

scribed in 13% of patients (5) using it as a depigmenting cream. Patch testing in our patient confirms that it is also a potential sensitizer when used to treat patients with vitiligo.

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Antimicrobials: preservatives, antiseptics and disinfectants

A. GOOSSENS, L. CLAES, J. DRIEGHE AND E. PUT

Department of Dermatology, University Hospital, Kapucijnenvoer 33, 3000 Leuven, Belgium

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Antimicrobials are widely used in topical medicaments, cosmetics and many household, industrial (biocides), and other products, such as paper, napkins, and shoes (1, 2).

Materials and Methods

Between January 1985 and December 1997, 8521 patients were investigated in our contact allergy clinic. Patch test allergens were supplied by Trolab (Hermal), Chemotechnique Diagnostics, or prepared in-house. The patch test materials were van der Bend[®] square test chambers on Mepore[®] acrylic tape, covered with Mefix[®]. Results were read 2, 3, or, usually, 4 days after application, in accordance with IDCRG guidelines.

Results

4567 patients (54%) had at least 1 positive reaction to the allergens tested. Tables 1, 2 give the antimicrobial allergens detected.

Discussion

The methyl(chloro)isothiazolinone mixture was the most common antimicrobial allergen. In a recent study (3), its frequency had almost halved in 1991–1996 relative to 1985–1990 (4), and reactions to formaldehyde and its releasers, such as quaternium-15, diazolidinyl urea, imidazolidinyl urea, DMDM hydantoin, and bromonitropropanediol had almost doubled. The newer preservative mixture containing methyldibromoglutaronitrile and phenoxyethanol (also called Euxyl[®] K400), which we have been routinely testing since April 1992, has now become increasingly important, the principal culprit being methyldibromoglutaronitrile (dibromodicyanobutane) (5). The spectrum of preservatives found to be allergens may differ from country to country (6, 7). Other

cosmetic preservatives identified were chloroacetamide, triclosan (mainly in deodorants), bradophen (in an “udder cream” used to treat hand dermatitis), captan (in hairdressing products), farnesol (in antiperspirants, cross-reacting with balsam of Peru), and bromonitrodioxane.

The parabens and thimerosal, most of the positive re-

Table 1. The most frequent antimicrobial allergens between 1985 and 1997 (%s are given for standard series substances) ($n=8521$)

Rank	Allergen	Number
1	methyl(chloro)isothiazolinone	143 (1.5%)*
2	thimerosal	136**
3	merbromine	94**
4	iodine	89
5	cetrimide	88
6	formaldehyde	80 (0.9%)
7	parabens	71 (0.8%)
8	chloramine	43
9	quaternium-15	32
10	nitrofurazone	29
11	quinoline mix	28 (0.3%)
12	benzyl alcohol	25***
	benzoic acid	25
	thiocyanomethylbenzothiazole	25
	chlorhexidine	25
13	glutaraldehyde	22
	methyldibromoglutaronitrile + phenoxyethanol	22
14	chloroacetamide	20
	diazolidinyl urea	20

* Methyl chloroisothiazolinone was not introduced into the standard series until March 1987.

** Thimerosal and merbromine are organic mercurials, so sensitivity to them is usually associated with reactions to other mercurials. In thimerosal, the thiosalicylic acid part may also be responsible for the reaction.

*** Benzyl alcohol is also a perfume component.

Table 2. The least frequent antimicrobial allergens (n=8521)

Rank	Allergen	Number
15	imidazolidinyl urea	18
16	alcohol	17
	hexamidine	17
17	chlorocresol	15
18	chloroxylenol	12
19	sorbic acid	11
	isopropyl alcohol	11
20	triclosan	9
21	phenoxyethanol	8
22	DMDM hydantoin	4
23	Bioban CS 1246*	3
	Bioban P 1487**	3
	Bioban CS 1135***	3
	bromonitropropanediol	3
	bradophen	3
24	benzalkonium chloride	2
	benzotriazole	2
	captan	2
	dodacin	2
	farnesol	2
	glyoxal	2
	octylisothiazolinone	2
	sodium hypochlorite	2
25	bromonitrodioxane	1
	chlorobutol	1
	dequalinium chloride	1
	methylolchloracetamide	1
	miristalkoniumchloride	1

* Bioban CS 1246=1-aza-3,7-dioxa-5-ethylbicyclo (3,3,0) octane.

** Bioban P 1487=4-(2-nitrobutyl) morpholine (70%) + 4,4-(2-ethyl-2-nitromethylene) dimorpholine.

*** Bioban CS 1135=3,4-dimethyloxazolidine (74.7%) + 3,4,4-trimethyloxazolidine.

actions to the 2nd of which are irrelevant (8), benzylalcohol (also used in perfumes), benzoic and sorbic acid, chlorocresol, benzalkonium chloride, and chlorbutol (both often used in eyedrops) are mainly medicament allergens.

The antiseptics found to be allergens were thimerosal and other mercurials (e.g., merbromine), cetrime, chloramine, nitrofurazone, quinoline derivatives (clioquinol, chlorquinaldol), chlorhexidine, alcohol, hexamidine, chloroxylenol, isopropyl alcohol, and sodium hypochlorite. Some of these may also produce contact urticaria, such as chloramine (9) and chlorhexidine (10).

Some of these antiseptics are also disinfectants. Formaldehyde, together with glyoxal and particularly glutaraldehyde, causes occupational contact dermatitis (also

airborne) in health care personnel. Dodacin (dodecylid-(aminoethyl)glycine) is mainly used for surface disinfection and was found to be the cause of allergic contact dermatitis in a swimming teacher.

The antimicrobial allergens, often called biocides, found in industrial products, such as soluble oils, water-based paints and glues, are formaldehyde, isothiazolinone derivatives, benzotriazole, chloroacetamide, and methylolchloroacetamide. The Biobans® were found to be specific causes of occupational dermatitis due to metalworking fluids, while formaldehyde is used more often in household products (11).

Thiocyanomethylbenzothiazole is used to preserve leather. Reactions to it were found in patients with shoe dermatitis. In all cases except 6, cross-sensitivity was found with other mercaptobenzothiazoles. Thus, it is difficult to determine whether it sensitizes primarily as a preservative agent or as a rubber additive in glues or rubber materials for shoes.

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