

CONTACT POINTS

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Hair dye allergy due to 3-nitro-*p*-hydroxyethylaminophenol

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Key words: 4-hydroxyethylamino-3-nitrophenol; allergic contact dermatitis; CAS no. 65235-31-6; cosmetics; hair dyes; patch testing.

Case Report

A 45-year-old woman had a history of contact dermatitis after she had used a colouring shampoo 10 years ago. She had changed to hair dye preparations of another firm and continued to colour her hair without problems. The patient, however, decided to use a new hair dye preparation belonging to group I (transient colouration). She applied the colouring preparation (Expression, Laboratoires Garnier, Saint-Ouen, France) as recommended by the manufacturer. Within 24 hrs, she developed itching, followed by acute head and neck dermatitis, with severe oedema. Lesions cleared with topical betamethasone.

Patch testing was performed with the revised international series (1), additional allergens, a hair dye series (Chemotechnique, Malmö, Sweden) and ingredients of the suspected hair dye preparations kindly provided by the manufacturer. Readings at D2/D3 showed a +++/+++ reaction to 3-nitro-*p*-hydroxyethylaminophenol tested at 1.35% in ethanol. Ingredients HC Red no. 3 and 4-amino-3-nitrophenol were negative. The suspected hair dyes, applied as is on the forearm and rinsed off after 20 min, gave a ++ reaction at D2. The patient was then open

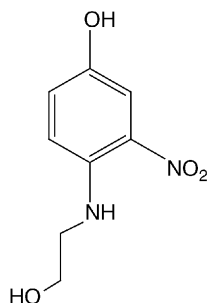


Fig. 1. Molecular structure of 3-nitro-*p*-hydroxyethylaminophenol.

tested with a group III (permanent) colouration containing oxidation dyes, without side effects, and was then authorized to use such dyes.

Discussion

3-Nitro-*p*-hydroxyethylaminophenol belongs to the aminophenol class and is also called 4-hydroxyethylamino-3-nitrophenol. It has CAS no. 65235-31-6 and condensed formula $C_8H_{10}N_2O_4$ (Fig. 1). It is used as a hair colorant, particularly in semipermanent hair dye preparations (2).

The main allergens in hair dyes remain *p*-phenylenediamine and derivatives (3), followed by toluene-2,5-diamine and aminophenols. In rare instances, however, patients with allergic contact dermatitis from hair dyes are not sensitized to PPD or other familiar haptens, and the offending hapten can instead be a colouring ingredient, such as 4-amino-3-nitrophenol (4), 2-aminomethyl-*p*-aminophenol (5) or 2,7-naphthalenediol (6), a viscosity stabilizer (7) or an antioxidant (8). This seems to be the first report of delayed-type allergy to this particular hair-colouring agent. In such a situation, when standard hair dye allergens remain negative, after a negative open test, PPD-based hair dyes remain a safe alternative.

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Allergic contact stomatitis from BIS-GMA and epoxy resins in dental bonding agents

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Key words: acrylates; allergic contact stomatitis; BIS-GMA; dental composite resins; dental patients; dimethacrylated epoxy resins; epoxy resin systems.

Case Report

A 43-year-old woman was referred for allergy testing before definitive replacement of dental restorations. In 2002, she had developed chronic stomatitis beginning a few hours after insertion of provisional dental bondings in her mouth, which were subsequently removed. Her dental practitioner, however, could not identify the composition of the material inserted. Patch testing performed elsewhere showed a strong reaction to BIS-GMA 2% pet.

In 1992, she had painful swelling of the oral mucosa for half a day following root canal treatment with the product AH 26 (Dentsply DeTrey, Konstanz, Germany), which according to the manufacturer contains bisphenol-A-diglycidylether and not BIS-GMA (1). Polymerization of the monomers in this product occurs in 8 h. The clinical history of the patient included, in 1974, an acute dermatitis of the face while using a 2-component ceramic glue for only 2 days.

Patch testing was performed with the standard series of the German Contact Dermatitis Group (DKG), the plastics and glues series of the DKG, the dental technician series of the DKG (both from Hermal, Reinbek, Germany) and a special epoxy resin series (study substances obtained from Hermal, in the course of the Epox 2002 study of the DKG). Patch tests were applied for 1 day with Finn Chambers[®] on Scanpor[®] tape (Epitest Ltd., Oy, Tuusula, Finland) to the upper back and further covered with Mefix[®] (Mölnlycke, Hilden, Germany). Readings were taken at D1, D2 and D3 by the criteria of the

DKG (2). Strong positive reactions were seen to epoxy resin 1% pet. (standard series of the DKG), bisphenol F epoxy resin 0.25% pet. and BIS-GMA 1% pet., and a weak reaction at D3 to diphenylmethane-4, 4'-diisocyanate 1% pet.

Dental restorations completely free of plastic materials and new amalgam fillings were then inserted by her dental practitioner and tolerated without any side effects.

Discussion

Epoxy resin systems frequently cause occupational allergic contact dermatitis (3), which may be airborne (4). Our patient had possibly been sensitized to epoxy resins at the age of 15 years at home while using ceramic glues. She, however, could not remember whether the glues were based on epoxy resin systems. In our experience, short contacts between epoxy resins and the skin for just a few days or weeks may be sufficient to sensitize. This may later cause problems when dental restorations based on epoxy resins or epoxy acrylates are used. In such cases, aliphatic acrylates may be used as a substitute (5). Ceramic glues or coating materials, however, used during home-working may also be the source of sensitization to diphenylmethane-4 and 4'-diisocyanate.

The origin of the sensitization to BIS-GMA in our patient also remains unclear. Sensitization was possibly induced through the dental composite resins (DCR) used in 2002, or cross-reaction has arisen between BIS-GMA and epoxy resins (5). BIS-GMA is the addition reaction product between bisphenol A and glycidyl methacrylate or an epoxy resin and methacrylic acid (6). Dimethacrylated epoxy resins find extensive use in industry. BIS-GMA is the most widely used epoxy dimethacrylate in DCR (7).

However, nonoccupational allergic symptoms from epoxy diacrylates or epoxy resins in dental acrylics are rare (8). Sensitization to both BIS-GMA and epoxy resins due to DCR has been described in dental technicians (9, 10), as well as in patients (5, 9, 11). This may also be due to free epoxy resin present, which may sensitize separately or simultaneously (6, 7). Some DCR based on epoxy dimethacrylates may contain

epoxy resins as an impurity (7, 9) while others do not (7, 10). However, because of the complexity of the acrylates present in DCR, it is difficult to know whether such patch test reactions are due to concomitant sensitization, to true cross-reactions (7, 12) or to previous sensitization as probably occurred in our patient. As seen in our patient, cross-reaction can also occur between bisphenol A and bisphenol F epoxy resins (11).

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Contact dermatitis due to disodium ethylenediamine-tetraacetic acid in cosmetics and shampoo

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Key words: allergic contact dermatitis;
cosmetics; disodium EDTA; shampoo.

Case Report

A 65-year-old woman had a 3-year history of recurrent pruritic erythema on her scalp, face and neck. Her symptoms gradually worsened in spite of topical corticosteroid application. Patch testing was performed with the cosmetics and shampoo that she had used. She showed positive reactions to a cosmetic lotion, cream and shampoo at days 2 and 3. Subsequently, she was patch tested with the ingredients of the shampoo. Only disodium ethylenediaminetetraacetic acid (EDTA) (0.1 and 1% aq.) was positive at days 2 and 3. All 3 positive cosmetic products were found to disodium EDTA. The skin eruption rapidly improved and did not recur after discontinuing the cosmetics that contained disodium EDTA.

Discussion

EDTA is well known as a chelating agent with a strong affinity for metals such as calcium, lead and magnesium. It is classed as a sequestering

agent and can bind metallic ions. It stops discoloration due to traces of metals in antibiotics, antihistaminics and local anaesthetics. It prevents oxidation by trace metals in cosmetic creams and lotions (1). EDTA can also be used in certain foodstuffs such as salad oil and wine.

Although EDTA is widely used, it is a rare sensitizer. In fact, only 4 cases of contact dermatitis due to salts of EDTA have been reported (2–5). A reasonable explanation is that the tetraacetate that binds each of the hydrogens attached to the nitrogen destroys the sensitizing properties of ethylenediamine (1). It should be kept in mind, however, that EDTA is still capable of inducing contact dermatitis.

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Airborne photocontact dermatitis due to the insecticide phoxim

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Key words: airborne photocontact dermatitis; insecticide; organophosphorus pesticide, phoxim.

Case Report

A 47-year-old woman was referred to our hospital with erythema on her cheeks, forehead and chin. 3 months before presentation, she had first noticed a strikingly itchy erythema with scaling on her face. The eruption subsided and worsened repeatedly. She developed an erythema especially after she sprayed phoxim (2-diethoxyphosphinothioxyloxyamino-2-phenyl-acetonitrile) in her garden to repel white ants or termites. There was a history of contact allergy to a hair dye a year before.

Patch testing was performed with phoxim and her cosmetics. She showed no reaction to either phoxim 0.1% aq. or her cosmetics at days 2 and 3. However, she had a positive (+) reaction (ICDRG criteria) to phoxim 0.1% aq. on photopatch testing with 5J/cm² UVA radiation. Photopatch testing with her cosmetics was negative. Stopping the use of phoxim resulted in disappearance of the dermatitis.

Comment

Phoxim, with the chemical structure shown in Fig. 1, is an organophosphorus insecticide widely used in Japan, especially for ants. In Japan, we construct houses of woods which easily succumb to the digestion of termites. As termites make tunnels and their entry site into the house is

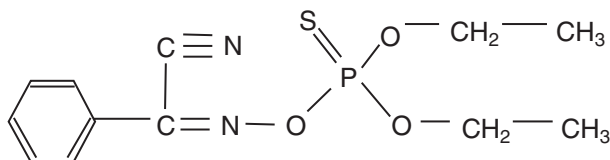


Fig. 1. Chemical structure of phoxim.

difficult to access, ridding a home of termites requires an extensive knowledge of house construction and termite biology. Spraying an insecticide over the garden is not enough for termite control. The patient would better have made contact with a professional termite control company.

The patient found winged termites in her garden in June and July. In Japan, winged termites emerge between April and July. We reported a previous airborne pesticide photocontact dermatitis occurring in June (1). Hot humid Japanese weather in June and July may facilitate the onset of airborne photocontact dermatitis.

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Occupational contact dermatitis from chrysanthemum in a mortician

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Key words: chrysanthemum; compositae; desensitization; edible plant; mortician; occupational allergic contact dermatitis.

Case Report

A 25-year-old mortician, who had worked in a funeral home for 2 years, was seen in December 2002 with pruritic erythema and scaling

on his face and hands, which he had developed 10 months before. He gave no history of exacerbation of skin lesions on sun exposure.

A screening phototest (1) showed a normal response to ultraviolet (UV) A and UVB. He was patch tested with flowers and leaves of chrysanthemum as is and 10% pet. of ether extracts of flowers and leaves (2), with the positive results shown in Table 1. 5 control subjects were negative to these same tests.

Topical corticosteroid therapy was not effective as he still handled chrysanthemums daily. Then, oral administration of juice from edible chrysanthemum leaves started to induce tolerance. The patient took juice containing 50 g of leaves stirred in water $\times 2$ daily for 3 weeks and stopped for a week. This desensitization regime was repeated $\times 2$. After this, the skin lesions markedly improved following slight erythema on the forehead. Patch tests were repeated and gave weaker responses to flowers and leaves of chrysanthemum (Table 1).

Discussion

Chrysanthemum, a member of the Compositae family of plants, is a well-known occupational sensitizer in gardeners and florists (3–5). In Japan, chrysanthemums are looked upon with favour at funerals to decorate the deceased person and to set up the bier. Morticians in Japan, therefore, may easily become sensitized to chrysanthemum. Our patient handled chrysanthemums daily as a mortician and may have acquired contact sensitivity occupationally.

Some chrysanthemums are edible plants originating from China and introduced into Japan during the

8th century. Flowers and leaves of this group of chrysanthemums are frequently eaten as a food plant in Japan. We attempted induction of oral tolerance in this patient by his drinking juice prepared from an edible chrysanthemum (6, 7).

Daily administration of the juice from water-stirred leaves resulted in remarkable improvement in the skin lesions and reduction of reactivity to patch testing. Our case suggests that the oral intake of edible chrysanthemums might be a possible desensitization method for occupational chrysanthemum dermatitis.

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Table 1. Patch test results

	Before desensitization		After desensitization	
	D2	D3	D2	D3
Flowers				
As is	++	++	?+	?+
Ether-extract	–	–	–	–
Leaves				
As is	++	++	?+	?+
Ether-extract	++	++	–	–

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Decrease in nickel allergy in Germany and regulatory interventions

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Key words: contact dermatitis; epidemiology; EU regulation; European Dir. 94/27/EC; nickel; women.

The vast majority of nickel-allergic women are sensitized through piercing with cheap jewellery, often as early as in childhood (1, 2). In addition, body piercing has become a widely popular fashion (3). At the beginning of the 90s, young women

were frequently found to be nickel-allergic, up to 20% at the level of the general population (4) and around 40% in clinical populations with contact dermatitis (5), making nickel the most frequent contact allergen. The great impact of nickel allergy on public health was recognized by several national and the European regulatory institutions. In 1992, the German Ministry of Health declared labelling mandatory ('contains nickel'), if a product remaining in prolonged contact with the skin (jewellery, tools and textile accessories) released more than $0.5 \mu\text{g}/\text{cm}^2/\text{week}$. In 1994, the EU prohibited trading in such products (6).

To evaluate the success of these interventions, we analysed the patch test results of 82 991 patients (women: 52 709 and men: 30 282) reported to the contact allergy surveillance network 'Information Network of Departments of Dermatology' (www.ivdk.org) between 1992 and 2001. During the observation period, the frequency of sensitization to nickel decreased significantly in women age 30 and below, namely, from 36.7 to 25.8% (Cochran-Armitage trend test: $P < 0.0001$), coinciding with the EU regulation (Fig. 1). Conversely, an increase was observed in the age group above (31–44 years), namely from 27.9 to 33.2%. This, most likely reflects nickel exposure in the 70s and 80s, as women most often have their ears pierced at a young age. The same trends were

reported from Denmark, where similar interventions took place (7).

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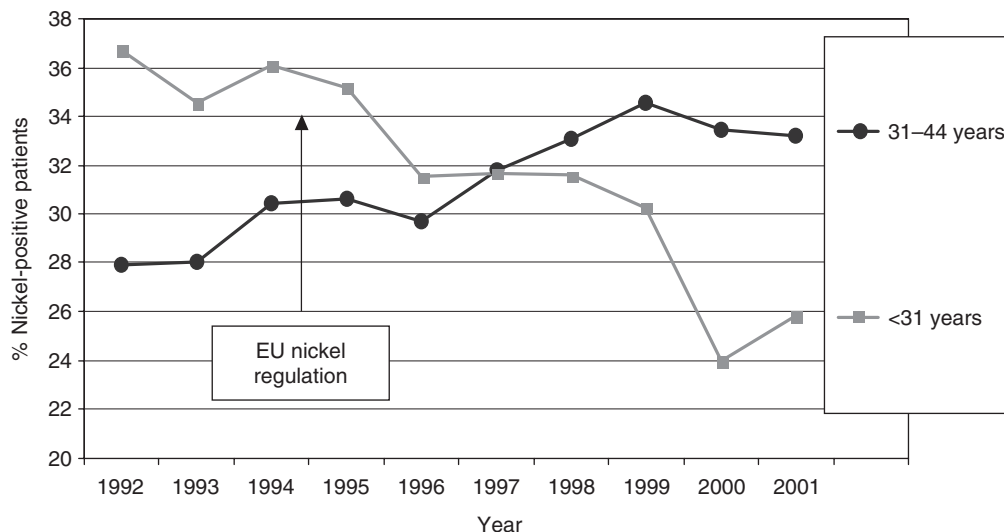


Fig. 1. Nickel allergy in women (2 age groups) (1992–2001). Data from the Information Network of Departments of Dermatology (IVDK)

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d-Limonene contact dermatitis from hand cleansers

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Key words: allergic contact dermatitis;
d-limonene; hand cleansers; occupational.

A 39-year-old painter and decorator was referred with a 4-year history of work-exacerbated hand eczema. He had a history of atopic eczema, and previous patch testing with the European standard series had been negative. Patch tests were repeated to an extended British standard series, d-limonene 2% pet. (Trolab[®], Hermal, Reinbeck, Germany), and a plastics and glues series (Chemotechnique Diagnostics, Malmö, Sweden). Readings showed a ++ reaction to d-limonene on D3 and D4 and a + reaction to lanolin alcohol (30% pet.) on D4. Further questioning revealed his work hand cleansers were Scrubs -in-a-bucket[®] water-free hand cleansing towels and Swarfega[®] orange, which contained d-limonene at concentrations of 7 and 1%, respectively. Avoiding these products has led to improvement but not resolution of the hand eczema. We have tested 270 consecutive patch test patients to dl-limonene 2% pet. in our department, and have not observed any other positive reactions. d-Limonene or oxidized citrus oil has different commercial uses depending on its concentration. It was first introduced, as a solvent and degreaser in concentrations around 95%. It is used

in water-free hand cleansers, in concentrations around 10–20% and is also frequently used as a fragrance in a wide range of technical and household products, and perfumes at concentrations around 0.005–2%. Pure d-limonene is irritant in high concentration, but its oxidation products, e.g. limonene oxide and limonene hydroperoxides, are allergenic.

Contact dermatitis from d-limonene primarily affects the hands, but can also involve the face and neck. Initial reports were of car mechanics exposed to degreasing agents, patients with occupational exposure to fruits, flavours and vegetables, and contact with cleaning products (1, 2). In a large European multicentre study of patch testing to limonene, an overall positive rate of 2.8% of 2273 patients was found (3). An air-exposed (autoxidized) preparation of 3% d-limonene was used, and the majority of contact allergy patients were administrative workers, nurses, and housekeepers. Only the nurses were likely to have had occupational exposure via hand washing, and the others were thought to have been exposed via household contact with peel oil in cooking or in fragrances.

Patch testing with 3% oxidized d-limonene (which is not commercially available) may detect more cases than 2% dl-limonene, possibly explaining our positive rate of only 0.3%. However, d-limonene should be considered as a potential allergen in patients with fragrance allergy or hand dermatitis.

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Occupational contact urticaria from the solid-phase peptide synthesis coupling agents HATU and HBTU

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Key words: contact urticaria; HATU; HBTU; solid-phase peptide synthesis coupling agent.

Case Report

A 29-year-old research scientist presented with a 2-week history of chest tightness, cough and rashes occurring while at work in a peptide synthesis laboratory. She had first developed symptoms of irritation of the eyes, streaming nose and coughing after 6 h of weighing HBTU (N-[(1H-benzotriazol-1-yl)(dimethylamino)methylene]-N-methylmethanaminium hexafluorophosphate N-oxide) and 9-fluorenylmethoxycarbonyl amino acids (f-moc amino acids), used in the process of solid-phase peptide synthesis (SPPS).

The symptoms were initially attributed to a viral upper respiratory tract infection and cleared spontaneously after 2 days rest at home. On return to work, she experienced further symptoms of chest tightness, coughing and an 'insect bite-like' rash. Her symptoms settled without treatment within 2 h of leaving work.

Over the next 5 days her symptoms at work progressively increased in severity, culminating in the development of very red, sore and itchy eyes, coughing and sneezing, and urticaria with angioedema affecting the exposed areas of the face (but not the areas protected by clothing or gloves) within 1 h of being at work. Past medical history was unremarkable apart from hay fever. Investigations showed that she had a normal total Immunoglobulin E (IgE) level and a negative IgE RAST to latex.

Prick tests to 0.16% HBTU in water, and 0.16% N-[(dimethylamino)-1H-1, 2, 3-triazolo[4,5-b]pyridine-1-yl-methy-

lene]-*N*-methylmethanaminium hexafluorophosphate *N*-oxide (HATU) in water elicited 5 mm and 10 mm urticarial responses, respectively, with appropriate positive and negative controls. There were no reactions to 0.16% O-(1*H*-6-chlorobenzotriazole-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate (HCTU), F-moc amino acids (F-moc-L-alanine monohydrate, N-F-moc-glycine, F-moc-L-threonine) or various other work-related materials. Prick tests in 2 control subjects were negative. There has been no recurrence of symptoms since avoiding exposure to HATU and HBTU.

Discussion

The annual incidence of occupational skin disease is approximately 12.9 cases per 100 000 workers (1–4). Occupational contact urticaria (OCU) accounts for only 3.5–4.7% of all occupational skin diseases with approximately 30% of cases of OCU have associated contact dermatitis. OCU occurs most commonly in health care workers and food industry workers (2, 4, 5).

In a Finnish series, OCU occurred most commonly in bakers, preparers of processed foods, dental assistants, veterinary surgeons and domestic animal attendants and farmers. Laboratory technicians/radiographers and laboratory assistants were the 10th and 13th most common occupations to develop OCU, respectively. The most important cause of OCU is currently related to latex glove use; however, in the Finnish series, the most common allergen was cow dander followed by natural rubber latex, flour/grains/cereals, foodstuffs and enzymes.

HATU, HBTU and HCTU (Fig. 1) are related guanidinium/uronium salts used in the biochemical process of SPPS (6–9), part of which involves the repeated formation of amide bonds ('coupling') with added reagents containing F-moc amino acids. HATU and HBTU exist as N (guanidinium salt) and O (uronium salt) isomers, and both accelerate the coupling process; however, the O isomers of HATU and HBTU are the more efficient couplers (9).

OCU from HATU and HBTU has not been previously reported, although the data sheets list both HATU and HBTU as potential sensitizers. Interestingly, there was no cross-reaction to the related compound HCTU, suggesting this agent may be used safely as an alternative coupling agent to HATU and HBTU.

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Allergic contact dermatitis from the epoxy resin plasticizer diglycidyl ether of propylene glycol

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Key words: contact dermatitis; diglycidyl ether of propylene glycol; epoxy resin.

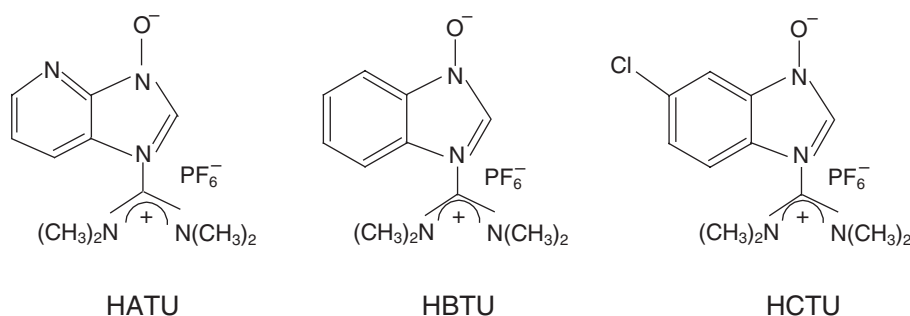


Fig. 1. The guanidinium/uronium salts HATU, HBTU and HCTU.

Case Reports

Case no. 1

A 38-year-old chemical processor presented with a 4-month history of an eczematous rash on his forearms, with subsequent spread to involve the knuckles. The rash occurred following the introduction of the manufacture of epoxy resin and accidental contact from a spillage sustained at work. There was no history of exposure to epoxy resin outside his working environment. The rash responded to treatment with topical betamethasone valerate. He was patch tested to the British Contact Dermatological Society (BCDS) series, epoxy resin series, plastics and plastic additives, an acrylates series and a number of work samples. He gave several positive reactions (Table 1). Testing of 30 controls to dilutions of diglycidyl ether of propylene glycol (DGEPG) was negative. Avoidance of the DGEPG led to complete resolution.

Case no. 2

A 46-year-old chemical processor presented with a 4-month history of an eczematous rash on the wrists (above the upper level of his gloves) and also on his genitals. He worked at the same factory as Case no. 1. Avoidance of DGEPG in his work environment led to complete resolution of his rash. Following a spillage in the factory, he, however, developed a facial eruption. There was no exposure to epoxy resin outside his working environment. He was patch tested to the BCDS series, epoxy resin series, plastics and plastic additives, an acrylates series and a number of work samples and showed several positive reactions (Table 1). Avoidance of these positive reactors led to complete resolution of his skin and ocular symptoms.

Discussion

Epoxy resins were first developed in the 1940s (1). The majority of epoxy

resins is based on esters of diglycidyl ether of bisphenol A (DGEBA). More recently, non-DGEBA type resins have been developed. An epoxy resin 'system' consists of 3 main components: epoxy resin (DGEBA or non-DGEBA), diluents and hardeners.

Allergy to epoxy resins occurs most commonly in the occupational setting (1), they being the 8th most common agent causing contact dermatitis (6.1%) in the United Kingdom. The incidence of epoxy resin allergy shows regional variations (2–6). 90% of patients with occupational dermatoses from epoxy resins present with symptoms on exposed areas of the hands and forearms. In addition, 50% of such patients have facial involvement. Mean exposure time to the development time of allergic contact dermatitis is approximately 31 months but appears to be less in patients who have contact urticaria and irritant contact dermatitis. Occupational skin disease resulting from epoxy resin systems can arise from most of their components (1–6).

Allergic contact dermatitis due to DGEPG has not been reported before. We report 2 cases from the same factory.

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Stethoscope earpiece-induced chemical depigmentation

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Key words: depigmentation; dermatitis; dibutyl phthalate; polyvinyl chloride; stethoscope.

Case Report

A 58-year-old male surgeon had developed itching followed by depigmentation on the neck and in the external auditory canal over the last 3 months. Topical corticosteroids were not effective in restoring pigmentation. The depigmentation was seen to coincide with the area of contact with the earpiece of the stethoscope. Instead of allowing the stethoscope to hang from the neck, he was advised to carry it in his pocket.

Phototherapy was then administered as follows: 0.5 ml of 0.75 g% of 8-MOP solution was added to 1 l of water with which a piece of cotton cloth was soaked, gently squeezed and placed over the neck for 15 min

Table 1. Patch test results

Case number	Epoxy resin D2/4	FK BPF/BPA resin 7500 1% pet. D2/4	Diglycidyl ether of propylene glycol (Araldite 3601) 1% pet. D2/4	Araldite DW132 Yellow 1% pet. D2/4	Araldite GY260 1% pet. D2/4	Other work Substances D2/4
1	+/+	+/+	-/+	-/-	-/-	-/-
2	++/++	++/++	-/+	++/++	++/++	-/-

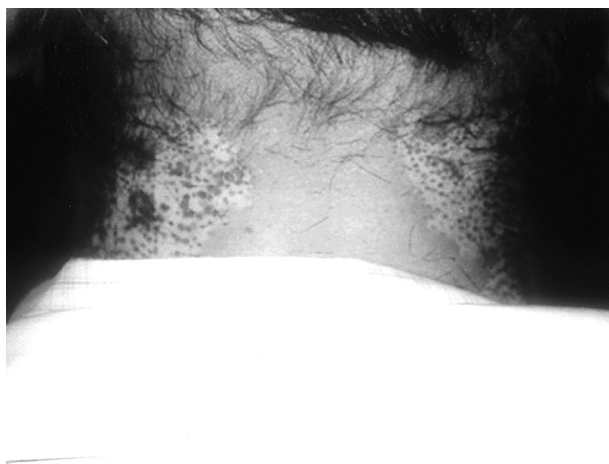


Fig. 1. Depigmentation in the area of contact with stethoscope earpiece.



Fig. 2. Repigmentation following treatment.

(1). He was then administered ultra-violet (UV) A 2× a week using a hand and foot UVA unit (V Care Systems, Bangalore, Karnataka, India). The upper frame of the unit can be tilted to enable exposure of the neck to UVA. Pigmentation started reappearing after 1 month of treatment (Fig. 1), the lesion repigmenting completely after 3 months (Fig. 2).

The earpiece was sent to the Indian Rubber Manufacturers Association for analysis and was reported to contain polyvinyl chloride (PVC), dibutyl phthalate and stearic acid-type additives. The presence of PVC was confirmed by burning characteristics, Belstein's test, action of 80% H_2SO_4 and concentrated HNO_3 , pyrolysis test and that of dibutyl phthalate and stearic acid-type additives by gas chromatography-mass spectrometry (GC-MS).

Comment

Chemical leukoderma following exposure to phenolic compounds and sulfhydryl compounds is reported (2). The various mechanisms responsible for chemical depigmentation have been hypothesized by Bleehen et al. (3) Depigmentation on the forehead from use of bindi is reported by Bajaj et al. (4) who identified para-tertiary-butylphenol (PTBP) as the depigmenting agent. Nickel causing stethoscope dermatitis around the neck is reported (5).

Frenk and Kocsis (6) reported depigmentation from adhesive tape. One such adhesive tape was of PVC with a natural rubber adhesive base containing a derivative of dihydroxy-

diphenyl methane (6). PVC and, more commonly, its additives, such as phthalates, are known to cause dermatitis (7). Fisher (8) reported plastic identification bracelets as a cause of PVC dermatitis in infants.

We report this case to highlight that chemicals other than phenols can also cause depigmentation. The surgeon was unwilling to undergo patch testing, either with shaving of the earpiece or relevant chemicals, after he was warned of the possibility of depigmentation at the patch-test site.

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Increased positive patch test reactivity to methyldibromoglutaronitrile

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Key words: antimicrobials; biocides; Euxyl™ K400; formaldehyde; methyldibromoglutaronitrile; preservatives. © Blackwell Munksgaard, 2003.

Since its introduction as a preservative in the mid-1980s, methyldibromo

glutaronitrile (MDGN) has emerged as an increasingly common cause of contact allergy in Europe. MDGN is present in EuxylTM K400 (MDGN and phenoxyethanol at 4:1 ratio). In 1997, EuxylTM K400 was replaced by MDGN in the extended standard series of patch tests in use at St John's Institute of Dermatology. This retrospective study compared the rates of positive patch tests to EuxylTM K400 0.5% petrolatum (pet.) from 1989 to 1997, and MDGN 0.3% pet. from 1997 to 2000, along with the corresponding rates of contact allergy to another common preservative, formaldehyde.

Patients and Methods

All patients who attended the St John's Institute of Dermatology patch test clinic from January 1989 to June 1997 were patch tested to EuxylTM K400 0.5% pet. From July 1997, all such patients were patch tested to MDGN 0.3% pet. Throughout the study period, from 1989 to 2000, patients were also patch tested to formaldehyde 1% aq. Finn Chambers[®] on Scanpor[®] tape (Epitest, Tuusula, Finland) were applied to the upper back, and the patches were read at D2 or D3 and D4 or D5.

Results

12 704 patients were patch tested from 1989 to 2000 (median age 39 years; 4442 males and 7297 females). There were 88 positive reactions to the patch tests in question (51 females and 37 males). The most commonly affected primary sites of eczema in

MDGN contact allergy were the head and neck (27% patients) and the hands (28%), followed by widespread eczema (20%) (Table 1). The most frequent sites of eczema in males were hands (40.6%) and head and neck in females (36.6%) (Fig. 1). This difference in the distribution of eczema between the sexes reflects the difference in exposure to products containing MDGN. There was a sharp increase in the number of positive reactions to the new preparation of MDGN, as compared with the positive reactions to EuxylTM K400 prior to 1997 (Fig. 2). In contrast, there was a gradual decline in the numbers of positive reactions to formaldehyde over the same period. There was a significant rise in positive patch tests to MDGN/EuxylTM K400, comparing the period 1989–1993 with 1994–2000 ($P < 0.01$). In comparison, there, however, was a fall in positive reactions to formaldehyde between the same periods ($P < 0.001$).

Discussion

That MDGN has become an important contact allergen was confirmed in this study. MDGN has been widely used as a preservative and is used in wash-off and leave-on cosmetics, moistened toilet paper, hand cleansers and detergents (1–4). It was introduced as a preservative in the mid 1980s and used increasingly by manufacturers as a preservative in cosmetics. It has been shown to be a weaker sensitizer than other preservatives such as methylchloroisothiazolinone plus methylisothiazolinone (MCI plus MI) in animal experiments (5). This increase in use is probably responsible for the increasing frequency of contact allergy to MDGN. The rates of contact allergy to it have been reported to be as high as those we have reported in many other centres (4, 6, 7).

Since the introduction of MDGN at 0.3% pet. in our extended stand-

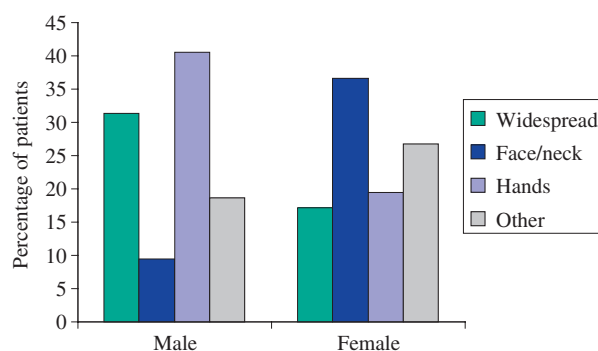


Fig. 1. Distribution of primary sites of eczema in methyldibromo glutaronitrile (MDGN) allergy.

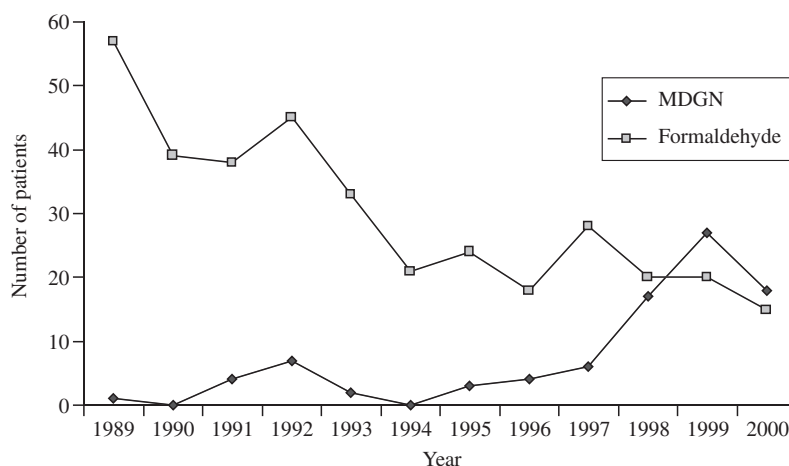


Fig. 2. Number of patients with positive tests. MDGN, methyldibromo glutaronitrile.

Table 1. Primary sites of eczema in patients with positive patch tests to methyldibromo glutaronitrile (MDGN)

Primary site	Number of patients (n = 88)
Head and neck	24
Hand	25
Widespread	18
Hand and foot	8
Trunk	3
Arm	2
Foot	2
Leg	1
Anogenital	2
Hand and face	3

ard series, the rate of positive results, however, has risen further, which might either reflect a false-positive irritant effect at this concentration or an under-detection at the previous concentration. We therefore recommend that any doubtful 0.3% MDGN-positive patch tests should be retested at a lower (0.15%) concentration. During 2000, we did retest all ?+ reactions to 0.3% MDGN at D2 with the lower concentration of 0.15% MDGN and found that all of these were negative. We believe that the more likely explanation for this finding is that MDGN 0.3% pet. can be weakly irritant, rather than that it is the lowest concentration capable of detecting contact allergy.

The relevance of a true-positive reaction to MDGN must then be carefully sought. The increasing incidence of MDGN contact allergy has led to a recent decision by the European Commission to prohibit MDGN in leave-on products and to permit its use at only up to 0.1% in wash-off products.

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Contact vitiligo appearing after allergic contact dermatitis from aromatic reactive diluents in an epoxy resin system

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Key words: allergic contact dermatitis; aromatic reactive diluent; epoxy resin; marble worker; occupational; phenylglycidyl ether; vitiligo.

Case Report

A 22-year-old man presented with a 1-year history of vitiliginous lesions on the backs of the fingers of both hands. He had been working as a

resinater in a marble factory for 5 years. Previously, he had a subacute eczema in these areas. The eczema cleared on leaving his job, but the vitiligo-like lesions remained. He did not have any other lesions of vitiligo. He gave no family history of vitiligo or of any other autoimmune diseases. Patch tests gave the results and are summarized in Table 1. After 2 years of follow up, the achromic areas have not changed, and new vitiligo-like lesions have not appeared in other locations, not even on those where patch tests were positive.

Discussion

Epoxy resins are a frequent cause of occupational allergic contact dermatitis (1–3). Epoxy resin systems contain a large number of chemicals. The most sensitizing are those based on diglycidyl ether of bisphenol A and cycloaliphatic-type epoxy resins, hardeners and reactive diluents.

Reactive diluents, mainly glycidyl ethers, are used to reduce the viscosity of the resin. They can be aromatic, such as phenylglycidyl ether and cresylglycidyl ether, or aliphatic such as butylglycidyl ether. They are irritant to the skin, eyes and respiratory mucosa. They can also sensitize, mainly mono- and di-glycidyl ethers of low molecular weight. Simultaneous positive reactions to 3 aromatic reactive diluents, similar to our case, have already been observed by other authors and can be interpreted as a cross-reaction, as all molecular structures involved have the same CH₂ group linked to the epoxy group (1).

Contact vitiligo or chemical leukoderma is an achromia secondary to the action of certain chemicals that can produce specific and selective melanocytopenia. This process is toxic and may or may not be accompanied by allergic contact dermatitis.

Table 1. Patch test results

Allergens	Results (D2/D4)
GEIDC standard series ^a	–/–
Plastics and glues series (Chemotechnique [®] , Malmö, Sweden)	–/–
Epoxy resins series (Chemotechnique [®] , Malmö, Sweden)	Phenylglycidyl ether 0.25% pet. ++/++
Own resins ^b	Phenylglycidyl ether 0.25% pet. ++/++
	Cresylglycidyl ether 0.25% pet. ++/++
	Hexanediyl diglycidyl ether 0.25% pet. ++/++
	Triphenyl phosphite 0.25% pet. ++/++

^aGEIDC = Grupo Español para la Investigación de Dermatitis de Contacto.

^bPatch testing on 10 controls was negative.

The list of melanotoxic chemicals includes phenols, catechols, hydroquinones and some agents with sulfhydryl groups (4). To our knowledge, contact vitiligo secondary to epoxy resins has previously been reported just once (5), and our case is the first to be associated with allergic contact dermatitis from an epoxy resin diluent.

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Anaphylactic reaction elicited by patch testing with diclofenac

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Key words: anaphylaxis; diclofenac; non-steroidal anti-inflammatory drugs; patch tests.

Some patients develop anaphylactic reactions during or shortly after

application of patch-test materials. Fortunately, this seems to happen rarely.

Case Report

A 39-year-old woman was referred to Department of Occupational Dermatology, because she had had an anaphylactic shock after using a sodium diclofenac (100 mg) suppository that was prescribed for a curettage. Within 5 min after insertion of the diclofenac, she developed swelling of the face and limbs, hypotension and respiratory insufficiency. She was treated in the intensive care unit. In the past, she had used diclofenac orally, after which respiratory problems had occurred, which were explained as hyperventilation. Also, she had noticed urticaria after taking ibuprofen and a propyphenazone/paracetamol/caffeine analgesic. No complaints had occurred after intake of paracetamol with codeine. There was no history of atopy, nor had she ever noticed any adverse reactions to other drugs.

She was patch tested with the European standard series on the back and with sodium diclofenac 1% pet. on the right upper arm. About 15 min after the application of the patch tests, the patient became dyspnoeic, hoarse and complained of headache and sputum production. Her blood pressure was 135/100 mmHg and her pulse regular. The patch test with diclofenac was removed immediately, and treatment was started with clemastine 2 mg intramuscular and salbutamol by inhaler; no wheal was seen at the patch-test site. 30 min later, she felt better, was no longer dyspnoeic and her blood pressure was 115/85 mmHg. After observation for a further hour, she was discharged home. All remaining patch tests were negative at D2 and D3. It was presumed that the anaphylactic reaction was elicited by diclofenac.

Discussion

Anaphylaxis is an immediate-type hypersensitivity reaction to an allergen caused by rapid cross-linking with specific immunoglobulin E (IgE) on tissue mast cells and peripheral blood basophils, causing cell degradation with the release of inflammatory mediators (1). In contrast, an anaphylactoid reaction is not IgE mediated but, similarly,

involves inflammatory mediators released from mast cells. This activation occurs both directly and indirectly, resulting from disturbances in arachidonic acid metabolism and the activation of complement (1). No previous sensitization is needed. Anaphylaxis due to the use of non-steroidal anti-inflammatory drugs (NSAIDs) has been described (1, 2). A relative high risk of developing anaphylaxis is noted in particular for diclofenac, ibuprofen and naproxen (2).

A few cases are described in the literature of anaphylaxis due to patch tests with antibiotics (3). Recent reports concern materials such as formaldehyde (4), natural rubber latex (5) and ammonium persulphate (6). To our knowledge, this type of reaction elicited by patch testing with diclofenac has not been described before. In this case, we presume that diclofenac must have been the cause of the anaphylactic reaction. In favour of this, are the history from the patient and the fact that she rapidly and completely recovered after removing the patch test with diclofenac, in combination with appropriate treatment (clemastine and salbutamol). No wheal, however, occurred on the patch-test site. It is hard to know whether the reaction was IgE mediated or not. However, the small amount of drug causing this severe and rapid reaction is in favour of an IgE-mediated process. This systemic reaction indicates rapid cutaneous penetration of sodium diclofenac.

Our case shows that anaphylactic reactions after patch testing with NSAIDs can occur. For this reason, we advise a period of observation after application of patch tests with NSAIDs when patients have a history of anaphylactic reactions to such drugs.

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Recurrence of pemphigus foliaceus after allergic contact dermatitis from triple antibiotic ointment

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Key words: allergic contact dermatitis; antibiotics; medicaments; pemphigus foliaceus.

Case Report

An 86-year-old woman had pemphigus foliaceus since 1997. She had originally been treated with systemic corticosteroid, but hyperglycemia had become difficult to control. This was then followed by gold sodium thiomalate but that was discontinued, because she developed thrombocytopenia. She had been managed with topical corticosteroid therapy since that time, along with oral doxycycline 100 mg $\times$ 2 daily. By May 2002, she was free of active lesions, and by August 2002, her skin was clear.

She re-presented in November 2002 with severe contact dermatitis

of the upper chest, where she had applied a topical triple antibiotic containing polymyxin B sulphate, neomycin and bacitracin. This was accompanied by an acute flare in her pemphigus over the chest, back and upper extremities, the most severe flare that she had experienced since her initial presentation in 1997.

Because of hyperglycaemia when on systemic corticosteroid, she was treated with topical corticosteroid and oral doxycycline. The condition remained active on her back (where she had difficulty in treating the lesions with topical medicaments) until June 2003. She was completely clear again by the end of July 2003.

Comment

Pemphigus can be precipitated by ultraviolet (UV) light (1) and other physical agents (2), drugs, infections, neoplasms and hormones (3). Several reports have attributed the mechanism to be via systemic absorption. Contact reactions, however, can cause local production of acantholysis (4) and pemphigus-like antibodies (5) associated with allergic contact dermatitis, as well as exacerbation of pemphigus from allergic contact dermatitis (6).

In 1973, Lynfield et al. (6) reported a patient with thymoma 16 years earlier, presenting with Senear–Usher pemphigus of 3 years' duration. This was localized to the upper chest and was found on a biopsy specimen on removal of a basal cell carcinoma. On the 2nd postoperative day, a prominent contact dermatitis appeared at the excision site, where it had been treated with tincture of benzoin. 11 days after surgery, a more widespread eruption of pemphigus erythematosus appeared, and this was treated with oral corticosteroid that was gradually tapered so that the patient was clear at 150 days on 15 mg of prednisone daily.

The present case history represents a recrudescence of pemphigus in a patient essentially in remission. A widespread flare occurred following a

severe contact reaction limited to the area on the upper chest, where a triple antibiotic ointment had been applied. Although it would have been desirable to confirm sensitivity by patch testing, I considered that it would have been unethical to do so, in view of the potential for aggravating her condition. One can postulate that the contact dermatitis freed desmoglein I and other allergens (7) involved in the pathogenesis. The risk-benefit ratio should be considered before patch testing patients with active or recently active pemphigus.

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