 and 1970.

In our patient, it is likely that small particles of carbon entered the skin through injuries caused by the metal strips in the 'steel bands'. It is possible that the first macule, which appeared while scouring pipes, contained carbon derived from graphite grease used in plumbing. Reactions to black tattoos are extremely rare (3), even though the pigment is likely

to persist indefinitely, and thus we expect him to remain asymptomatic.

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Allergic contact dermatitis from colophonium, turpentine and ebony in a violinist presenting as fiddler's neck

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Key words: allergic contact dermatitis; colophonium; musicians; turpentine; violinist.

Case Report

A 28-year-old violinist had suffered from eczema on the neck, left jaw and upper left shoulder, where the violin touched her skin, for 1.5 years prior to presentation. She studied violin at a conservatory and noticed worsening of the eczema and itching especially after practising the violin for 9 h a day in preparing for her examination. No involvement of the hands or other parts of the exposed skin was reported. Treatment with topical corticosteroids for several weeks had not procured recovery. There was a positive family history

of atopy, the patient herself having suffered from atopic eczema.

Clinical examination showed eczematous and erosive lesions in the area where the violin touched the neck, jaw and shoulder, which involved over half of the neck. The back of the hands showed discrete erythema, the palms and finger tips not being involved.

Patch testing with the standard series, synthetic resins and glues and additional metals, ebony wood and the lacquer of the violin were performed, according to the guidelines of the German Contact Allergy Group. Finn Chambers were removed after D2. D2 and D3 readings showed positive reactions to colophonium (++), turpentine (+), formaldehyde (+), ebony (+) and the lacquer of the violin (+).

Comment

Allergic contact dermatitis in musicians, especially in violinists has been reported from colophonium, exotic woods, propolis and nickel, this last being the most frequent allergen in musicians playing stringed instruments (1). Although contact dermatitis from colophonium might be expected to be common in musicians, it has rarely been reported. Ramirez and Eller (2) described a case of sensitization to colophonium in a violinist in 1930, followed by Fisher in 1981 (3), Murphy et al. in 1999 (4) and Angelini and Vena in 1986 (5). All these published cases (3 violinists and 1 violoncellist) were of allergic contact dermatitis of the hands, mostly fissured or pompholyx type.

Positive patch tests to both colophonium and turpentine as a result of a cross-reaction in our patient has not previously been reported in a violinist. However, it is not surprising because the rosin used by violinists is usually made of colophonium and turpentine oil, both components being isolated from the resin of conifers by distillation (6). Abietic acid and its isomers play an important role as sensitizers in rosin. The adducts of rosin and maleic anhydride, so-called maleic resins are used extensively in varnishes and lacquers (3), which might explain the positive reaction to the violin lacquer in our patient. A positive reaction to ebony has also been reported recently in this context (1). The important differential diagnosis is fiddler's neck, a mild irritant contact dermatitis, which indeed is much more

common. However, our patient had developed an allergic contact dermatitis from ebony, turpentine and colophonium in the location of fiddler's neck instead of in the more typical area of the palms and fingertips. Therefore, allergic contact dermatitis should be considered as a differential diagnosis, suggesting that in cases of irritant contact dermatitis on the neck of violinists, delayed-type allergy should be excluded by differential diagnostic allergy testing.

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Role of patch testing in antimicrobial drug eruptions

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Key words: antimicrobial drugs; beta-lactams; cutaneous adverse drug reactions; fluoroquinolones; India; medicaments; patch testing; positive patch tests; sulfonamides.

The incidence of adverse drug reactions (ADRs) in the general population is 6–30% (1), cutaneous ADRs (CADRs) accounting for the majority. Antimicrobials are the commonest group of drugs (40%) causing CADRs (2, 3). The most commonly used such drugs are beta-lactams (penicillins and cephalosporins), fluoroquinolones and sulfonamides.

Materials and Methods

30 consecutive patients clinically diagnosed or giving a history suggestive of CADRs due to these 3 groups of antimicrobials were enrolled in a patch test study. Patients presenting with maculopapular eruptions, fixed drug eruptions (FDE), eczematous lesions, lichenoid drug rash and delayed urticaria were included in the study. Patients of age less than 18 years, those who had developed Stevens–Johnson syndrome or toxic epidermal necrolysis, had been on oral corticosteroids within the last 4 weeks (>20 mg/day) or topical corticosteroids for the last 1 week, and pregnant and lactating women were excluded. 20 patients without any history of CADR were included as controls.

All patients and controls were patch tested according to the guidelines of Contact and Occupational Dermatoses Forum of India with the drugs summarized in Table 1. Patch test readings were taken on day (D) 2 and D4 and graded as recommended by International

Table 1. List of drugs patch tested

Penicillin G	100 000 U/ml of water
Amoxicillin	20% in pet.
Piperacillin	20% in pet.
Cephalexin	20% in pet.
Cefadroxil	20% in pet.
Cefaclor	20% in pet.
Ceftriaxone	20% in pet.
Cefazoline	20% in pet.
Cefuroxime	20% in pet.
Ceftazidime	20% in pet.
Cefpirome	20% in pet.
Ceftizoxime	20% in pet.
Co-trimoxazole	20% in pet.
Lomefloxacin	20% in pet.
Ciprofloxacin	20% in pet.
Norfloxacin	20% in pet.
Levofloxacin	20% in pet.
Sparfloxacin	20% in pet.

Contact Dermatitis Research Group. Readings that were ?+ even at D4 were not regarded as positive. In the case of FDE, topical provocation was considered as positive when a clearly demarcated erythematous reaction was seen lasting for at least 6 h.

Results

Of the 30 patients, 13 (43%) were female and 17 (57%) were male. Their ages ranged from 22 to 69 years, with a mean of 38 ± 13 years. 13 (43%) patients had positive patch test results to 1 or more drugs. Only 1 patient, who was allergic to sulfonamides, showed +++ positivity and the remaining 12 patients had + positivity. The mean interval between drug eruption and evaluation was 1 (maximum 6) years in patch test-positive patients, whereas it was 6 (maximum 20) years among patch test-negative patients, this difference being statistically significant ($P < 0.01$). The mean interval between drug intake and onset of drug reaction was longer in patients with a positive patch test when compared to patients with a negative patch test (106 versus 60 h), though this difference was not statistically significant ($P > 0.05$). Table 2 summarizes the frequency of various clinical patterns of drug eruptions and patch test positivity within them. 1 patient had both FDE and eczematous lesions.

Among the 30 patients, 11 gave a history suggestive of allergy to sulfonamides. 1 patient who gave a doubtful history of allergy to ciprofloxacin and rofecoxib showed positivity to sulfonamides on patch testing. 11 patients gave a history of allergy to fluoroquinolones. 3 patients gave a history of sensitivity to cephalosporins and 2 to penicillins. Cross-reactivity was observed in a single case between cefadroxil and amoxicillin. There were no side effects from patch testing in any of the patients. All 20 controls showed negative patch tests.

Discussion

Earlier studies have shown a variable frequency of positive patch tests ranging from 7 to 87% (4–7) in CADR from various groups of drugs, including antimicrobials. 29 of 30 cases had positive patch tests in a selected group of patients with CADR from beta-lactams (8). Blanca et al. (9) have documented that patients who are allergic to certain drug usually loses this hypersensitivity on long-term follow up. The results of our study are consistent with this finding as we have found a significantly longer interval between drug eruption and evaluation in patients with negative patch tests in comparison with those with positive patch tests. We observed the highest positivity of patch testing in patients with FDE (50%), followed by maculopapular eruptions (46%), eczematous eruptions (33%) and urticarial eruptions (33%), whereas Alanko et al. (4) showed 87% positivity of patch testing in FDE (Table 2). In FDE, only previously involved sites showed patch test positivity.

In our study, there was no significant association between the frequency of drug exposure and patch test positivity ($P > 0.05$). Only 1 patient showed cross-reactivity between amoxicillin and cefadroxil. As patients with allergy to beta-lactams were few in our study, it is difficult to comment upon the true incidence of cross-reactivity between penicillins and cephalosporins. Most of the cephalosporins implicated in our patients belong to the 2nd and 3rd generation groups, which have very little cross-reactivity with penicillins (10). There were no significant side effects from the patch testing in our study. Like previous reports (10), we have found no association between body surface area of involvement and patch test positivity. None of the age-matched controls showed positivity to the allergens tested.

To conclude, a frequency of 43% patch test positivity in patients with

CADRs to antimicrobials was observed in our study. Those patients having a relatively long-standing history of drug allergy had a significantly lower frequency of positivity. There was no significant association between patch test positivity and body surface area of involvement or frequency of exposure. The highest positivity rate was observed in patients with FDE. As antimicrobials are the commonest group of drugs causing CADR, patch testing may be recommended as a safe initial method of investigation in the diagnosis of CADR due to antimicrobials.

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Table 2. Clinical pattern and frequency of patch test positivity

Clinical pattern	Frequency	Positivity
Maculopapular	13	6 (46%)
Fixed drug eruption	8	4 (50%)
Eczematous	6	2 (33%)
Urticarial	3	1 (33%)
Exfoliative dermatitis	1	0 (0%)

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Allergic contact dermatitis from VP/eicosene copolymer (Ganex® V-220) in an emollient cream

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Key words: allergic contact dermatitis; cosmetics; film-former; Ganex V-220; polyvinylpyrrolidone; repeated open application test; VP/ eicosene copolymer.

Case Report

A 59-year-old non-atopic man, with a 6-month history of xerosis and pruritus of the hands, lower arms and legs, was prescribed daily applications of an emollient cream (Lipikar baume®, La Roche-Posay, France). Within a month, he developed itchy, vesicular dermatitis of the limbs. Patch testing was performed with the SIDAPA (Società Italiana di Dermatologia Allergologica e Professionale) standard series and the patient's emollient cream as is. Readings at D2 and D3 were negative except for a mild erythematous-oedematous (+) reaction to the emollient cream. The cream was discontinued and the patient improved within 3 weeks. A repeated open application test performed with the cream in the antecubital fossa was positive within 3 days.

The manufacturer kindly provided samples of the ingredients of the cream, appropriately diluted for patch testing. 6 months after resolution of his dermatitis, the patient was further patch tested with these substances and the emollient cream again. Readings performed at days 2, 3 and 4 showed a delayed but clearly positive erythematous-oedematous reaction to VP/eicosene copolymer 10% pet. (+ at D4), plus a weak

erythematous reaction to disodium stearyl glutamate 30% pet. (?+ at D4). The cream as is reacted positively (+/+) at D3 and D4.

15 controls were patch tested with VP/eicosene copolymer, disodium stearyl glutamate and the emollient cream. No positive reactions were seen, except for a weakly erythematous one to disodium stearyl glutamate in an atopic patient who also showed weak irritant reactions to metal salts and lanolin alcohol.

Comment

The patch test reaction to VP/eicosene copolymer was considered allergic and clinically relevant, while the nature of the reaction to disodium stearyl glutamate was doubtful and possibly irritant.

VP/eicosene copolymer, also known as Ganex® V-220 F, is a film-former/waterproofing agent that belongs to the family of copolymers of vinylpyrrolidone and long-chain α -olefins. These polymers are used as emulsifiers and dispersants in non-aqueous systems, desensitizers/wax dispersants in melt-cast explosives, dye dispersants for candles and shoe polish, and water-resistant film-formers in wood coatings.

To the best of our knowledge, the Ganex®-alkylated polyvinylpyrrolidones have not previously been described as contact allergens. We unexpectedly identified VP-eicosene copolymer as contact allergen in an emollient preparati widely prescribed by dermatologists as a treatment for dry skin conditions.

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Allergic contact dermatitis from direct dyes for hair colouration in hairdressers' clients

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Key words: allergic contact dermatitis; cross-sensitivity; direct dye; hair colouring; hairdressers' clients; HC Red B54; HC Yellow 7.

Among hair-dye allergens, *p*-phenylenediamine (PPD) is the most frequent sensitizer in hairdressers' clients. Guerra et al. (1) reported a study in which contact sensitization to hairdressing allergens among hairdressers' clients was detected in 18.7% of a group of 281 patients with contact dermatitis. A high rate of sensitization to PPD (7.3%) was detected in these patients, but contact sensitization to *o*-nitro-*p*-phenylenediamine (ONPPD) occurred in only 4.6% of patients. Frosch et al. (2) found a positive reaction to PPD in 19% of 104 patients, with ONPPD showing a 7.7% rate of sensitization. Allergic contact dermatitis from direct dyes for hair colouration is unusual (1–4).

Case Reports

Case no.1

A 50-year-old non-atopic housewife had a history of allergic contact dermatitis from PPD in permanent hair colouring. In April 2002, 2 days after the 2nd application of a violet semi-permanent hair dye, Renovative® (L'Oréal, Paris, France), she reported itchy, erythematous-oedematous, scaly plaques located on the neck. Multiple lesions on the eyelids, behind the ears, neck and upper extremities developed over a short time. The lesions subsided in 2 weeks with frequent shampooing and oral corticosteroids.

Patch tests were performed with the Spanish standard series, a hairdresser series, the Renovative® hair dye and its components. Patch tests at D2 and D4 were positive (++) to PPD 1% pet., caine mix 7% pet. and black rubber mix 0.6% pet. of the standard series; 4-PPD base 1% pet., 2,5-diaminotoluene sulfate 1% pet., 2-nitro-4-phenylenediamine 1% pet., 3-aminophenol 1% pet. and 4-aminophenol 1% pet. of the hairdresser series; and Renovative® and one of its components, HC Yellow 7 1% and 10% pet. 25 controls patch tested with HC Yellow 7 10% pet. were negative at D2 and D4.

Case no. 2

A 43-year-old woman, a clerk and ex-hairdresser – she had had to leave the job after 6 months due to hand dermatitis – had a history of allergic rhinoconjunctivitis, and allergic contact dermatitis from nickel, PPD and disperse dyes in a textile series (Orange 3, Yellow 3 and Red 1). In January 2002, hours after the 2nd application of a L'Oréal semi-permanent hair dye, Farandol® (L'Oréal), she reported itchiness on her scalp, which subsided in 7 days without dermatitis. In May 2002, 2 days after applying a coral-red semi-permanent hair dye, Igora Fleur 7-88® (Schwarzkopf, Düsseldorf, Germany), she experienced itchy erythematous-crusty plaques on and behind the ears and on the neck. These lesions subsided in 4 weeks after frequent shampooing and topical corticosteroids.

Patch tests were performed with the Spanish standard series, a hairdresser series, the hair dye Farandol and its components, and Igora® and its components. Patch tests at D2 and D4 were positive (++) to nickel sulfate 5% pet. and PPD 1% pet. of the standard series; 4-PPD base 1% pet., 2,5-diaminotoluene sulfate 1% pet., 2-nitro-4-phenylenediamine 1% pet., 3-aminophenol 1% pet. and 4-aminophenol 1% pet. of the hairdresser series; Farandol® and one of its components, 4-amino-3-aminophenol 0.2 pet. and 1% pet.; and Igora® and one of its components, HC Red B54 1% pet. 25 controls patch tested with 4-amino-3-aminophenol 1% pet. and HC Red B54 1% pet. were negative.

Comment

The reported cases correspond to allergic contact dermatitis from HC Yellow 7, 4-amino-3-nitrophenol and HC Red B54 in hair dyes used in patients with a history of PPD allergic contact dermatitis. Positive patch tests to different dyes may be interpreted as primary sensitizations because some dyes belong to permanent, some to semipermanent and some to temporary hair-dyeing products. However, cross-sensitizations to different azo dye and paramino compounds, as has been described in some reports (5, 6), or concomitant contact allergy, should also be considered.

HC Yellow 7 (CAS 104226-21-3) is an azo dye whose chemical structure corresponds to 1-(4-aminophenylazo)-2-methyl-4-(bis-2-hydroxyethyl)-aminobenzene. It is an orange powder incorporated into semi-permanent and temporary hair lotions at a maximum concentration of 0.25%. In experimental studies, this compound was minimally irritant but showed evidence of contact sensitization (7).

4-amino-3-nitrophenol (CAS 610-81-1) is an orange dye whose chemical structure belongs to the nitro-aminophenol group. This compound can safely be used in semi-permanent and permanent hair-dye formulations at a maximum concentration of 3.0%. However, as permanent hair dyes are mixed with hydrogen peroxide before application, the maximum in-use concentration should not exceed 1.5%. Cosmetic products containing this substance should carry a label warning of a risk of sensitization (8). We have found a previous report of a patient with a positive patch test to 4-amino-3-nitrophenol, though patch testing with PPD was negative (9).

HC Red B54 (CAS 65235-31-6) is a dark red dye whose chemical structure corresponds to 1-hydroxy-3-nitro-4-β-hydroxyethyl-aminobenzene. This compound can safely be used in semi-permanent and permanent hair-dye formulations at a maximum concentration of 6.0%. When mixed with hydrogen peroxide, the maximum in-use concentration should not exceed 3%. In experimental studies, this compound has shown evidence of contact irritation. Delayed-type hypersensitivity to HC Red B54 has also been reported, with negative standard hair-dye allergens (10).

Some authors have investigated safer hair dyes for hairdressers who are already sensitized to para-phenylenediamine (5, 11). Disperse Yellow 9, Disperse Red 11 and Disperse Blue 3 hair dyes could be an option in patients with contact allergy to PPD (5). New generation hair dyes, FD & C and D & C, have appeared on the market. 40 hairdressers sensitized to PPD, 2,5-diaminotoluene sulfate and 2-nitro-4-phenylenediamine were tested but showed no positive reactions to FD & C and F & D dyes (11).

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Piroxicam-induced erythema multiforme

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Key words: cutaneous adverse drug reactions; erythema multiforme; non-steroidal anti-inflammatory drugs; piroxicam; positive patch test.

Patch testing is a safe and easy way to identify the causative drug in some systemic drug eruptions (1).

Case Report

A 31-year-old man had been treated 2 years ago with oral piroxicam (20 mg/day) and amoxicillin-clavulanic acid (500 mg $\times$ 3/day) for arthritis. During treatment with these drugs, he developed the target lesions of erythema multiforme (EM) on his palms and soles and a pruritic erythematous circular lesion on his penis. He discontinued treatment after 1 month and the skin lesions progressively resolved without any scaling or postinflammatory hyperpigmentation. 1 year later, he received a tablet of piroxicam (20 mg) for pharyngitis, and 24 h later, similar mucocutaneous lesions appeared in the same locations. Piroxicam was discontinued and he was treated with oral antihistamines and corticosteroids, improving in 1 week. He later tolerated amoxicillin.

Patch tests were performed on the patient's back with piroxicam, meloxicam and tenoxicam in 10% dimethyl sulfoxide (previously shown not to be an irritant in controls), as previously described (2). These were ++ to piroxicam on days 1, 2 and 4, but negative to the other oxicams. Prick and intradermal tests with benzylpenicilloyl polylysine, minor determinant mixture, benzylpenicillin, amoxicillin and amoxicillin-clavulanic acid, as well as a single blind-controlled oral challenge test with amoxicillin-clavulanic acid, were negative.

Discussion

Piroxicam is a widely prescribed anti-inflammatory drug. The cutaneous

adverse drug reactions to piroxicam that have been reported are mainly urticaria, photosensitivity reactions and fixed drug eruption, and less frequently EM, Stevens-Johnson syndrome, toxic epidermal necrolysis, pemphigus vulgaris or erythema annulare centrifugum (3, 4).

Patch tests with piroxicam have been found to be positive in most cases of photosensitivity reactions and in various reports of fixed drug eruption when applied on residual pigmented lesions (1–3, 5). Osawa et al. demonstrated a positive patch test in 20.7% of patients with possible drug-induced EM (6). Patch testing is a specific but poorly sensitive test, which when positive can avoid a systemic drug-challenge test (1).

There are few reports of oxycam-induced EM (7–12), and most of these have clinical features of Stevens-Johnson syndrome, which some consider to be a distinct disorder (13, 14), while others propose fixed drug eruption, EM, Stevens-Johnson syndrome and Lyell's syndrome to be a disease spectrum with different degrees of severity (15).

Reported cases (7–12) may be documented by biopsy, but few have been investigated by patch testing. Katoh et al. (11) described a case of piroxicam-induced Stevens-Johnson syndrome with a negative result on patch testing with 1% piroxicam in petrolatum, yet a positive oral-challenge test with piroxicam; the patch test concentration and vehicle used might have been suboptimal.

To our knowledge, this is the 1st report of piroxicam-induced EM confirmed by a positive patch test. We found no cross-reactivity on patch testing with other oxicams (meloxicam and tenoxicam).

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