

Short Communications

Contact lupus erythematosus

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Key words: lupus erythematosus; contact allergy; carvone; spearmint; late patch test reactions; isomorphic phenomenon. © Munksgaard, 2000.

Case Report

A 63-year-old woman presented with burning mouth syndrome. For many years, she had been treated with oral hydrocortisone for Addison's disease. Over the last 10 years, she had had recurrent light-induced subacute cutaneous lupus erythematosus (SCLE), predominantly on the face, neck and upper extremities, with associated arthralgia. A skin biopsy confirmed the diagnosis of lupus erythematosus. Immunofluorescence staining was negative. She was ANA and SSA (Ro) positive.

She was patch tested with TRUE TestTM panels 1 and 2, and the following toothpaste additives: carvone 5%, 2%, 1% pet., spearmint mix 5% pet., peppermint mix 5% pet., menthol 5% pet., anethole 5% pet., eugenol 5% pet. and cinnamal 1% pet., and also with the Chemotechnique dental series, using Finn Chambers[®] on Scanpor[®] tape. Readings on D3 and D7 showed a follicular reaction to mercury 0.5% pet. and a + reaction to cinnamal 1% pet. All other tests were negative.

On D19, the patient returned with late patch test reactions to carvone 5%, 2%, 1% pet. and spearmint mix 5% pet. These were all clinically consistent with SCLE and a biopsy was confirmatory of such a diagnosis (Fig. 1).

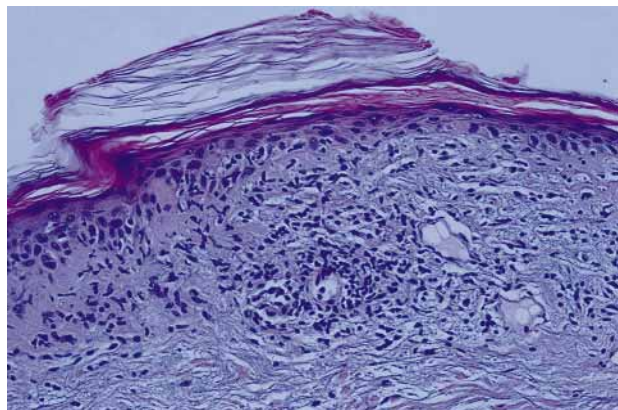


Fig. 1. Interphase dermatitis with basal vacuolar change and scattered necrotic keratinocytes. The epidermis is thinned with compact orthokeratosis. There is sparse interstitial mucin in the upper dermis. There is no spongiosis.

Subsequently, she was re-tested and showed no early eczematous reactions, but, with the same delay, identical late reactions. Allergen avoidance for some months did not diminish the burning mouth symptoms and the positive tests were considered of no clinical relevance to her mouth complaints.

Discussion

The development of various skin diseases can be provoked locally by direct skin contact with exogenous factors (isomorphic phenomenon), including allergens (1–4). The patient described by Stransky (1) had perioral contact LE following allergy to toothpaste ingredients. It has, to our knowledge, not been described previously that patch testing can result in the development of cutaneous LE at test sites.

Various cytokines are involved in LE (5). We speculate that spearmint mix and carvone (though not cinnamal) could cause a sub-clinical irritant reaction, which provoked the late response observed. Carvone is a terpene and 1 of the main constituents of spearmint oil, its sensitizing potential being high (6). Doubtful reactions are common among patients tested with carvone at 5% pet., though lower concentrations are not irritant (7). A more specific stimulus than marginal irritancy cannot, therefore, be excluded.

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Occupational allergic contact dermatitis from trichlorozincates of 4-(dimethylamino)benzenediazonium (Diaz A) and 3-methyl-4-(pyrrolidin-1-yl)benzenediazonium (Diaz Y) and thiourea in diazo copy paper

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Key words: 4-(dimethylamino)benzenediazonium: CAS 6087-56-5; CAS 52572-38-0; 3-methyl-4-(pyrrolidin-1-yl)benzenediazonium; diazo A; diazo Y; diazo copy paper; occupational; allergic contact dermatitis; thiourea; office workers. © Munksgaard, 2000.

Diazo copy papers contain up to 40 different chemicals, many of which are contact allergens (Table 1, 1–26).

handling diazo papers and his hand dermatitis had cleared on follow-up 6 months later.

Case Report

A 32-year-old office clerk, at the Finnish National Road Administration, was referred for investigation of recalcitrant palmar eczema, which had started 10 years earlier. At work, his main duty was to file newly diazo-copied maps.

2 patch test sessions were performed. In the 1st, a modified European standard series was negative, while thiourea (Trolab, 0.1% pet.) gave ++, and 5 of his own papers + to ++, patch test reactions. The manufacturers then kindly supplied us with samples of 29 chemicals used in the products. 2 such chemicals were positive: trichlorozincates of 4-(dimethylamino)benzenediazonium (Diaz A) (Fig. 1) 1% pet., ++; 0.32% pet. ?+; 0.1% pet. –; 1%–0.1% aq. ++; 0.32–0.01% aq. +; 3-methyl-4-(pyrrolidin-1-yl)benzenediazonium (Diaz Y) (Fig. 1) 2%–0.5% pet. ++ (lower %s not tested). Kathon CG® 0.02% aq. (Chemotechnique Diagnostics AB, Malmö, Sweden) elicited a ++ reaction of uncertain relevance. Many other chemicals, e.g., resorcinol, 2,7-dihydroxynaphthalene (23) and 4 other diazo salts, were negative.

Following diagnosis, the patient was able to avoid

Discussion

Several methods can be used for copying drawings and manuscripts: all except xerography have caused allergic contact dermatitis (1, 10, 17). The ammonia used to develop diazo paper may cause irritation (1, 7). Diazonium salts interact with coupling agents present in diazo paper to form azo dyes (9). The coupling agents are generally phenol or resorcinol derivatives. Other components such as stabilizing agents are also present. Antioxidants, e.g., thiourea, prevent yellowing of the non-image area.

The allergen in diazo paper is usually p-diethylaminobenzene diazonium chloride (diazodiethyl aniline hydrochloride, DDA), which is reduced to an amine that may cross-react with para-phenylenediamine (9, 14) (Table 1). Cross-reactions do not seem to occur with other azo compounds. DDA is no longer a sensitizer after it is UV-irradiated (21, 22, 24). Thus, patch tests only with *non-irradiated* paper are positive.

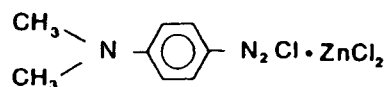
4-(dimethylamino)benzenediazonium trichlorozincate, CAS 6087-56-5 (other CAS numbers 13533-17-0, 15667-48-8, 22112-42-1, 24688-67-3 and 42493-39-0,

Table 1. Allergic contact dermatitis from diazo paper

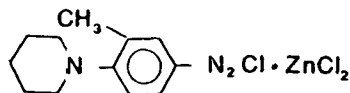
causative chemical/agent	Refs.
diazo copy paper	7, 9, 12
diazodiethylaniline	2, 8, 14, 16, 18, 19, 21, 22
4-(dimethylamino)benzene-diazonium trichlorozincate (Diaz A)*	6
3-methyl-4-(pyrrolidin-1-yl)benzenediazonium trichlorozincate (Diaz Y)*	3
2,7-dihydroxynaphthalene	23
dimethylthiourea	4
thiourea*	5, 6, 11, 15, 20*
nickel	25
chromate	26

* Allergen in present patient.

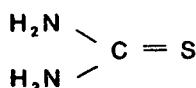
** Photoallergy from photocopy paper.



4-(Dimethylamino)benzenediazonium trichlorozincate (Diaz A)



3-Methyl-4-(pyrrolidin-1-yl)benzenediazonium trichlorozincate (Diaz Y)



Thiourea

Fig. 1. Chemical structures of 4-(dimethylamino)benzenediazonium trichlorozincate (Diaz A), 3-methyl-4-(pyrrolidin-1-yl)benzenediazonium trichlorozincate (Diaz Y) and thiourea.

50768-81-5), $C_8H_{10}N_3Cl_3Zn$, synonyms, e.g., Diaz A, 4-N,N-dimethylaminobenzene diazonium chloride and 4-N,N-dimethylaminobenzene diazonium chloride zinc chloride dihydrate, has a MW of 319.93 as an anhydride. Diaz A is a poison by ingestion, and allergic contact dermatitis has previously been reported (6), the patient also being allergic to thiourea. Patch testing was positive to Diaz A at 0.1% aq. In our patient, pet. seemed to be the better vehicle, 0.01% pet. eliciting a positive reaction.

3-methyl-4-(pyrrolidin-1-yl)benzenediazonium trichlorozincate, CAS 52572-38-0, $C_{11}H_{14}N_3Cl_3Zn$, synonyms, e.g., Diaz Y, 4-diazo-2-methylpyrrolidinobenzene zinc chloride and 3-methyl-4-pyrrolidinobenzenediazonium zinc chloride, has a MW of 360. Crijs et al. (3) reported a patient with allergic contact dermatitis from Diaz Y, who had patch test reactions to 2 diazo solutions at 1% aq.). These solutions contained 4-diazo-2-methylpyrrolidinobenzene zinc chloride, i.e., Diaz Y, which gave positive patch test reactions (++; 10%, 2% and 1% aq). In our patient, 0.5% pet. provoked a ++ patch test reaction, but we did not test at lower concentrations.

In conclusion, we report a patient who became sensitized to 3 chemicals used in diazo copy paper, Diaz A, Diaz Y and thiourea. All chemicals have previously been reported to be sensitizers in diazo copy paper, but not in the same person.

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Contact sensitivity to Tween 80 in a child

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Key words: Tween 80; allergic contact dermatitis; polyoxyethylene sorbitan monooleate; polysorbate 80; emulsifiers; children; medicaments; antivirals. © Munksgaard, 2000.

Tween 80 (INCI name, polysorbate 80; polyoxyethylene sorbitan monooleate) is a mixture of esters and ethers of sorbitan, a heterocyclic ether and polyalcohol, derived from sorbitol by dehydration (1). This non-ionic surfactant is a dispersing agent for injectable drugs and an emulsifier in cosmetics, pharmaceuticals and foods (2).

20,000 products analysed according to the FDA) (1). Previous patients sensitized to it have usually been adults, who had made much use of topical preparations before. Our case is a reminder that children may also become sensitized.

Case Report

A 9-year-old boy presented with an itchy erythematous dermatitis of the lower lip. He had a 6-month history of recurrent facial-oral herpes simplex virus treated with topicals without improvement. Patch tests with the GIRDCA standard series, a preservatives series and his topicals revealed positive reactions to Esavir[®] cream as is and Tween 80 0.25% pet. at D2 and D3 (+/++). He was negative to acyclovir 5% aq./PG. Lesions improved on avoiding topical preparations containing Tween 80.

Discussion

Allergic contact dermatitis from Tween 80 is not common (2–5), although this emulsifier is widely used (246/

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Sensitizing potential of cobalt chloride in the open epicutaneous test (OET)

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Key words: open epicutaneous test; guinea pig model; cobalt chloride; contact allergy; active sensitization, patch testing technique. © Munksgaard, 2000.

Cobalt chloride (CoCl₂) is a potent allergen in the guinea pig maximization test (GPMT) (1) and useful in studies on cross-reactivity and in repeated open application tests (ROATs) (2–4). The open epicutaneous test (OET) is an interesting alternative to the GPMT.

Materials and Methods

Cobalt II chloride (CoCl₂ · 6H₂O) p.a. from E. Merck, Darmstadt, Germany.

Vehicle: Water.

Experimental animals. Albino guinea pigs (Dunkin Hartley), average weight 300 g.

Open epicutaneous test (OET). The procedure of Klecak (5, 6) was followed.

(I) Irritation

Determination of minimal irritating and maximal non-irritating concentrations: on Day (D) 0 a single application of 0.025 ml of CoCl₂ in water was applied on a flank area 2 cm². Reactions were read 24 h later according to an all-or-none criterion. The protocol suggests

Table 1. Defining maximal non-irritating and minimal irritating concentrations of CoCl₂ after a single open application; 42 guinea pigs were tested; 24-h reading

CoCl ₂ conc. (%)	0.1	0.3	1.0	3.0	4.5	6.0	7.5
Pos. guinea pigs (%)	0	2	0	12	36	45	69

100, 30, 10, and 3% of the test material, but we found in pilot studies that the higher concentrations caused fatalities and therefore chose the range in Table 1.

(II) Induction

On D 1, application of 0.1 ml of the test material was performed on a flank area 8 cm². The applications were repeated daily for 3 weeks. The sites were left uncovered and were read daily prior to the next application. 6 guinea pigs per induction concentration, as well as a vehicle control group, were used – a total of 48.

(III) Challenge

Open. On D 21, the established maximal non-irritating concentrations of CoCl₂ were applied (0.025 ml on 2 cm²), as described above (see D 0), to see whether any shift in eliciting concentration had taken place.

Patch testing. The protocol (5, 6) recommends a 2nd open challenge at D 35, but we carried out regular patch testing. The guinea pigs were patch tested using Finn Chambers (Epitest Ltd Oy, Tuusula, Finland) with readings 24 and 48 h after removal of the patches. The CoCl₂ concentrations were 1.0, 0.3, and 0.1%, with a vehicle control (pet.).

Results

Irritation. The maximal non-irritating concentrations were found to be 1–3% (Table 1). 5 guinea pigs (12%) reacted to 3%, but according to the protocol (5), the minimal irritant concentration is the lowest causing mild erythema in at least 25%. However, we used 1% in subsequent studies.

Challenge. Open challenge on D 21 showed that 50–83% of the guinea pigs reacted to 1% (Table 2), i.e., a clear shift in eliciting concentration. There was no clear dose-response relationship for the induction concentrations used.

Patch testing on D 35 showed that 50–100% of the animals reacted to 1% and 0–67% to 0.3% CoCl₂. A dose-response relationship was seen for the induction concentrations used.

Discussion

Repeated open epicutaneous application of CoCl₂, according to the OET method, was sufficient to induce contact allergy (Tables 2, 3), there being no need for intradermal administration, Freund's complete adjuvant (FCA) or occlusion. A minimal sensitizing concentration could not be defined but was less than 0.1% CoCl₂ (Table 2). The minimal eliciting concentration was 0.1% on open testing (Table 2) as well as on patch testing (Table 3).

In previous studies (2–4) of CoCl₂ using ROATs, some FCA pre-treated control animals reacted late during the treatment period. Of 75 such control animals, 11 (8%) reacted within 7–10 days of treatment with 0.1% CoCl₂,

Table 2. Results of open testing on D 21 with the previously established maximal non-irritating test concentrations of CoCl₂ (Table 1); no. and % of reacting guinea pigs in relation to concentrations used for induction; 24-h reading

		CoCl ₂ concentration (%) used for induction														Contr. n=6 n
		0.1		0.3		1.0		3.0		4.5		6.0		7.5		
		n=6		n=6		n=6		n=6		n=6		n=6		n=6		
		n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	
CoCl ₂																
test conc. (%)	1.0	5	83	4	67	3	50	3	50	4	67	4	67	4	67	0
test conc. (%)	0.3	3	50	1	17	1	17	0	0	1	17	0	0	1	17	0
test conc. (%)	0.1	1	17	0	0	0	0	0	0	0	0	0	0	0	0	0

Table 3. Results of patch testing with CoCl₂ on D 35; no. and % of reacting guinea pigs in relation to concentrations used for induction; the tests were read 24 h after removal of the patches

		CoCl ₂ concentration (%) used for induction													
		0.1		0.3		1.0		3.0		4.5		6.0		7.5	
		<i>n</i> =6		<i>n</i> =6		<i>n</i> =6		<i>n</i> =6		<i>n</i> =6		<i>n</i> =6		<i>n</i> =6	
		<i>n</i>	(%)	<i>n</i>	(%)	<i>n</i>	(%)	<i>n</i>	(%)	<i>n</i>	(%)	<i>n</i>	(%)	<i>n</i>	(%)
CoCl ₂															
patch test	1.0	4	67	3	50	4	67	5	83	5	83	6	100	6	100
conc. (%)	0.3	0	0	2	33	2	33	2	33	3	50	1	17	4	67
	0.1	0	0	0	0	0	0	1	17	1	17	0	0	1	17
pet. contr.	0	0	0	0	0	0	0	0	0	1	17	0	0	0	0

and on subsequent patch testing, some were found to be allergic to CoCl_2 . These findings did not support the suspicion that the test preparation was irritant. On the other hand, CoCl_2 -sensitive guinea pigs reacted early (D 2–3) in ROATs (2). The treatment period in the OET was 21 days compared to 7–10 days in the ROATs (2–4), which might be significant. On the other hand, in the ROAT studies, the guinea pigs had received FCA.

In a previous study (2), it was suggested that reactivity to CoCl_2 in ROATs, seen in guinea pigs induced with NiSO_4 , was due to the repeated treatments rather than to cross-reactivity. The ease with which CoCl_2 sensitivity was induced in the present study supports this. In a study on persistence of patch test reactions, CoCl_2 was the only allergen with many *new* positives on retesting after 5 years (7). 3 possibilities for this were discussed, but there might be a 4th. Based on our findings, could it have been due to patch test sensitization?

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Allergic contact dermatitis from cetrimide and cetearyl alcohol in Burnol-plus[®] cream

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Key words: cetrimide; cetearyl alcohol; Burnol-plus[®] cream; allergic contact dermatitis; over-the-counter topical medicaments. © Munksgaard, 2000.

Case Report

A 53-year-old Chinese housewife presented with a 1-week history of a pruritic facial rash. She self-medicated with several over-the-counter topical medicaments, including Eurax[®] and Burnol-plus[®] creams. The rash spread to the trunk and extremities. She had a past history of eczema on her legs for 2 years. Clinically, there was marked erythema and swelling of both upper eyelids. An exudative erythematous oedematous plaque was noted on her right cheek, with extension to the neck. Erythematous patches were present on the trunk and extremities. There was complete resolution of the rash following cessation of self-medication and treatment with topical and systemic corticosteroids.

The patient was subsequently patch tested to our Na-

tional Skin Centre (NSC) standard series, including cetearyl alcohol 20% pet., Burnol-plus[®] cream as is, Eurax[®] cream as is and ingredients of Burnol-plus[®] cream listed on the container, including cetrimide. She gave a ++ reaction to Burnol-plus[®] cream as is, and + reactions to cetearyl alcohol 20% pet. and cetrimide 0.1% aq. (Table 1). On enquiry of the manufacturer, we found the base of the cream to contain cetearyl alcohol. We concluded that the patient had had allergic contact dermatitis from cetrimide and cetearyl alcohol in Burnol-plus[®] cream.

Discussion

Cetrimide is a mixture of quaternary ammonium compounds and is generally regarded as a rare and very weak sensitizer (1–3). It is better known as an irritant that can cause cutaneous necrosis and chemical-burn-like skin lesions (4–5).

Cetearyl alcohol is a mixture of long-chain fatty alcohols. It is commonly found as a stabilizer, emollient and base for pharmaceuticals and cosmetics. A high prevalence of contact allergy to it has been found in patients with leg ulcers (6–8), though true contact allergy is ap-

Table 1. Positive patch test results

Patch test	D3 reading
cetearyl alcohol 20% pet.	+
Burnol-plus [®] cream as is	++
cetrimide 0.1% aq.	+

parently rare (9). Positive patch test reactions to cetearyl alcohol should be interpreted with caution, as they may be irritant reactions that cannot be confirmed by repeated open application tests (10).

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2 cases of occupational dermatitis due to mercury vapor from a broken sphygmomanometer

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Key words: mercury exanthem; occupational contact dermatitis; sphygmomanometer; mercury vapor; contact allergy; health care workers; hospital staff; ophthalmologist; nurse. © Munksgaard, 2000.

2 types of dermatitis develop due to mercury allergy, one local and the other systemic (1). Mercury exanthem is a systemic type that follows inhalation of mercury vapor, many cases of which have been reported (2–34), most caused by broken thermometers, sometimes occupationally (27, 30).

Case Reports

Case no. 1:

A 26-year-old ophthalmologist used a broken sphygmomanometer to measure a patient's blood pressure on 19 September 1996. 2 days later, there was an itchy erythema on her thigh with high fever (39°C), followed by generalized exanthem. Moreover, she had miliary pustules on erythematous skin. Laboratory data were normal. Histological examination showed liquefaction and

perivascular lymphocytic infiltration. She was treated with a systemic corticosteroid, an antihistamine and a topical corticosteroid. Her skin lesions disappeared within a week, without pigmentation. On patch testing, she showed positive reactions to mercury and its compounds (Table 1).

Case no. 2:

A 26-year-old nurse, with previous allergy to egg and walnut, worked near a broken sphygmomanometer on 18 October 1997. That night, she had slight fever (37°C) and noticed itchy erythema on the backs of her knees and buttocks. She was taking no drugs nor using any externally. She showed strongly positive reactions to mercury and its compounds (Table 2). She was treated with a systemic corticosteroid, an antihistamine and a topical corticosteroid. Her skin lesions disappeared within a few days, without pigmentation.

We measured the release of mercury vapor from the broken sphygmomanometer to which patient no. 1 was exposed with a gas detector tube (length-of-stain type: Mercury vapor no. 40, Gastec Co. Ltd). A Tedlar bag (10 l polyvinyl fluoride film bag, GL Sciences Inc., Japan) was closed after placing the broken sphygmomanometer inside, then filled with 10 litres of air with activated charcoal. After 24 h at room temperature, the concentration of mercury vapor was 9.9 mg/m³ (aprox. 0.01 mg in 10 l).

Table 1. Patch test results (ICDRG reading at D4)

Test substances	Conc./veh.	Case no. 1	Case no. 2
ammoniated mercuric chloride	1% pet.	+	++
mercuric chloride	0.05% aq.	+	++
mercury	1% pet.	+	++
thimerosal	0.1% pet.	+	++
thimerosal	0.05% pet.	–	++

Table 2. Acute toxic symptoms caused by mercury vapor

Concentration of mercury vapor in the air (mg/mm ³)	Symptoms	Exposure time
>10	pneumonia, diarrhea, nephropathy	1–2 days
>1	diarrhea, proteinuria, hematuria, tremor, stomatitis	~1 month
>0.5	tremor, stomatitis, proteinuria, excitation	2–5 months
>0.2	tremor, proteinuria, subjective psychoneurosis	6 months–1 year
>0.1	subjective psychoneurosis, senilism	several years

Table 3. Japanese cases of mercury exanthem

	Summary of 57 cases	Case no. 1	Case no. 2
age (years)	3–73 (mean 27)	26	26
male:female	24:33	female	female
causative products	broken thermometer: 46 mercurial ointment: 5 broken fluorescent lamp: 1 dental treatment (amalgam): 2 vaccine: 2 patch test with mercuric tape: 1	broken sphygmomanometer	
past history of Mercurochrome dermatitis	yes: 28 no: 12 unknown: 17	unknown	unknown
duration from exposure to onset dermatological symptoms	7 h to several days widespread maculopapular	2 days widespread maculopapular fever (38°C–39°C)	1 day erythema on hip and back of knee slight fever (37°C)
systemic symptoms	temperature <37.5 fever up >38°C: 8 lymph node swelling: 1 general fatigue: some cases	lymph node swelling	
patch test result with mercuric chloride (D4)	46 cases positive	+	++

Discussion

We breathe its vapor when exposed to mercury at room temperature. Acute toxic symptoms (Table 2), or generalized mercury exanthem may develop. In the Japanese literature, 57 cases of mercury exanthem have been reported, 46 from broken thermometers (Table 3). Almost all cases are positive to mercuric chloride on patch testing. Mercurochrome may be the original source of sensitization (Table 3), Hernandez et al. (35) reporting immediate hypersensitivity. Osawa et al. (36) reported a correlation between gold and mercury sensitivity.

The concentration of mercury vapor from the broken sphygmomanometer in case no. 1 was found to reach 9.9 mg/m³ (about 0.01 mg/10 l) over 24 h. The permissible level of mercury vapor in the work place is 0.05 mg/m³ (37) and a concentration of 9.9 mg/m³ may cause acute toxic symptoms. No previous case of occupational mercury exanthem from a broken sphygmomanometer has been described. In Japan, mercury sphygmomanometers are used in 70–90% of hospitals and clinics. Rudzki et al. (38) reported that 5.4% of dentists, 7.2% of surgeons and 2.4% of other physicians showed positive patch tests to mercury compounds. Adachi et al. (39) reported that the positivity rate of ammoniated mercuric chloride was 7.3% in 1994. Thus, the risks of occupational mercury exanthem and mercury toxicity should be emphasized in hospital workers.

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Corticosteroid-delayed contact sensitivity and cross-reactions provoked by 20-mm patch test exposure

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Key words: psoriasis; contact urticaria; benzoic acid, corticosteroids; medicaments; budesonide; hydrocortisone-17-butyrate; triamcinolone acetonide; amcinonide; cross-sensitivity. © Munksgaard, 2000.

Case Report

A 39-year-old woman with psoriasis had had symptoms of urticaria for 2–3 weeks. Following the use of corticosteroid-containing topical medicaments, erythema, oedema and intense itching developed. The European standard series, our fragrance series (benzoic acid, cinnamal, vanilla, camphor and menthol) and the Epifarm steroid series (dexamethasone, prednisolone, amcinonide, budesonide, betamethasone-17-valerate, clobetasol-17-propionate, hydrocortisone-17-butyrate and triamcinolone acetonide) were applied as patch tests to the back for 20 min. After the 20-min application, at the site of the benzoic acid test, contact urticaria was manifest,

which persisted to 40 min. During further observation of the test reactions, a +++ reaction to budesonide was observed at D2 and D3. Also, at D2 and D3, hydrocortisone-17-butyrate and triamcinolone acetonide were +++, along with amcinonide (+++) at D3.

Discussion

The 1st case of corticosteroid contact allergy was reported by Burckhardt in 1959 (1), the 1990s seeing an increasing number of reports (3, 4, 6), frequently with patch test positivity to several preparations (2, 5, 7, 9), partly due to cross-reactivity (10).

In our patient, multiple reactions are explained both

by use of several medicaments (budesonide, triamcinolone and hydrocortisone), and by reported cross-reactions (amcinonide and triamcinolone acetonide in group B), plus hydrocortisone butyrate in group D. The unusual feature of this case was that multiple, partly cross-reactivity-based delayed reactions (amcinonide is not available in Hungary), following a 20-min exposure, developed without contact urticaria, in contrast to our former observations (8).

According to the history, for the urticarial symptoms of this patient, benzoic acid appeared to be the relevant allergen. The sensitization to corticosteroids may have resulted in the erythematous, oedematous, itching flare of symptoms in psoriasis and maybe in a Köbner effect.

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Exudative granulomatous reaction to hyaluronic acid (Hylaform®)

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Key words: hyaluronic acid; Hylaform®; wrinkles; allergy; medicaments; cosmetic surgery; plastic surgery; dermatological surgery. © Munksgaard, 2000.

Patient and Methods

An exudative reaction that increasingly turned granulomatous occurred in a 53-year-old woman 2 days after the injection of hyaluronic acid (Hylaform®) for perioral wrinkles. The peak of the eczematous reaction was reached after 4 to 6 days, and it healed after a further 4–5 days.

From the 3rd day on, papular skin changes, which had completely regressed after 6 weeks, could be felt. The patient had undergone the same treatment at a cosmetician's 18 months before, without complications.

Patch tests with the European standard series, ointment bases, and plastic-resin-adhesive series from Hermal, as well as with Hylaform®, were read at D1, D2 and D3. A scratch and intracutaneous test with Hylaform® was carried out with readings after 20 min, 6, 24, 48, 72 h, and 6 days. A biopsy was taken from the site of the intracutaneous test on the left volar forearm after 30 days. The ingredients of Hylaform® were unfortunately not made available to us by the manufacturer.

Results

On patch testing, no Type IV sensitization was provable. The intracutaneous test showed a crescendo reaction, be-

ginning after 24 h and increasing until the 6th day. From the 3rd day on, a granuloma, which was no longer detectable after 6 weeks, could be felt. Histological examination showed a foreign body granuloma with evidence of basophilic material similar to mucin, probably corresponding to Hylaform®.

Discussion

Hylaform® is a viscoelastic gel that is increasingly being used for patients who have become sensitive to bovine collagen or wish immediate treatment without prior skin testing (as is indicated with collagen).

After the injection of Hylaform®, a distinct exudative granulomatous reaction, which could be reproduced on intracutaneous testing and which was confirmed histologically, occurred in our patient, the 1st such report. Sensitization probably resulted from the same substance injected beneath the wrinkles 18 months earlier. Similar reactions during treatment with collagen (Zyderm®/Zyplast®) have been described (1, 2). In these cases, immunological processes were assumed, though no demonstrable allergic reaction could be found. Barr et al. (2) spoke rather of histological changes, as appear with granuloma annulare, necrobiosis lipoidica and rheumatic nodules. The histological findings were also simi-

lar to those resulting from insect bites. However, these authors did not entirely exclude an allergic component.

Local side-effects after collagen injections, such as erythema and eczema along the tracks caused by the injections, appeared in 1.3% of 7000 patients in a study by Castrow & Krull (3). In most cases, these disappeared within the first 4–6 months, some however remaining visible even after 1 year. Such side-effects during the treatment of wrinkles with hyaluronic acid have not been described before, though undesired concomitant reactions were observed after intra-articular injection for the treatment of osteoarthritis of the knee by Puttick et al. (4). Here, pain, erythema and swelling, which continued for 3 weeks, appeared within 24 h.

Whether immunological or allergic processes occur with injections of hyaluronic acid cannot be determined. The reproducibility of the reaction in the intracutaneous test points to an allergic reaction; the formation of granulomas and the histological appearance point more to an immunological pathogenesis. The complete regression within 6 weeks is remarkable, because this is a considerably shorter period of time than with collagen. Granulomatous reactions have also been increasingly observed by the university clinics in Frankfurt and Regensburg.

In summary, this case report indicates that a thorough explanation, including all side-effects, and an intracutaneous test with later readings, are recommendable before reinjection of hyaluronic acid in the treatment of wrinkles. It should be required that Hylaform® be injected only by doctors. It is essential to change the leaflet in the package to include this necessary information.

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A cluster of 6 cases of occupational allergic contact dermatitis from (meth)acrylates

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Key words: acrylates; (meth)acrylates; occupational; allergic contact dermatitis; material safety data sheets; cross-sensitivity; engineering. © Munksgaard, 2000.

Methacrylate (MA) monomers are transformed into tough polymeric resins by light, heat and oxygen, and utilized as coatings, mouldings and adhesives in fields as disparate as dentistry, cosmetics, printing, film developing, medical equipment and the car industry (1, 2). Al-

though all MAs, have the potential to sensitize occupationally, increased side-chain length up to C₁₂ may increase this potential (3).

Case Reports

6 men aged between 27 and 65 years of age were seen in our contact dermatitis clinic over 14 months. All were employed by the same engineering company assembling and testing power steering units for vehicles. They attended with recalcitrant dermatitis mainly of the hands and forearms symmetrically, that typically would resolve on holidays, or in other work areas. Their job was to test power steering assemblies for oil leaks in a pressurized test rig. Prior to such testing, a plug on the steering assembly casing had been bonded using a Loctite™ acrylate adhesive. Long-sleeved protective overalls were provided, but generally worn with the sleeve rolled part-way up each arm, and gloves, though available, were not routinely worn because of loss of manual dexterity and interference with work.

Patch testing was performed to the European standard series and an MA series using IQ Chambers™ (Chemotechnique, Malmö, Sweden). All readings were

Table 1. Positive results of patch tests with the European standard series and MA series in 6 patients sensitive to acrylic resins

Allergen	No. positive patch tests
mercapto mix	1
mercaptobenzothiazole	1
methyl methacrylate	3
2-hydroxyethyl methacrylate	4
2-hydroxypropyl methacrylate	4
ethyleneglycol dimethacrylate	4
triethyleneglycol dimethylacrylate	6
1,4 butanediol dimethacrylates	4
1,6 hexanediol diacrylate	1
tetrahydrofurfuryl methacrylate	3
tetraethyleneglycol dimethylacrylate	6
n, n-dimethylaminoethyl methacrylate	3
n-butyl methacrylate	1

made at D2 and D4 and graded according to the ICDRG criteria by the same observer (BNS). The results are presented in Table 1.

2 individuals reacted only to the ethylene glycol derivative MAs (triethyleneglycol dimethacrylates, tetraethyleneglycol dimethacrylates), the remaining 4 cases having positive reactions to between 7–10 of the 14 MAs tested.

Discussion

Previous papers have reported occupational sensitization to MA in the motor industry, including 4 gearbox testers, 3 from the same factory (4). The adhesive used in the factory where our patients worked was Loctite 542TM, which consists of 95% polyethylene glycol dimethacrylate by weight. According to the material safety data sheet (MSDS), the product does not contain any other MA. As discussed in previous papers (5), it is unclear whether the multiple patch test reactions represent cross-sensitivity or concomitant sensitization. If the MSDS is correct, cross sensitization is suggested. Animal studies show that ethylene glycol dimethacrylate has only a weak ability to induce cross-reactivity with other MAs (6); if this is true in humans, it favours traces of other MAs being present in LoctiteTM.

Our patients illustrate that those at risk of sensitization to MAs may not necessarily be those workers directly using them.

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Occupational allergic contact dermatitis from thiocolchicoside

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Key words: thiocolchicoside; CAS 602-41-5; Muscoril[®] cream; muscle relaxant; medicaments; contact allergy; occupational; physiotherapist; health care workers. © Munksgaard, 2000.

Thiocolchicoside (3,10-di(demethoxy)-3-glucopyranosyloxy-10-methylthiocolchicine) is a semi-synthetic derivative of colchicoside (1). Administered orally, parenterally or topically, the drug is a muscle relaxant, anti-inflammatory and analgesic, widely used in algo-rheumatic disorders. Although topical thiocolchicoside preparations are widely used, contact allergy seems rare (2, 3).

Case Report

A 47-year old physiotherapist was referred with a 1-month history of erythematous desquamative dermatitis on the hands and forearms, accompanied by pruritus and burning. She suspected topical thiocolchicoside (Muscoril[®] cream), handled in her work, as the cause. We advised her to stop all further contact with this cream and the dermatitis cleared, without any therapy, in about 2 weeks. She had no personal or family history of atopy.

She was subsequently patch tested with the European standard series, Muscoril[®] cream (as is) and thiocolchicoside 0.25%, 0.5%, 1%, 3% and 5% pet. In addition, the other components of Muscoril[®] cream, and several other products that she used daily in her work, were

tested. Positive reactions were seen only to Muscoril[®] cream and to thiocolchicoside (Table 1).

Concurrently with her positive patch tests to thiocolchicoside, she had a flare-up of dermatitis on the hands and forearms. 11 controls tested with 1% thiocolchicoside were all negative. The patient has continued to work with no further problems since avoiding this particular topical preparation.

Table 1. Patch test results

Allergen	(%)	D2	D3	D5	D7
European standard series		–	–	–	–
Muscoril [®] cream	as is	–	?+	+	+
thiocolchicoside	0.25% pet.	–	–	+	+
thiocolchicoside	0.50% pet.	?+	+	+	+
thiocolchicoside	1% pet.	+	++	+	+
thiocolchicoside	2% pet.	++	++	++	+
thiocolchicoside	5% pet.	++	++	++	+
other constituents of Muscoril [®] cream		–	–	–	–

Discussion

To our knowledge, this is the 1st case report of occupational contact dermatitis from thiocolchicoside. Only 2 documented cases of photocontact (2) and contact (3) allergy to thiocolchicoside appear to have been reported, both non-occupational.

In their case, Foti et al. (3) patch tested with 0.5%, 1%, 3% and 5% pet. thiocolchicoside, which was positive only at 1% and above; the authors recommended 2% pet. for future patch testing. On the basis of our experience, we believe that 1% pet. may be adequate for patch testing with thiocolchicoside.

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Contact allergy to fragrance mix – a 10-year study

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Key words: patch testing; fragrance mix; fragrance mix constituents; fragrance series; contact allergy. © Munksgaard, 2000.

The mix of 8 fragrances at 8% pet., known as the fragrance mix (FM) in the standard series of allergens, is considered a good marker of fragrance allergy (1–3).

Patients, Methods and Results

In a 10-year period (July 1989 to June 1999), out of 2600 consecutive patients (1741 female, 859 male) patch-tested with the Portuguese standard series, 283 (10.9%) had a positive reaction to the FM (185 female and 98 male, with a mean age of 43.6 years). Frequency was similar for females (10.6%) and males (11.4%), but males were older (mean age of 41.9 and 47.1 years, respectively). The % of atopic patients was similar to that of the whole population (18.0% versus 22.0%) though 2× as many patients (30) had a leg ulcer (10.6% versus 5.1%).

93 patients (32.9%) reacted only to the FM; 190 had other positive reactions, mainly to Myroxylon Pereirae (120–42.4%), nickel (60–21.2%), lanolin (42–14.8%), thimerosal (40–14.1%) and colophonium (30–10.6%); Myroxylon Pereirae, lanolin and colophonium were over-represented compared to the whole population tested.

Cosmetics were responsible for FM sensitivity in 121 patients (42.7%). In 62 patients (21.9%), FM reactivity was attributed to topical medicaments and 42 patients were allergic to plants (14.8%). An occupational cause (cutting fluids) was suspected in 1 patient. No relevance was found in 57 patients (20.1%).

Of the 283 FM-reactive patients, 226 patients (142 female and 84 male) were tested separately with the 8 constituents at 1% pet. and sorbitan sesquiolate at 20% pet., and 67 were also tested with other fragrances and flavours available from Chemotechnique or Hermal. Of

these 226, 133 (58.9%) reacted to components of the mix (60 reacted to 1 and 73 to 2 or more fragrances), 13 (5.7%) also reacted to sorbitan sesquiolate and 7 (3.1%) reacted only to fragrances not included in the FM. Of all the fragrances tested, positive reactions occurred most frequently to oak moss, isoeugenol, eugenol, cinnamal, ylang-ylang oil, clove oil, cananga oil and geraniol (Table 1). Oak moss and cinnamal were more frequent

Table 1. Reactivity to the main fragrances in FM-reactive patients

Allergen	Patients tested no.	Positive reactions no.	Positive reactions (%)
oak moss 1%	226	50	22.1
isoeugenol 1%	226	45	19.9
eugenol 1%	226	33	14.6
cinnamal 1%	226	30	13.3
geraniol 1%	226	19	8.4
cinnamic alcohol 1%	226	18	7.9
hydroxycitronellal 1%	226	15	6.6
α -amyl-cinnamal 1%	226	10	4.4
sorbitan sesquiolate 20%	226	13	5.7
ylang-ylang oil 2%	67	9	13.4
clove oil 2%	67	9	13.4
cananga oil 2%	67	7	10.4
geranium oil Bourbon 2%	67	5	7.5
sandalwood oil 2%	67	4	6.6
lavender absolute 2%	67	4	6.6
neroli oil 2%	67	4	6.6
rose Bulgarian oil 2%	67	3	4.5
orange oil 2%	67	3	4.5
lemon oil 2%	67	3	4.5

in males and reactivity to sorbitan sesquiolate occurred mainly in patients allergic to topical medicaments (11.2%).

Discussion

Among our patients, reactivity to the FM is high (10.9%), though within the range found in most European centres. Similarly to other series, less than 60% of our patients react to a component of the FM (1, 3). Oak moss was the main allergen responsible (22.1%), though less frequent than the 45% detected in our previous study (4). 3.1% of the patients reacted only to fragrances not included in the FM, namely ylang-ylang oil, clove oil and cananga oil, which, nevertheless, contain substances in common with the FM constituents (1, 3). Although it may seem encouraging to know that these patients also react to the current FM, this is not the rule in other studies (3, 5), and hence it may be worth devel-

oping newer mixes with these fragrances, as is currently being studied (5).

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Screening for p-phenylenediamine (PPD) in hair-care products by thin-layer chromatography (TLC)

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p-phenylenediamine (PPD), a colorless compound, is a known skin sensitizer (1). Most cases of contact allergy to PPD occur from hair dyes, either in the user or the hairdresser. Besides allergic contact dermatitis, other reactions, such as contact urticaria (2, 3) and anaphylaxis (4, 5), have been described.

The presence of PPD in hair dye is not always documented, especially in hair dye products from developing countries. The objective of this study was to determine the presence of PPD in unlabelled hair dyes in Singapore that are sold over the counter.

Materials and Methods

All available over-the-counter hair dyes were purchased from medicinal shops and pharmacies in Singapore city. In all, 16 hair dyes were purchased (Table 1). The presence of PPD was qualitatively detected using thin-layer chromatography (TLC), in the following manner.

Sample and standard preparation

Samples – hair dyes were dissolved in ethanol and filtered prior to TLC.

Standard – 0.1 g of PPD was dissolved in 3 ml of ethanol. The standard was obtained from Sigma-Aldrich Inc. and its purity of PPD was >98%.

Sample analysis

Using capillary tubes, a small amount of the sample was placed on a pre-coated silica gel F254 plate and run using a solvent containing methyl alcohol and ammonia

Table 1. Presence of PPD in hair dye products

Products	Form	Presence of p-phenylenediamine (PPD)			
		(i)	+ve	(ii)	–ve
* Gui Hua	powder	(i)	+ve		
Henara	powder		–ve		
Henna Plus	powder		–ve		
Henna Plus	mouse		–ve		
* Henna Plus	cream	(i)	–ve	(ii)	–ve
Belmac	cream		–ve		
Betz	cream		–ve		
Bigen	cream		–ve		
Gui Hua	cream		–ve		
Ultronic	cream		–ve		
Wu Fu Ru	cream		–ve		
* Yee Lok	cream	(i)	–ve	(ii)	–ve
Zymay	cream		–ve		
Fa Zhi Bao	liquid		–ve		
Ford Excel Color	liquid		–ve		
Vitrie	gel		–ve		

* These hair dyes contained 2 parts, (i) and (ii), each of which was analysed separately.

(100:1.5). The spray reagent was 0.5 g of p-dimethylaminobenzaldehyde in 50 ml of a mixture containing 60 volumes of ethanol and 40 volumes of sulfuric acid.

Results

The results of the study are presented in Table 1. TLC showed the presence of PPD in 1 of the dyes that had 2 parts – Gui Hua powder.

Discussion

Many types of hair dye do not contain PPD. In general, PPD-containing dyes come in 2 bottles to be mixed (6): the first contains PPD and couplers (additives) in a soap solution; the other contains the developer, usually an oxidizer such as hydrogen or urea peroxide. The peroxide activates the PPD, which binds with the coupler to produce the desired color. The allergenic potential of permanent hair dyes lies with the PPD or its oxidation products alone, and not with the additives. This also applied to related dyeing agents such as *p*-toluenediamine and methyl-*o*-aminophenol.

By Singapore law, hair dyes that contain PPD can be

dispensed only by a registered pharmacist. The hair dye must also carry the label that it contains PPD and that it may cause skin allergy. This study demonstrates that, in spite of such legislation, unlabelled PPD-containing hair dye can still be bought over the counter, which can be a cause of skin reactions in sensitized persons.

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Contact dermatitis and adverse oral mucous membrane reactions related to the use of dental prostheses

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Key words: dental patients; dental prostheses; allergic contact stomatitis; allergic contact cheilitis; lichen planus; beryllium; rhodium; vanadium; (meth)acrylates; gold. © Munksgaard, 2000.

Since our previous publication (1), we have patch tested 520 patients, with dental prostheses, using an expanded series containing 33 metals (Table 1). No dental staff were included in this study, nor in the former study (1).

Patients and Methods

520 patients were patch tested with the following allergens: (a) TRUE Test standard series; (b) Chemotechnique dental screening series; (c) Special metal series (Table 1).

Results

120 of the patients studied were male and 418 female. 231 patients were negative (62 male and 169 female) and 289 patients gave 1 or more positives (41 male and 248 female). Symptoms are shown in Table 2 and signs in Table 3. Table 4 shows the most frequent allergens.

Discussion

Our results agree with recent publications (2, 3). Our special metal series includes (4) gallium (5), zirconium

and yttrium (6, 7), iridium (8) and indium (9). Minagi et al. (10) have published a new method for identifying such metals in dental prostheses in situ. Titanium is regarded as the metal of the future (11). With regard to resins, the following were considered useful additions to the series: 4-methacryloyloxyethyl trimellitic anhydride (4-META) (12); the PMDM system (13) and the new HEMA additive based on PVA and acryloyl chloride (14); the antibacterial monomer methacryloyl dodecylpyridinium bromide (MDPD) (15); and 'compomers' (16) containing barium-aluminium fluorosilicate, carbonic acid dimethacrylate, ytterbium trifluoride and strontium difluoride. In the future, 'ormocers' (organically modified ceramics), which contain new multifunctional urethane and thioether oligo(meth)acrylate alkoxsilanes as gel/sol precursors, will be developed as organic/inorganic copolymer composites in dental restorative materials (17).

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Table 1. Special metal series

Allergen	% pet.
gold sodium thiosulfate	0.5%
palladium chloride	1.5%
zinc chloride	2%
ammonium heptamolybdate	1%
tin chloride	1%
gallium chloride	5%
indium chloride	5%
chromium trioxide	0.5%
ferric chloride	2%
beryllium chloride	1%
tantalum chloride	1%
iridium chloride	1%
silicon tetrachloride	2%
copper sulphate	1%
rhodium chloride	2%
metallic mercury	0.5%
platinum chloride	0.5%
silver nitrate	0.5%
tungsten metal	5%
tungsten carbide	2%
cesium chloride	2%
magnesium chloride	2%
manganese chloride	2%
titanium oxide	5%
cadmium chloride	1%
columbium chloride	2%
vanadium chloride	1%
antimony chloride	1%
strontium chloride	2%
tellurium dioxide	2%
ytterbium sulfate	2%
yttrium oxide	2%
ruthenium oxide	2%

Table 3. Signs in 520 patients with dental prostheses

Signs	Male	Female	Total
erythema	48	114	142
ulcers (aphthous)	24	71	95
lichen planus	18	96	114
papules	18	33	51
cheilitis	4	34	38
erythema migrans linguae	6	18	24
gingivitis	9	22	31
glossitis	12	18	30
angular cheilitis	4	18	22
total	143	424	576

Table 4. Most frequent allergens^{a)} in 520 patients with dental prostheses: relevance current (C), past (P) or unknown (U)

Allergens	No. of positives	Male			Female		
		C	P	U	C	P	U
nickel	163	3	0	0	60	100	0
cobalt	67	3	0	0	32	30	2
palladium	63	3	0	0	32	24	4
beryllium	22	8	0	2	8	0	4
rhodium	17	3	0	0	8	0	6
vanadium	17	3	0	0	10	0	4
chromium	12	0	5	0	2	2	3
platinum	11	0	0	0	4	2	5
columbium	9	0	0	0	0	0	9
thimerosal	8	0	0	2	5	1	0
PPD	8	0	0	0	0	8	0
gold	7	0	0	2	3	1	1
formaldehyde	7	0	0	0	0	5	2
caine mix	7	0	1	1	0	3	2
PPD mix	7	0	1	0	0	2	4
colophonium	7	0	0	1	3	1	2
gallium	6	0	0	0	2	0	4
cadmium	6	0	0	1	3	0	2
thiuram mix	5	0	0	0	2	3	0
mercury metal	5	0	0	0	3	2	0
Fragrance mix	5	0	0	0	2	1	2
carba mix	5	0	0	0	2	3	0
methyl methacrylate	4	0	0	0	2	0	2
antimony	4	0	0	0	0	0	4
eugenol	4	0	0	0	3	0	1
zinc	4	0	0	0	3	0	1
ethyleneglycol dimethacrylate	3	0	0	0	3	0	0
triethyleneglycol dimethacrylate	3	0	0	0	3	0	0
2-hydroxyethyl methacrylate	3	0	0	0	3	0	0
tetrahydrofurfuryl methacrylate	3	0	0	0	3	0	0
Myroxydon Pereirae	3	0	0	0	2	1	0
N,N-dimethylaminoethyl methacrylate	3	0	0	0	3	0	0
epoxy resin	3	1	0	0	2	0	0
p-tert.-butylphenol-formaldehyde resin	3	0	0	0	2	1	0
copper	3	0	0	0	0	1	2
neomycin	2	0	0	0	0	2	0
methylhydroquinone	2	0	0	0	2	0	0

^{a)} Single positive reactions, of past or unknown relevance, were also found to iridium, aluminium, strontium, manganese, magnesium, silver and tin in the special metals series.

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