

CONTACT POINTS

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Occupational asthma and IgE-mediated contact dermatitis from sapele wood

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Key words: airborne; asthma; carpenter; IgE; occupational; protein contact dermatitis; sapele wood.

Case Report

A 35-year-old man had a medical history of atopic disease, with rhinitis, asthma and flexural dermatitis since childhood. He had worked as a carpenter since he was 18 years old. After 1 year in this work, he reported more severe relapsing episodes of asthma, rhinitis, conjunctivitis and widespread dermatitis but not urticarial lesions. He improved only on weekends and holidays. Every time he returned to work, he experienced a worsening of symptoms and these were so severe that he occasionally required systemic corticosteroids.

He was first referred to our Department of Dermatology (Hospital de Cabueñes) when he was 35 years old. Dermatological examination showed disseminated erythematous, excoriated, lichenified plaques, more severe in exposed areas of the face, neck and forearms.

Patch tests were performed, according to the recommendations of the International Contact Dermatitis Research Group, with the European standard series, resins, glues, plastics

and acrylates all of which were negative. Also, the patient was patch tested to the sawdust of the various woods that he used in his work (iroko, oak, maple, beech, pine, cherry, sapele and chestnut), both 'as is' and at 10% in pet., and all of these tests were also negative.

Prick tests were then performed. The positive control was histamine 10 mg/ml and saline 0.9% the negative control. We considered a prick test-positive if the diameter of the wheal was at least 3 mm larger than the negative control. Positive prick tests (Leti, Barcelona, Spain) were obtained with latex (diameter wheal 20 mm) and *Dermatophagoides pteronyssinus* (diameter wheal 15 mm). Negative prick tests were obtained with other common aeroallergens (other mites, molds, pollens and animal allergens) and with all the previously mentioned wood extracts. Intradermal testing was also negative for these woods.

Total serum immunoglobulin E (IgE) was more than 2000 kU/l, and we detected high levels of allergen-specific IgE antibodies to latex (more than 100 kU/l) by radio-allergosorbent test (RAST) (UniCAP System, Pharmacia, Uppsala, Sweden). RAST to woods was not performed. Immunoblotting was performed according to the method described by Towbin et al. (1). Several IgE-specific bands were detected to latex and a different molecular weight (60 kDa) band was detected to sapele but not to the other 7 woods.

We concluded that the worsening of both his asthma and his dermatitis was IgE-mediated and occupational, caused by airborne contact with sapele wood. We found no latex sources in his working environment, but he recognized recreational exposure as he reported swelling of the lips when blowing up balloons.

The patient was informed and he gave up working as a carpenter, after which he experienced a great improvement in both cutaneous and respiratory symptoms.

Discussion

IgE-mediated contact dermatitis was first described by Seeberg (2) in 1952 from contact with beef and pork meat. In 1967, Hjorth and Roed-Petersen (3) reported 10 new cases of this disease caused by food, mainly fish, and they termed it protein contact dermatitis (PCD).

PCD is a chronic recurrent dermatitis caused by contact with proteinaceous material. It is mostly occupational and mainly develops on the hands and forearms of food handlers. Its pathogenic origin is not fully understood, but it may be mediated by IgE bound to Langerhans cells receptors. Intact skin may be a limiting factor, and atopic or irritant contact dermatitis may first be necessary for high molecular weight proteins to penetrate the skin (4). Patch tests are negative and the responsible allergen is usually detected by prick test or by allergen-specific IgE in serum. Occasionally, as in the case, we report that specific IgE antibodies may be detected in the serum although prick testing is negative (5).

Jansen et al. (6) reviewed the reported cases of PCD up to 1993 and concluded that 4 main groups of proteins may cause this disease: animal proteins, grains, enzymes and vegetables (fruits, spices, plants and latex). Since then, multiple further sources of PCD have been reported. Sapele wood is the source of PCD found in our patient. Wood has previously been described as a cause of occupational asthma (7) and allergic contact dermatitis (8), but it has not been found in a Medline search of PCD and wood. Specifically, sapele is a tropical tree widely distributed in Africa and its wood is used in carpentry due to its durability and attractive appearance. We have found only 1 previously reported case of sensitization to sapele wood in a carpenter's son, although presenting as asthma and angioedema rather than dermatitis (9).

Otherwise, several studies have shown that allergy to latex is associated with cross-reactivity to other plants

and woods (10). Our patient was sensitized to latex from non-occupational sources and immunoblotting did not demonstrate the existence of cross-reactivity between proteins in latex and sapele wood.

In conclusion, we propose that wood should be included in the list of vegetable sources of PCD and that carpentry should be considered an at-risk occupation to develop this kind of IgE-mediated dermatitis. It is also important to remember that allergic contact dermatitis may occasionally occur despite negative patch test results and that correct diagnosis may then depend on prick testing, RAST or other immunological assays such as immunoblotting.

Acknowledgement

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Potassium peroxymonosulfate-induced contact dermatitis

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Key words: allergic contact dermatitis; antibacterials; biocides; potassium peroxymonosulfate; preservatives.

Case Report

A 55-year-old man presented with a 1-year history of a pruritic eruption beginning on the anterior legs and spreading to the thighs and torso, sparing the areas under his briefs and axillary vaults bilaterally. The head and neck were uninvolved. Coinciding with the skin eruption, he began to experience intermittent wheezing. He had no previous history of asthma, or atopy. Patch testing to the Chemotechnique (Malmö, Sweden) North American standard series and an additional 15 allergens showed no positive reactions except for a questionable reaction to potassium dichromate, thought to represent an irritant reaction. Further

elicitation of daily habits revealed that he had purchased a hot tub before the onset of the rash and wheezing. Investigation into the hot tub additive revealed the ingredient as potassium peroxymonosulfate. Avoidance of the hot tub resulted in clearance of both the rash and the pulmonary symptoms. Subsequent patch testing revealed a + reaction to potassium peroxymonosulfate (5% in pet.) at day 7 (Aldrich CAS no. 22,803–6). Of note, he was also patch tested to Chemotechnique's ammonium persulfate 2.5% in pet. and was negative at day 7.

Potassium peroxymonosulfate is a potassium salt used as a disinfectant and is found in oral hygiene formulations, pool and spa disinfection (in this capacity, patients may commonly recognize it as 'shock'), paper recycling, printed circuit board etching, wool shrink proofing, laundry bleaches and precious metal extraction processing (1). It is not commonly recognized as an allergen. One previous report does exist of potassium peroxymonosulfate-induced dermatitis in a sheep farmer (2). Swimming pools and spas are typically sanitized using either a chlorine donor or a bromine donor [usually in the form of bromochlorodimethylhydantoin (BCDMH)]. In addition, most pools now periodically add shock treatments to eliminate algae and also the chloramines or bromamines created by the interaction of sanitizing chemicals and faecal material. Potassium peroxydisulfate (potassium persulfate) and less commonly potassium peroxymonosulfate (potassium monopersulfate) are used in pools and spas which employ BCDMH as the primary sanitizing agent. In contrast, chlorinated pools often use calcium hypochlorite as shock treatment.

Some sulfate salts may cause both Type IV and Type I hypersensitivity reactions in susceptible individuals (3). Our patient was tested to ammonium persulfate to investigate a possible cross-reaction and did not react. However, one of the authors (AS) has identified 6 patients allergic to potassium persulfate shock treatment who patch tested positive to ammonium persulfate. Ammonium persulfate is available from a standard vendor (Chemotechnique), and it is possible that ammonium persulfate may be useful for screening for allergy to potassium persulfate but

not always useful for screening for potassium peroxymonosulfate allergy, as in this case.

We conclude that potassium peroxymonosulfate was the cause of our patient's rash and, through aerosolized exposure, was also the cause of the pulmonary symptoms, both of which cleared after avoidance of this product. Pool or spa chlorination with the use of calcium hypochlorite as shock treatment is a recommended alternative in patients allergic to either persulfate shock treatments or to BCDMH.

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Electron-beam treatment of allergic granuloma due to gold pierced earrings

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Key words: allergic granulomas; electron-beam treatment; gold allergy; gold pierced earring.

Case Report

A 37-year-old woman presented in August 2000 with subcutaneous tumours on both earlobes. The

patient had a history of atopic dermatitis and allergic rhinitis. She had started to wear 18 carat gold pierced earrings on both earlobes approximately 11 years ago. Due to the itching that developed a few months after she began wearing the earrings, she stopped using them. She restarted wearing the earrings 6 months after the first manifestation, which resulted in renewed itching the next day. Therefore, she again discontinued wearing the pierced earrings. 2 years after this incident, the growth of subcutaneous tumours on both earlobes was noticed. Patch testing showed that the patient was positive to gold sodium thiosulfate, and she received intraoral metal removal as well as treatments including oral administration and local injection of corticosteroids, oral administration of antiallergic and 3 tylectomies. However, the tumours kept recurring. At our first medical examination, we detected subcutaneous soft-elastic tumours (5 × 3 cm), with severe itching and erythematous papules on the skin, from the auricle to her earlobes and lower jaw.

Histopathological analysis of the tumours showed dermal and subcutaneous infiltration of dense cells with lymphoid follicles. The infiltrating cells were mostly lymphocytes without any evidence of cytologic atypia. Infiltrating eosinophils were also noted. Haematology showed slightly increased white blood cells (7300/mm³), eosinophils (13%), and immunoglobulin E (7300 U/ml). Other than these, no abnormal values were noted on laboratory testing.

Cranial–cervical CT scan indicated soft-tissue tumours, which were seen in the subcutaneous tissue region between both earlobes and the parotid glands, the tumours and parotid glands being closely in contact with each other. Moreover, magnetic resonance images showed multiple nodes in the region from outside and inside both parotid glands towards the deep cervical region. Patch testing showed that the patient was positive to 0.5% gold sodium thiosulfate, 0.5% chloroplatinate and 0.05% mercuric chloride.

Based on these results, the patient was diagnosed as having an allergic granuloma due to gold pierced earrings. We tried both systemic corticosteroid and immunosuppressant therapy, but these were withdrawn due to adverse effects. Therefore, we

turned to electron-beam irradiation at a total dose 20 Gy to both sides, which resulted in both disappearance of the tumours. Tumour recurrence was noted 5 months after irradiation in both non-irradiated sides of the submandibular region, which prompted us to retreat the patient with an electron beam at the sites of recurrence. The recurrent tumours were eliminated, though psoriasis was observed as an adverse effect of the electron beam. The patient is currently tumour free and doing well 18 months after the last treatment.

Discussion

Conventionally, gold is thought rarely to cause contact dermatitis, as it is insoluble and difficult to ionize. However, the recent popularity of wearing gold pierced earrings has triggered more frequent reports of contact dermatitis caused by gold (1–4).

In addition to contact dermatitis, dermopathy due to gold pierced earrings includes nodular lesions, epidermal cysts and keloids (5). Here, we report a case in which a patient experienced recurrent enlargement of subcutaneous tumours on both earlobes for 9 years after she stopped wearing the earrings. The patient was resistant to a number of treatment regimens. Therefore, she was treated with electron-beam irradiation, with a favourable result of tumour disappearance and no recurrence.

No significant infiltration of eosinophils within lymphoid follicles was detected, and thus we excluded Kimura disease as a possible diagnosis. Considering that the patient had worn 18 carat gold pierced earrings for 6 months, 2 years prior to manifesting subcutaneous tumours, and because the patch test was positive to gold sodium thiosulfate, we thought that the gold in the pierced earrings was the causal factor.

Many cases of allergic granuloma have been reported which cannot be cured by conservative therapies such as external application of corticosteroids or local corticosteroid injections, and consequently require surgical excision (5, 6). We tried various treatments for this patient, but the tumours remained intractable and progressive. Therefore, electron-beam treatment was elected. To our

knowledge, the use of electron-beam irradiation has not previously been reported for this type of tumour. Prior to treatment, the patient was given sufficient information regarding adverse effects and the possibility that the tumour might become malignant. Upon understanding the consequences, she firmly requested this treatment, and we chose to apply electron-beam irradiation. The initial irradiation was effective in eliminating the intractable tumours on both sides. However, about 5 months later, the tumours recurred in both non-irradiated sides of the submandibular region. We retreated these recurrent tumours with the electron beam, and the patient has since been free from tumours thus far. Based upon the facts derived from this case, we conclude that electron-beam irradiation may be considered, provided a patient has a thorough understanding of possible adverse effects.

The tumours in the present case recurred for a long period of time, despite surgical excisions. In general, contact dermatitis due to gold pierced earrings exhibits symptoms of acute dermatitis accompanied by skin induration, with subsequent dermal nodulation. Such nodules tend to remain for several months, even after discontinuation of pierced earring use. Sensitization to gold in general seems unlikely. In contrast, direct contact between gold and dermis by wearing pierced earrings causes ionization, resulting in sensitization. The gold incorporated in the dermis is difficult to eliminate, and dermal immunoreaction remains even after epidermal inflammation is ameliorated. As gold is an element, it cannot be degraded by macrophages. Furthermore, dermal turnover is slower than epidermal turnover, causing the antigen to remain at the local site for a long time (7). Therefore, once nodulation manifests on the earlobes, it is difficult to eliminate.

No tumour recurrence distant from a primary lesion has been reported so far. Accordingly, our case, in which the tumour recurred in the submandibular regions after treatment of tumours on the earlobes, was considered to be rare. Electron-beam treatment is thought to trigger apoptosis or necrosis of the macrophages which incorporated gold particles, resulting in the elimination of tumours. However, we

assumed that the gold particles were not eliminated, but rather absorbed into the lymph node, and elicited an allergic reaction again at the resorption site, thereby causing tumour recurrence.

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Allergic contact dermatitis from *Boswellia serrata* extract in a naturopathic cream

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Key words: allergic contact dermatitis; *Boswellia serrata*; naturopathic cream; plant extracts.

The application of medicinal plant extracts to the skin may produce

adverse effects including irritant contact dermatitis, phytophotodermatitis and allergic contact dermatitis (1).

Case Report

A 28-year-old woman with atopic background had a 2nd degree burn from hot water on her thigh in September 2001. She was initially treated with topical antiseptics, antibiotics and antihistamines; some days later, she stopped these treatments and went to a naturist, who prepared and sold her a cream made with natural plant extracts. After 5 days of application, an intense eczematous local cutaneous reaction with bullae developed on her thigh, requiring systemic and topical corticosteroids to heal.

Patch tests with the GEIDC standard series, antimicrobial series, her previous topical medicaments and the naturopathic cream as brought in by the patient gave positive results to nickel, colophonium, balsam of Peru, hexyl resorcinol, benzoyl hydroxybenzoate (considered non-relevant for this patient) and to the naturopathic cream (+++) at both 2 and 4 days. The patient then went back to the naturopath, who gave her the composition of the cream: resin extract of *B. serrata*, rosemary oil, olive oil and virgin beeswax. A second patch test with all of these components was made, with the results summarized in Table 1. Patch tests with *B. serrata* resin extract (0.1% pet.) were performed on 12 healthy volunteers, and no reactions were observed. A diagnosis of allergic contact dermatitis from *B. serrata* resin extract was then made.

Some months later, the patient applied the same cream to her husband for a muscle pain, developing a fresh allergic contact dermatitis on her own hands.

Discussion

B. serrata is a tree from the Burseraceae family commonly found in India, northern Africa and the Middle East. Strips of its bark yield a gummy oleoresin which contains oils, terpenoids and gum. Its active principle consists of 4 pentacyclic triterpenes, β -boswellic acid (Fig. 1) being the major one. Extracts of this oleoresin have been used as a

Table 1. Patch tests with the ingredients of the naturopathic cream, including *Boswellia serrata* extract dilutions

	D2	D4
<i>B. serrata</i> extract		
0.1% pet.	+	++
0.1% alc.	+	++
1% pet.	+++	+++
1% alc.	+	+++
5% pet.	++	+++
5% alc.	++	+++
10% pet.	++	+++
10% alc.	++	+++
Rosemary oil	—	—
Olive oil	—	—
Virgin beeswax	—	—

folk medicine for centuries in Ayurvedic medicine in India. Boswellic acids have anti-inflammatory properties inhibiting leukotriene biosynthesis via non-competitive inhibition of 5-lipoxygenase. *Boswellia* extract tablets have been employed for asthma, arthritic conditions and ulcerative colitis and other chronic inflammatory diseases (2–4). Topical administration for cutaneous burns and ulcers or as a cosmetic agent is increasingly being used in Western countries, although there is limited scientific evidence about its safety and effectiveness (2–4).

We have not found other side effects described from the topical application of *B. serrata* extract. Indeed, it is not included in some recently published lists of botanical extracts that may cause dermatitis (5, 6). So, to the best of our knowledge, this is the 1st report of allergic

contact dermatitis from *B. serrata*. Its increasing use, because of its anti-inflammatory and cosmetic properties, will probably lead to further reports of its side effects. When contact dermatitis is suspected, a patch test with *B. serrata* 0.1% pet. is recommended.

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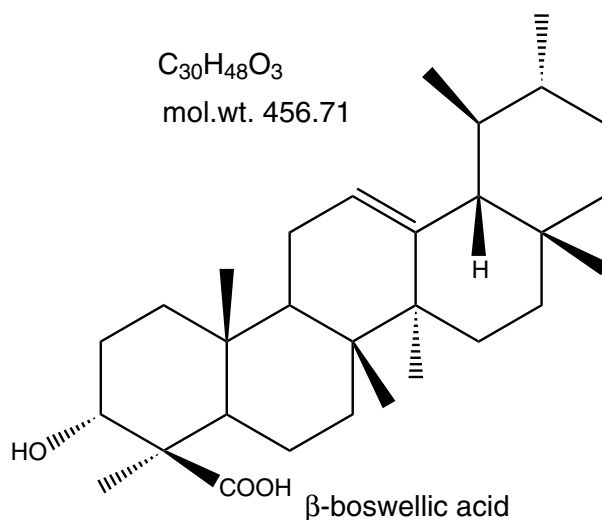


Fig. 1. Chemical structure of β-boswellic acid.

The dangers of making mint sauce

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Key words: allergic contact dermatitis; *Mentha spicata*; plants; spearmint.

Case Report

A 64-year-old man developed erythema and blistering over the dorsal and palmar aspect of his hands, a few hours after picking mint from his garden. He had 2 further episodes which on each occasion occurred following the picking and chopping of mint to prepare mint sauce. He was patch tested to the British Contact Dermatitis Society standard series, the departmental plant and fragrance series and to the leaf and stalk from spearmint (*Mentha spicata*) (as is). At day (D)4, he developed ++ reactions to the leaf and stalk of the spearmint only. Patch testing with peppermint oil was negative. We patch tested 20 healthy volunteers to the leaf and stalk of spearmint, but there were no positive reactions at D4. The patient was advised to avoid contact with spearmint and has because remained free of symptoms.

Discussion

Mentha spicata (spearmint) is a member of the Lamiaceae family. There are about 30 herbaceous species of mint and more than 200 subspecies, varieties, forms and hybrids. *Mentha spicata* is commonly grown throughout Europe and the USA. Its leaves are essential in making mint sauce, and oil of spearmint is used in the manufacture of medicines, toothpastes, chewing gums and soft drinks.

Allergic contact dermatitis from mint was first described in 1940 in 2 bartenders who made drinks with the leaves of peppermint (*Mentha x piperita* var *citrate*) (1). Both were negative to the leaves of spearmint. Since then, peppermint oil has been reported as a cause of allergic contact dermatitis in fragrance (2), toothpaste flavours (3) and food handlers (4).

Reports of allergic contact dermatitis from spearmint are rare. Cases of contact cheilitis from spearmint oil in toothpaste flavours (3, 5, 6) and a chewing gum finisher (7) have been documented. The only case of allergic contact dermatitis from spearmint at any other site was that of a 64-year-old woman who developed vesicobullous lesions on the knee after repeated applications of compresses made with an infusion of *Mentha spicata* leaves (8). Carvone is one of the main constituents of spearmint oil and has been implicated as the main allergen, although in a human maximization test, carvone (1% pet.) did not sensitize (9).

We believe that this is the 1st report of allergic contact dermatitis from direct contact with *Mentha spicata* leaves, which in our case resulted from the preparation of mint sauce.

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Allergic contact dermatitis from para-phenylenediamine in Bigen® powder hair dye

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Key words: allergic contact dermatitis; Bigen® powder hair dye; hair dye; para-phenylenediamine.

Case Report

A 40-year-old Indian man presented with acute dermatitis on the scalp, ears, pre-auricular areas and neck a day after dyeing his hair. He had been using hair dye to conceal his greying hair for the last one and a half years and dyed his sideburns every week. Apart from occasional mild stinging, no previous reaction to the hair dye used had been experienced. He had a preference for Bigen® hair dye which is heavily marketed to those from the Indian subcontinent. This is a powder hair dye which is mixed with water to form a paste prior to application.

On examination, he had an erythematous papular eruption on his scalp and ears, which were crusted and exudative. A similar rash was seen on his pre-auricular areas and neck, where it was more confluent with evidence of hyperpigmentation and lichenification. Sensitization to para-phenylenediamine (PPD) in the powder hair dye used was suspected, and he was patch tested to the European standard series and an azo-dyes series. He developed a +++ reaction to PPD 1% pet. and + cross-reactions to Disperse Orange 3 and Disperse Red 17, both also at 1% pet. His dermatitis resolved with topical corticosteroids but some post-inflammatory hyperpigmentation remains.

Discussion

In a study of PPD allergy at St John's Institute of Dermatology, the female: male was 2:1. This is in keeping with other European centres (1). However, the converse is true in the Indian subcontinent and the Middle East, where

men are more likely to develop PPD allergy than women (2–4). This reflects cultural differences, there being a greater use of hair dye for scalp and facial hair by men in these areas.

PPD is a potent allergen mainly encountered in hair dyes. Allergic skin reactions to temporary black henna tattoos, which often contain high concentrations of PPD, are increasingly reported (5). Cross-sensitization to Disperse Orange 3, among other textile dyes, is also commonly reported (6). Under European Union (EU) directives, PPD is allowed in hair dyes at a maximum concentration of 6% (i.e. 3% as used by the consumer when mixed with peroxide).

Bigen® powder hair dye is manufactured by a Japanese company (Hoyu) and distributed in the UK and Southeast Asia. Using high performance liquid chromatography, Brancaccio and colleagues (5) demonstrated that PPD was present in Bigen #59 Oriental black hair colour at a concentration of 12.3%. Such concentrations would be considerably higher than those legally permitted in the EU and would increase the risk of sensitization to PPD were the substance not sufficiently diluted.

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**Erythrodermic
phytophotodermatitis
after application of
aqueous fig-leaf extract
as an artificial suntan
promoter and
sunbathing**

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Key words: erythroderma; fig;
phytophotodermatitis; phytophototoxic
contact dermatitis.

Case Reports

A 40-year-old Italian man and his wife presented with extensive skin lesions. On examination, generalized dusky erythema, oedema, vesicles and bullae, especially on the thighs and the trunk of the man and the face and the trunk of the woman, were seen. Their 9-year-old boy was only partially and less severely affected. All 3 were fair skinned, type III according to Fitzpatrick's classification (1), and they had come to Greece in July for a holiday. They had severe pain rather than pruritus.

2 days earlier, they had prepared themselves an aqueous extract using boiled tap water and fresh-ground fig leaves, which they had collected from the surrounding countryside. The concoction was of unknown concentration. Soon after, they applied this homemade artificial suntan promoter all over their skin and exposed themselves to the burning midday sun to acquire a quick tan, except for their son who came in contact accidentally with both the mixture and the sun. Few hours later, as they were soaked in perspiration, they felt increasing

burning and pain, but they thought this was mild sunburn. By the time, the initial erythema developed into erythroderma, and in some areas evolved into vesicles and bullae, the pain became severe.

Personal and family history was negative. Full blood count revealed only leucocytosis (20 300 and 13 500/ μ l, respectively, for the man and the woman). Routine haematological and biochemical tests were otherwise normal, as well as urine analysis and chest X-ray.

They were admitted to a dark room and treated with wet compresses, baths, emollients, topical corticosteroids 2 times daily and oral methylprednisolone 0.5 mg/kg daily and acetylsalicylic acid 325 mg daily. 2 weeks later, they left in remission but with residual partial hyperpigmentation, tapering the corticosteroids and with the suggestion to avoid the sun, shield with clothing and apply sunscreens every 2 hr.

Discussion

Phytophotodermatitis describes the reaction to sunlight of skin previously in contact with certain species of plants and is a phototoxic reaction. Furocoumarins are a chemical component common to the plant families Compositae (e.g. milfoil, yarrow), Umbelliferae (e.g. parsley, celery, parsnip, carrot), Leguminosae (bavchi, scurf pea), Rutaceae (e.g. lime, bitter orange) and Moraceae (fig), which all are capable of inducing photodermatitis (2, 3).

The Moraceae comprises 53 genera with around 1400 species, approximately 800 of which are in the genus *Ficus* (4). Studies (5, 6) have detected furocoumarins in all parts of *Ficus carica* (fig) including the milky sap. The leaf and shoot saps contain 2 photoactive furocoumarin compounds, psoralen and bergapten. These are more plentiful in the leaf and are also present in the leaf extract. Tests revealed that psoralens and bergapten were present throughout the growing season and that psoralens were always the more plentiful.

The phototoxic response is due to the presence of these compounds and primarily to the presence of psoralen, as the concentration of this compound is significantly greater and it is at least 4 times more photoactive

on human skin than bergapten (6, 7). Contact with the leaf sap or shoot sap followed by sun exposure may therefore lead to such a phototoxic reaction. The increased incidence of fig phytophotodermatitis during spring and summer can be attributed to the higher concentrations of furocoumarins during these 2 seasons, in addition to other factors such as heat, humidity and increased exposure during the fruiting season (5, 6).

In our cases, we believe that the aqueous extract of fig leaves, rich in psoralens in this season, was the culprit of the phototoxic reaction, enhanced by the heat and humidity of perspiration and the susceptibility of their fair skin, as they did not mention contact with any other phototoxic agent. The use of boiled ground fig leaves in these cases shows that, even after boiling temperatures, furocoumarins are still capable of eliciting phytophotodermatitis and, to our knowledge, this has not been reported before.

The clinical appearance (dusky erythema, oedema, linear streaks, vesicles and bullae) on sun-exposed areas and the severe pain were both characteristic of phytophototoxic contact dermatitis.

There have been reported anaphylactic reactions after ingestion of fresh fig (8) and to *Ficus benjamina* (9), which seems to share some common allergens. Our patients did not show any manifestations of such a reaction. Leucocytosis in both the man and the woman, in our opinion, was attributable to the extensive skin inflammation (10).

Treatment of the acute reaction is symptomatic. Severely affected individuals may need hospital admission, wet compresses and paraffin gauze dressings, together with potent analgesia. Corticosteroids may be helpful if the eruption is oedematous. Hyperpigmentation may persist for several months and is best left untreated. Areas affected by phototoxic reactions may remain hypersensitive to UV light for several months or years and subsequent sun protection is advisable (11).

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Allergic contact dermatitis from tetracaine in the beauty industry

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Key words: allergic contact dermatitis; amethocaine; beauty industry; caine mix; local anaesthetics; medicaments; nurse; occupational; tetracaine.

Tetracaine (amethocaine) is an amino-benzoate ester found in topical anaesthetics. It is a recognized contact sensitizer amongst healthcare professionals. This case highlights the susceptibility of workers in the beauty industry.

Case Report

A 46-year-old right-handed nurse presented with a 6-month history of hand dermatitis. This predominantly affected the fingertips and was more marked on the right hand, with the thumbs, index and middle fingers demonstrating dermatitis. There was no personal history of atopy.

She worked as a nurse performing collagen injections in the beauty industry. Her job involved applying topical anaesthetics, Emla® cream (AstraZeneca UK Ltd, Kings Langley, UK) or Ametop® gel (Smith and Nephew Healthcare Ltd, Hull, UK), to the patients' skin prior to collagen injections. She had worn latex gloves but changed to vinyl gloves when the dermatitis developed. However, she had not always used gloves prior to the onset of her hand dermatitis and, occasionally, her hands were in direct contact with the topical anaesthetic products.

Patch testing was performed to the British standard series, and additional cosmetics and preservatives, medicaments, rubber and nursing series, as well as to Emla® cream and Ametop® gel, and the individual constituents of a local anaesthetic series. The results confirmed that she was allergic to the local anaesthetic agent tetracaine (Table 1).

Comment

Tetracaine (amethocaine) is a known cause of allergic contact dermatitis

in healthcare personnel, including chiropodists, dentists, oculists and laser-clinic nurses (1–4). Non-occupationally induced cases have also been reported, particularly in patients using antihaemorrhoidal ointments (5) or urethral lubricants (6).

Ametop® gel is an effective local anaesthetic for topical application, containing tetracaine 4%. Tetracaine is an aminobenzoate ester and a more potent sensitizer than the amide anaesthetics (4) found in Emla®, which contains lidocaine 2.5% and prilocaine 2.5%. As it is now commonly used in the expanding beauty industry, personnel working in this field are at increased risk of becoming sensitized.

Initially, our patient did not always wear gloves when applying Ametop® gel to patients' skin. She is likely to have become sensitized from direct skin exposure and her hand dermatitis persisted despite the routine use of gloves. We contacted the manufacturer for information concerning breakthrough time of Ametop® gel with latex and vinyl gloves but unfortunately data were not available.

This case highlights the importance of employee education in the beauty industry to increase awareness of the potential sensitizing agents of topical anaesthetics, and emphasizes the lack of available information regarding penetration rates of some topical preparations through gloves, which should be addressed.

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Table 1. Patch test results

	Day 2	Day 4
Caine mix III 10% pet. (cinchocaine, tetracaine and lidocaine)	++	++
Ametop® gel (as is)	++	++
Emla® cream (as is)	–	–
Tetracaine 1% pet.	++	Not tested

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**Active sensitization to
para-phenylenediamine
and its relevance:
a 10-year review**

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Key words: active sensitization; clinical relevance; contact allergy; para-phenylenediamine.

Para-phenylenediamine (PPD) is a primary intermediate in permanent hair dyes and a common contact allergen. It is patch tested routinely in the European standard series. Individuals may be sensitized to PPD by patch testing (1). As a consequence, some authors have recommended removal of PPD from the European standard series (2). Our review aimed to determine the rate of PPD sensitization when testing with PPD and its clinical relevance. This was undertaken by examining the frequency of PPD sensitivity in patients who had never been patch tested, compared with that in those who were having repeat patch testing who had therefore been exposed to PPD under patch test conditions. We reviewed the records of all patients patch tested at St John's between 1990 and 2000.

Patients and Methods

From January 1990 to December 1999, 13 300 patients with suspected contact dermatitis were tested with the European standard series. We selected and obtained the records of all patients during this time period who had a positive patch test to PPD-free base 1% pet.

Results

Of the 13 300 patients tested, 1035 had previously been patch tested on at least 1 occasion, representing 7.9% of this population. This proportion varied from 5.6% in 1994 to 11.1% in 1991, but there was no clear trend and it otherwise remained fairly constant during the 10-year period. The total number of PPD-positive reactions (+ to +++) over the 10-year period in the whole population was 449 (3.4%). The number of PPD-positive reactions in the 1st-time testers was 419 (3.4%), compared with 30 (2.9%) in the repeat testers.

Of the 30 patients in the retest group who tested positive for PPD (24 women and 6 men), 17 had been exposed to hair dye in the past, 6 were as a consequence of recent exposure and 4 were cross-reactions from other agents (Disperse Yellow 3, Disperse Orange, Disperse Orange and Red, and IPPD, respectively). 3 patients had a positive reaction but of unknown significance. In these patients, there was no clear exposure other than patch testing. 1 case was complicated by multiple positive reactions and clinical evidence of polymorphic light reaction.

Discussion

Active sensitization is a complication of patch testing and has been reported with a number of substances including PPD, isothiazolinones, sesquiterpene lactones and methacrylates. Para-phenylenediamine has intermittently been banned in a number of European countries; most recently in Sweden in 1964. However, as the advent of the European Union and stricter regulation of the concentration allowed (currently 3%, though the actual concentration used is rarely above 2%), PPD is used throughout the European Union.

Para-phenylenediamine at concentrations greater than 10% is known to act as an active sensitizer in up

to 100% of individuals (3). It is this fact that has led some authors to suggest the removal of PPD from the European standard series, and testing for PPD sensitivity only when clinically suspected. Late reactions occurring up to 7 days after application are often attributed to late sensitization. However, sensitization can only be proved if repeat patch testing to the original allergen is then positive.

It is known that there is a marked interindividual variability in eliciting a reaction to PPD on patch testing, with regard to both the exposure time and the concentration required (4, 5). This may mean that some late reactions are true-positive reactions rather than representing active sensitization.

Our study has shown that the rate of PPD sensitivity in the 1st-time patch testers is 3.4% compared with 2.9% in the repeat patch testers. Of the 30 patients positive to PPD in the retest group, 3 patients had no documented history of PPD exposure. Hence, if these 3 patients' PPD sensitivity were due to sensitization from their 1st patch test, this would equate to a sensitization rate of 0.3%. These figures assume that the 1035 are a random sample from the 13 300 and that someone sensitized was just as likely to be retested as someone unsensitized. In addition, this assumes that the only manner of sensitization between tests (in the absence of a contact history) is the patch test itself. This would tend to exaggerate the risk of sensitization, as it does not take into account incidental sensitization in the environment between tests.

Our review is an attempt to determine the clinical relevance of PPD sensitization. If PPD is actively sensitizing individuals, then the rate of PPD-positive reactions should be higher in repeat testers rather than in new patients due to exposure to the allergen during patch testing. Our figures over a 10-year period do not reveal an increase in the rate of PPD sensitivity in patients who have been previously patch tested, while the maximal sensitization rate was less than 0.3% in retested individuals and may well be considerably less.

Though the clinical assessment of a patient with suspected allergic contact dermatitis will give clues to possible sensitizers, it is not sufficient to

patch test only with initially suspected sensitizer, as unsuspected sensitizers used for patch testing frequently turn out to be the actual cause of the dermatitis (6). With this in mind, and in view of the above data, the risk of PPD sensitization seems low enough to warrant its continued inclusion in the European standard series.

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A simple spectroscopic technique proposed for scanning the depigmenting potential of azo dyes

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Key words: azo dyes; chemical leucoderma; CT DNA; interaction; para-phenylenediamine.

Para-phenylenediamine (PPD), a building block for azo dyes and the major component of hair dyes, has recently been implicated in producing depigmentation (1, 2). In India, such cases of hair dye depigmentation have frequently been observed in the past few years, more so because the introduction of black henna. Black henna, touted to be a herbal product, in fact contains 16–25% of PPD w/w in powder form. Azo dyes like Crocein Scarlet Moo and Solvent Yellow 3, components of alta (alta is a scarlet red solution applied by a certain sect of Indian women on their feet during religious and social functions), have also been documented to produce depigmentation in patients by patch testing (3, 4). As it is impractical and unethical to scan large number of dyes for their depigmenting effect in patients, a spectroscopic laboratory assay was devised by interacting calf thymus DNA (CT DNA) with known depigmenting and other azo dyes, as well as food, cosmetic and drug dyes, to observe any differences in their interaction.

Materials and Methods

The optical density (OD) of different dyes, as well as of CT DNA, was fixed at 1 at their respective $\lambda_{\max}$. The solution of CT DNA was prepared in $\times 1$ Tris-HCl (pH 8.0), and the solutions of dyes were prepared in double distilled water. The dyes were mixed with CT DNA in equal concentrations of their OD and the UV/visible spectra were recorded. It is well known that UV/visible spectra of organic molecules depend on chromophore present. The specific $\lambda_{\max}$ for DNA is normally taken as 260 nm. Each one of the azo dyes has its own specific $\lambda_{\max}$ depending upon its chromophore. In the case that the 2 molecules do not interact with each other when mixed together, the $\lambda_{\max}$ values are not found to change. However, if there is molecular interaction, the $\lambda_{\max}$ can undergo hypsochromic

(shift towards lower wavelength)/bathochromic (shift towards higher wavelength) shift.

The molecular interaction may be of different types. There are 3 primary ways in which molecules may interact with DNA, viz, by electrostatic forces, as minor or major groove binders (5) or as intercalators. Thus, the binding may affect the conformational stability of the DNA helix, causing a significant shift in its UV/visible spectra.

Results and Comment

A significant shift in $\lambda_{\max}$ of CT DNA was observed with PPD, Disperse Orange 1, Brilliant Crocein Moo, Solvent Yellow 3 and Ponceau 4R, while no such shift was observed with other dyes (Table 1).

The interaction of DNA with small molecules in its environment is the physical means of control and regulation of cells. The wide range of biological effects of intercalating drugs has provided a major stimulus to the study of this process. In fact, the activity of a large variety of substances, such as antibiotics, anti-cancer and antimalarial agents as well as aromatic carcinogens, has its primary origin in intercalation.

Intercalation involves the insertion of a planar molecule between the adjacent DNA base pairs, perpendicular to the double helix backbone. This gives rigidity to the helix, the resulting unwinding of base pairs increases the length of DNA and causes some distortion in the backbone (such as bends). These changes are specific for each intercalator species. Many studies have been carried out using DNA-binding dyes to determine physical characteristics of the nucleic acids (6, 7).

Significant shift in $\lambda_{\max}$ of CT DNA by the known depigmenting dyes could be due to the intercalation of dyes with DNA, resulting in damage to the cells which could be melanocytes in this case. The shifts produced by Ponceau 4R (a drug and cosmetic dye) and Disperse Orange 1 seem difficult to explain, but further studies involving the interaction of these dyes with melanocytes *in vitro* might help to explain these seemingly paradoxical readings. The present study suggests that this simple laboratory technique might be helpful in scanning the depigmenting potential of various azo dyes.

Table 1. Spectroscopy results

Name of dye	$\lambda_{\max}$ of dye (nm)	$\lambda_{\max}$ of CT DNA (nm)	Shift in $\lambda_{\max}$ of CT DNA (nm)
Brilliant Crocein MOO/Crocein Scarlet Moo	510	260	10
Para-phenylenediamine	400	260	25
Fast Garnet GBC/Solvent Yellow 3	380	260	10
Disperse Orange 1	483	260	20
Ponceau 4R	510	260	10
Disperse Yellow 3	357	260	—
Disperse Orange 3	443	260	—
Brilliant Blue	625	260	—
Erythrosine	525	260	—
Tartrazine	425	260	—
Metanil Yellow	440	260	—
Rhodamine	550	260	—

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