Acta Dermatovenerol Croat 2004;12(4):261-267 CLINICAL ARTICLE

Retrospective Survey of Patch Testing at Department of Dermatology and Venerology, Zagreb University Hospital Center in Zagreb, Croatia

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Received: 16.07.2004.
Accepted: 08.09.2004.

SUMMARY Epicutaneous (patch) test is a standard test to confirm contact allergy. During a six-year period (1998-2003), contact allergic dermatitis was diagnosed in 4132 (65%) of 6341 patients using standard patch test with a Croatian series of allergens according to the International Contact Dermatitis Research Group (ICDRG). The most common clinical diagnoses related to contact allergy (male; female) were contact allergic dermatitis (65.4%; 72.2%); atopic dermatitis (15.9%; 11.7%); contact irritant dermatitis (7.0%; 6.6%) and nummular eczematoid dermatitis (4.2%; 2.4%). According to occupation, positive patch test reaction was most commonly observed in workers, whereas 65% of patients showed positive reactions to one or more substances. There was an increased frequency of positive patch test reactions to potassium dichromate, nickel sulfate, thimerosal and neomycine sulfate, along with a significant decrease in the frequency of positive patch test reactions to cobalt chloride, carba mix, wood tars, detergents, parabens mixture, urushiol and rubber mixture. We strongly recommend keeping up-to-date with the epidemiology of contact allergy in Croatia.

KEY WORDS contact sensitivity; epidemiology; patch testing

INTRODUCTION

Patch test (epicutaneous) is a gold standard for the diagnosis of allergic contact dermatitis. The diagnosis is not usually apparent from history or physical examination, and without patch testing it is impossible to delineate the underlying allergen (1). An early diagnosis has been reported to improve response to treatment (2,3). Several studies have assessed the reproducibility of different patch test systems with different results (4-12). The most prevalent allergens showed great variability from study to study (4,13). We embarked upon this study to shed more light upon the epidemiology on contact allergy in Croatia. This study of contact allergy was so designed as to reassess the reproducibility of patch testing in concordance with clinical diagnoses and physical examination. In our previous studies we have depicted nickel and neomycin as frequent contact allergens (4,12). We recommend

keeping up-to-date with the epidemiology of delayed hypersensitivity.

PATIENTS AND METHODS

The study was carried out at Allergy Clinic, Department of Dermatology and Venerology, Zagreb University Hospital Center, Zagreb, Croatia. We reviewed medical records of 4132 patients with positive results of patch testing during the period from 1998 to 2003. There were 2940 (71.2%) female and 1192 (28.8%) male patients, median age 40 years, with different clinical diagnoses (male; female): contact allergic dermatitis (65.4%; 72.2%); atopic dermatitis (15.9%; 11.7%); contact irritant dermatitis (7.0%; 6.6%); nummular eczematoid dermatitis (4.2%; 2.4%); psoriasis vulgaris (2.9%; 0.6%); seborrheic dermatitis (0.9%; 1.1%); stomatitis (0.1%; 0.6%); pruritus simplex (0.9%; 0.6%); vasculitis (0.4; 0.4%); other inflammatory dermatoses (0.3%; 0.7%), and other (1.8%; 3.1%) (Table 1). Details on age, sex, presenting complaint, history of allergy, clinical diagnoses and occupational history are presented in Table 2. There were 645 (15.6%) students, 1342 (32.5%) workers, 325 (7.9%) medical and allied professions, 892 (21.6%) office workers, 233 (5.6%) housewives, 505 (12.2%) pensioners and 190 (4.6%) others (Table 2). We included patients suspected to have allergic contact dermatitis based on clinical grounds and who had undergone patch testing with a Croatian standard patch test series of allergens (Table 3). We excluded patients who received topical or systemic steroids, immunosuppressive drugs or those suffering from chronic illnesses. The standard patch test battery allergens were tested on the upper back. Using a standard technique with Beiersdorf scanpor tape according to the International Contact Dermatitis Research Group (ICDRG), the test was read at 48 and 72 hours (14,15). Test results were interpreted using the fol-

Table 2. Subjects with positive patch test reaction according to occupation

Year	1998 - 2003			
Sex	Male		Female	
N	1192		2940	
Occupation	n	%	n	%
Students	273	22.90	372	12.65
Workers	249	20.89	1093	37.18
Medical and related professions	71	5.96	254	8.64
Office workers	225	18.88	667	22.69
Housewives	0	0.00	233	7.93
Pensioners	296	24.83	209	7.11
Others	78	6.54	112	3.81
Total	1192	100.00	2940	100.00

Table 1. Clinical diagnoses in relation to positive patch test reaction 1998-2003*

Year	1998				1999				2000				2001				2002				2003				TOTAL			
Sex	M		F		M		F		M		F		M		F		M		F		M		F		M		F	
	234		602		235		498		176		463		194		542		181		422		172		413		1192		2940	
Diagnosis (N)	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	no	%	no	%	no	%	no	%	no	%
CAD	135	57.7	445	73.9	145	61.7	349	70.1	116	65.9	326	70.4	126	64.9	379	69.9	130	71.8	317	75.1	128	74.4	308	74.6	780	65.4	2124	72.2
CD	19	8.1	42	7.0	18	7.7	36	7.2	14	8.0	28	6.0	12	6.2	35	6.5	7	3.9	25	5.9	13	7.6	27	6.5	83	7.0	193	6.6
AD	48	20.5	64	10.6	38	16.2	65	13.1	29	16.5	57	12.3	36	18.6	82	15.1	24	13.3	39	9.2	15	8.7	37	9.0	190	15.9	344	11.7
DEN	7	3.0	14	2.3	8	3.4	9	1.8	6	3.4	9	1.9	9	4.6	16	3.0	11	6.1	14	3.3	9	5.2	10	2.4	50	4.2	72	2.4
Psoriasis vulgaris	12	5.1	4	0.7	13	5.5	5	1.0	5	2.8	5	1.1	2	1.0	3	0.6	0	0.0	0	0.0	3	1.7	1	0.2	35	2.9	18	0.6
Seborrheic dermatitis	1	0.4	5	0.8	1	0.4	7	1.4	3	1.7	7	1.5	2	1.0	0	0.0	3	1.7	8	1.9	1	0.6	4	1.0	11	0.9	31	1.1
Stomatitis	0	0.0	2	0.3	0	0.0	3	0.6	0	0.0	4	0.9	0	0.0	2	0.4	1	0.6	2	0.5	0	0.0	6	1.5	1	0.1	19	0.6
Pruritus simplex	5	2.1	4	0.7	5	2.1	1	0.2	0	0.0	4	0.9	1	0.5	3	0.6	0	0.0	1	0.2	0	0.0	4	1.0	11	0.9	17	0.6
Vasculitis	1	0.4	3	0.5	2	0.9	5	1.0	1	0.6	1	0.2	0	0.0	2	0.4	0	0.0	0	0.0	1	0.6	0	0.0	5	0.4	11	0.4
Other inflammatory dermatoses	1	0.4	8	1.3	1	0.4	9	1.8	0	0.0	1	0.2	2	1.0	1	0.2	0	0.0	0	0.0	0	0.0	1	0.2	4	0.3	20	0.7
Other	5	2.1	11	1.8	4	1.7	9	1.8	2	1.1	21	4.5	4	2.1	19	3.5	5	2.8	16	3.8	2	1.2	15	3.6	22	1.8	91	3.1

*Abbreviations: M=male; F=female; CAD=contact allergic dermatitis; CD=contact irritant dermatitis; AD=atopic dermatitis; DEN=dermatitis eczematoides nummularis

Table 3. Croatian standard series of contact allergens

Test substance	Concentration (%)	Vehicle
Potassium dichromate	0.25	petrolatum
Cobalt chloride	1.0	petrolatum
Nickel sulfate	2.5	petrolatum
Formaldehyde	1.0	water
p-Phenylenediamine	1.0	petrolatum
Balsam of Peru	25.0	petrolatum
Epoxy resin	1.0	petrolatum
Colophony	20.0	petrolatum
White mercury precipitate	10.0	petrolatum
Benzocaine (Anesthesin)	5.0	petrolatum
Carba mix	3.0	petrolatum
Mercapto mix	2.0	petrolatum
Rubber mixture (PPD mix)	0.6	petrolatum
Fragrance mix	8.0	petrolatum
Thiuram mix	1.0	petrolatum
Wood tars	12.0	petrolatum
Paraben mixture	15.0	petrolatum
Neomycin sulfate	20.0	petrolatum
Quaternium 15	2.0	petrolatum
Thimerosal	0.1	petrolatum
Detergents	2.0	water

lowing scale: negative reaction (0); macular erythema (?); erythema/infiltration and possibly papules (1+); erythematous papules and/or vesicles (2+); spreading blisters and/or crust with ulceration (3+); and irritant reaction (IR), whereby 1+, 2+ and 3+ were considered a positive allergic reaction (14).

RESULTS

During the six-year period, contact allergic reactions were recorded in 4132 (2940 female and 1192 male) of 6341 patients. Analysis of contact hypersensitivity in patients according to site of skin lesions revealed hands and forearms to be the most commonly affected areas, followed by the face and neck, and to a much lesser extent other parts of the body. The patients with positive patch test reactions to the Croatian standard series of allergens are presented in Table 4 and Figure 1. The most frequent allergens were nickel sulfate, potassium dichromate, neomycin sulfate, cobalt chloride, carba mix and wood tars. In 2003, the most common allergens were nickel sulfate (43.4%), cobalt chloride (21.7 %), potassium dichromate (19.3%), thimerosal (18.8%), and neomycin sulfate (16.2%). During the 6-year period of observation, there was an increased frequency of positive reactions to thimerosal (from 0.0% in 1998 to 18.8% in 2003) and neomycin sulfate (from 14.6% to 16.2%), and a steadily high positivity to potassium dichromate (from 16.5% to 19.3%) and nickel sulfate (from 35.4% to 43.4%) (Table 4). A significant decrease was observed in the frequency of positive reactions to cobalt chloride (from 33.1% to 21.7%), carba mix (from 35.2% to 6.3%), wood tars (from 15.6% to 7.9%), rubber mixture (from 7.7% to 3.8%), detergents (from 40.8% to 7.2%), para(*p*-)phenylenediamine (from 6.5% to 3.9%), parabens (from 5.0% to 2.1%), balsam of Peru (from 10.2% to 9.1%) and colophony (from 2.8 % to 1.5 %). Sixty-five percent of the patients showed positive reactions to one or more chemicals on patch testing, with three allergens *per* patient on an average. The three most common allergens were carba mix, cobalt chloride and potassium dichromate in male, and nickel sulfate, cobalt chloride and carba mix in female patients. Statistical analysis of three allergens showing a rising frequency during the 6-year period yielded the following values: potassium dichromate ^{2}=4.92, p=0.418; nickel sulfate ^{2}=16.88, p=0.0047; and thimerosal ^{2}=46.98, p=0.0001. A statistically significant frequency increase was recorded for nickel sulfate and thimerosal. On the other hand, a statistically significant decreasing trend was observed for the frequency of cobalt chloride (^{2}=36.87, p=0.0001), carba mix (^{2}=546.44, p=0.0001) and wood tars (^{2}=42.77, p=0.0001).

DISCUSSION

In contrast to the study by Bourke *et al.* (6), our results confirmed patch test reproducibility. We found no discordance in positive patch tests according to age, sex, history of allergy and presence of multiple allergies. The prevalence of positive patch test results (65%) was similar to the finding reported by the North American Contact Dermatitis Group (NACDG) (66.5%) (16). The reason for the lower rate in our series is uncertain. Many other studies (14,17) have described rates of positive patch testing similar to our and lower than that of NACDG. Our finding also underscores the impor-

Table 4. Results of positive patch testing in 4132 patients 1998-2003

Year	1998		1999		2000		2001		2002		2003		Total	
Positive subjects (N)	836		733		639		736		603		585		4132	
Allergen	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Potassium dichromate	138	16.5	146	19.9	106	16.6	130	17.7	103	17.1	113	19.3	736	17.8
Cobalt chloride	277	33.1	267	36.4	200	31.3	243	33.0	203	33.7	127	21.7	1317	31.9
Nickel sulfate	296	35.4	275	37.5	251	39.3	310	42.1	263	43.6	254	43.4	1649	39.9
Formaldehyde	28	3.3	10	1.4	20	3.1	13	1.8	7	1.2	13	2.2	91	2.2
p-Phenylenediamine	54	6.5	62	8.5	15	2.3	17	2.3	19	3.2	23	3.9	190	4.6
Balsam of Peru	85	10.2	99	13.5	71	11.1	78	10.6	45	7.5	53	9.1	431	10.4
Epoxy resin	39	4.7	37	5.0	13	2.0	19	2.6	14	2.3	21	3.6	143	3.5
Colophony	23	2.8	15	2.0	11	1.7	9	1.2	12	2.0	9	1.5	79	1.9
White mercury precipitate	82	9.8	104	14.2	68	10.6	78	10.6	49	8.1	62	10.6	443	10.7
Benzocaine (Anesthesin)	42	5.0	49	6.7	17	2.7	24	3.3	17	2.8	29	5.0	178	4.3
Carba mix	294	35.2	256	34.9	207	32.4	30	4.1	27	4.5	37	6.3	851	20.6
Mercapto mix	23	2.8	21	2.9	17	2.7	13	1.8	5	0.8	13	2.2	92	2.2
Rubber mixture (PPD mix)	64	7.7	55	7.5	31	4.9	43	5.8	19	3.2	22	3.8	234	5.7
Fragrance mix	182	21.8	149	20.3	102	16.0	143	19.4	96	15.9	117	20.0	789	19.1
Thiuram mix	47	5.6	43	5.9	24	3.8	21	2.9	31	5.1	24	4.1	190	4.6
Wood tars	130	15.6	130	17.7	84	13.1	85	11.5	55	9.1	46	7.9	530	12.8
Paraben mixture	42	5.0	26	3.5	7	1.1	25	3.4	10	1.7	12	2.1	122	3.0
Neomycin sulfate	122	14.6	90	12.3	63	9.9	96	13.0	56	9.3	95	16.2	522	12.6
Quaternium 15	0	0.0	9	1.2	5	0.8	13	1.8	12	2.0	11	1.9	50	1.2
Thimerosal	0	0.0	52	7.1	111	17.4	119	16.2	87	14.4	110	18.8	479	11.6
Detergents	341	40.8	140	19.1	173	27.1	128	17.4	88	14.6	42	7.2	912	22.1

tance of testing for additional allergens beyond a standard tray (17).

Nickel sulfate was the most common allergen encountered in our study with a mean of 39.9%, which is in discordance with other reports ranging from 14.2% to 29.5% (14,16,18-20). A similar high rate (37%) was found in patients with predisposition to atopic dermatitis and positive patch test reactions to nickel (21). Systemic contact dermatitis elicited nickel in all 20 patients in the study by Dou Xia *et al*. (22). The statistically significantly increased frequency of nickel sulfate (p=0.0047) in our study could be explained by its wide use in everyday life.

The increased frequency of fragrance allergy found in our group of patients (19.1%) has also been reported by NACDG and others (13,18,21, 23,24). The presence of fragrances, not only in perfumes but also in a wide variety of cosmetic products and toiletries containing fragrances, is likely to account for the increased allergy to fragrances. Neomycin sulfate accounted for 14.6% (1998) and 16.2% (2003), and similar rates have been reported elsewhere (13). We found that 12.6% of our patients developed allergy to neomycin sulfate during the 6-year period, which may reflect the extent of the use of this topical antibiotic in the treatment of skin infections. The incidence of contact allergy to neomycin in 1998 was 14.6%, similar to our results in 2003 (16.2%) (11). Contact allergy to neomycin combined with cross-reaction with other aminoglycoside antibiotics is also becoming ever more present (11). Bacitracin, a commonly used antibiotic, showed an increased allergy rate (9.2%) as reported by NACDG. It may cause not only delayed, eczematous contact dermatitis but also an immediate reaction, which may reflect a decrease in the use of bacitracin as a prophylactic antibiotic often used in surgical procedures. Positive patch test reactions to bacitracin often appear at 96 hours. Katz and Fisher report on bacitracin as a unique topical antibiotic sensitizer in nine patients (25).

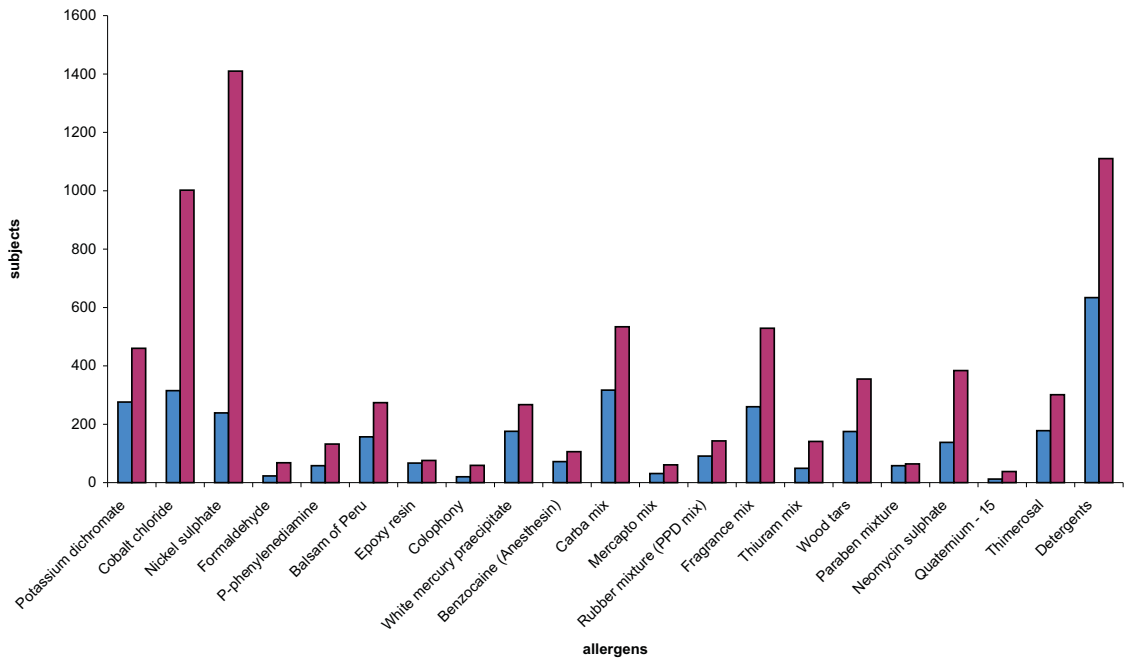

Figure 1: Distribution of positive patch-test reaction to standard Croatian series of allergens in 4132 patients according to sex and allergens between 1998 and 2003. Blue bars – male; red bars – female.

Cobalt chloride is a common sensitizer with a prevalence rate from 8.0% to 13.5% in several series (13,16,18,26,27). Our patients showed a prevalence rate of 21.7% in 2003, which is consistent with most of other studies (13,16,26).

In our study, balsam of Peru was also a common allergen during the 6-year period (mean 10.4%; 10.2% in 1998; 13.5% in 1999; 11.1% in 2000; 10.6% in 2001; 7.5% in 2002; and 9.1% in 2003), which is consistent with the NACDG report (13,16). Consistently with other reports (1,13,16), formaldehyde induced 2.2% of positive reactions in 2003, however, patients with suspected occupational skin diseases may have 4.0% of positive reactions to formaldehyde (19).

Quaternuim 15 is a preservative present in many cosmetics and personal hygiene products. Our finding of 1.9% of positive reactions to quaternium 15 in 2003 is incomparable to NACDG finding (16). A study conducted in Turkey reports on a 0.6% prevalence of allergic reactions to quaternium 15 (26), a rate we recorded in 2000. The higher incidence observed in our study may have resulted from regional variation and difference in personal habits that contributed to the increased exposure to quaternium 15 in our patients.

Thiuram, an important occupational allergen in rubber industry, caused positive reactions in 4.1% of our patients in 2003, which is consistent with some reports (19,20) but lower than the rate reported by others (13,16). This could be explained by the fact that our patients are not involved in occupations that may put them at risk of exposure to thiuram. The high mean rate (17.8%) of reactions to potassium dichromate in our study can be explained by low preventive measures. It has been reported to induce positive patch test reactions in 9.4% to 11.8% of cases (19,26,29). Uter *et al.* (28) report on a significantly higher rate of allergic contact sensitization to para amino compounds such as *p*-phenylenediamine (14.1%) than the mean rate observed in our study (4.6%). The rate of allergy to *p*-phenylenediamine observed in the present study (3.9% in 2003) was lower than the rates reported elsewhere (13,16,19,28). This may have resulted from a decreased use of hair dyes among our patients because of awareness of their allergic potential. Use of alternative pigments in hair dyes may contribute further to the decrease of positive reactions to *p*-phenylenediamine. Rubber workers and hairdressers are high-risk occupational groups for sensitization to *p*-phenylenediamine compounds.

Thimerosal is a mercury derivative used as a preservative in various products, including cosmetics, ophthalmic and otorhinolaryngologic medication, and vaccines. A lack of relevance of thimerosal reactions induced by patch testing has been reported and the reaction may be the result of past exposure and vaccinations (30). NACDG report on 10.4% and 10.9% of reactions to thimerosal (13,16). Our finding of 0.0%, 7.1%, 17.4%, 16.2%, 14.4% and 18.8% of reactions to thimerosal during the 6-year period (1998-2003) of patch testing may be attributable to the frequent use of thimerosal as a preservative in cosmetics and vaccines. Positive reactions to the rest of patch-tested substances in our study were variably comparable to those of NACDG (13,16). The ICDRG, using a standard technique for patch testing, evaluated patients with suspected allergic contact dermatitis to detect delayed type contact sensitivity and to identify new allergens (29).

CONCLUSION

Our own results and literature data on the ever increasing incidence of allergic contact dermatitis from frequent contact allergens such as nickel, cobalt, carba mix, fragrance mix, potassium dichromate, thimerosal, and neomycin sulfate clearly point to the increasing need of preventive measures to fight this morbidity. The use of alternative and hidden chemicals may result in an increased frequency of reactions to certain substances such as thimerosal. Therefore, patterns of allergen frequencies can change and may raise our concern about emergence of new allergens. We strongly recommend keeping up-to-date with the epidemiology of contact allergy and the results of patch testing to substances that may cause allergic contact dermatitis in patients with inflammatory dermatoses.

References

1 Belsito DV. The diagnostic evaluation, treatment, and prevention of allergic contact dermatitis in the new millennium. J Allergy Clin Immunol 2000;105:409-20.

2 Rajagopalan R, Anderson R. Impact of patch testing on dermatology – specific quality of life in patients with allergic contact dermatitis. Am J Contact Dermatitis 1997;8:215-21.

3 Rajagopalan R, Kallal JE, Fowler JF, Sherertz EF. A retrospective evaluation of patch testing in patients diagnosed with allergic contact dermatitis. Cutis 1996;57: 360-4.

4 Lipozenčić J, Milavec-Puretić V, Lakoš-Jukić I, Marinović B, Ljubojević S, Basta-Juzbašić A. Changing epidemiology of contact dermatitis in Zagreb, Croatia. Allergy 2002;73 (Suppl 37):305.

5 Ingber A, Sasson A, David M. The seasonal influence on patch test reactions is significant in Israel. Contact Dermatitis 1998;39:318-9.

6 Bourke JF, Batta K, Prais L, Abdullah A, Foulds LS. The reproducibility of patch test. Br J Dermatol 1999;140: 102-5.

7 Dooms Goossens A, Lesaffre E, Heidbuchel M, Dooms M, Degreef H. UV sunlight and patch test reactions in humans. Contact Dermatitis 1988;19:36-42.

8 Kranke B, Aberer W. Seasonal influence on patch test results in Central Europe. Contact Dermatitis 1996;34: 215-6.

9 Hosoi J, Hariya T, Denda M, Tsuchiya T. Regulation of the cutaneous allergic reaction by humidity. Contact Dermatitis 2000;42:81-4.

10 Katsarou A, Koufou V, Kalogeromitros D, Armenaka M, Papaioannou D, Stratigos J. Seasonal influence on patch test results in Greece. Photodermatol Photoimmunol Photomed 1992;9:232-4.

11 Lipozenčić J, Milavec-Puretić V, Trajković S. Neomycin – a frequent contact allergen. Arh Hig Rada Toksikol 1993;44:173-80.

12 Katsarou A, Kalogeromitros D, Armenaka M, Koufou V, Stratigos J. The influence of climatic factors on patch test results in Athens. Contact Dermatitis 1993;28: 301-2.

13 Marks JG, Belsito DV, De Leo VA, Fowler JF Jr, Fransway AF, Maibach HI, *et al*. North American Contact Dermatitis Group patch-test results, 1996-1998. Arch Dermatol 2000;136:272-3.

14 Wahlbeg JE. Patch testing. In: Rycroft RJG, Menne T, Frosch PT, *et al.,* eds. Contact dermatitis. Berlin: Springer-Verlag, 1992;239-68.

15 Čvoriščec B, Buneta D, Lipozenčić J, Kanceljak-Macan B, Stipić-Marković A. Imunodijagnostički postupci *in vivo*. In: Dekaris D, Čulo F., eds. Klinička imunologija u nas. Zagreb: Naprijed, 1990;222-43.

16 Marks JG, Belsito DV, De Leo VA, Fowler JF Jr, Fransway AF, Maibach HI, *et al*. North American Contact Dermatitis Group patch test results for the detection of delayed-type hypersensitivity to topical allergens. J Am Acad Dermatol 1998;38:911-8.

17 Saripalli YV, Achen F, Belsito DV. The detection of clinically relevant contact allergens using a standard screening tray of twenty-three allergens. J Am Acad Dermatol 2003;49:65-9.

18 Lee TY, Lam TH. Patch testing of 490 patients in Hong Kong. Contact Dermatitis 1996;35:23-6.

19 Dickel H, Kuss O, Schmidt A, Diepgen TL. Occupational relevance of positive standard patch-test results in employed persons with an initial report of an occupational skin disease. Int Arch Occup Environ Health 2002;75:423-34.

20 Cooper SM, Shaw S. Eyelid dermatitis: an evaluation of 232 patch test patients over 5 years. Contact Dermatitis 2000:42:291-3.

21 Brasch J, Schnuch A, Uter W. Patch-test reaction patterns in patients with a predisposition to atopic dermatitis. Contact Dermatitis 2003;49:197-201.

22 Dou Xia, Liu LL, Zhu XY. Nickel-elicited systemic contact dermatitis. Contact Dermatitis 2003;48:126-9.

23 De Groot AC, Colnraads PJ, Bruynzeel DP, Jagtman BA, van Ginkel CJW, Noz K, *et al*. Routine patch testing with fragrance chemicals in The Netherlands. Contact Dermatitis 2000;42:184-5.

24 Buckley DA, Rycroft RJG, White IR, Basketter DA, McFadden JP. Concomitant sensitivity between fragrances. Br J Dermatol 2001;145 (Suppl 59):99-100.

25 Katz BE, Fisher AA. Bacitracin: a unique antibiotic sensitizer. J Am Acad Dermatol 1987;17:1016-24.

26 Akasya-Hillenbrand E, Ozkaya-Bayazit E. Patch test results in 542 patients with suspected contact dermatitis in Turkey. Contact Dermatitis 2002;46:17-23.

27 Lim JT, Goh Cl, Ng SK, Wong WK. Changing trends in the epidemiology of contact dermatitis in Singapore. Contact Dermatitis 1992;26:321-6.

28 Uter W, Lessmann H, Geier J, Becker D, Fuchs T, Richter G. The spectrum of allergic (cross-)sensitivity in clinical patch testing with "para amino" compounds. Allergy 2002;57:319-22.

29 Albert MR, Gonzales S, Gonzales E. Patch testing reactions to a standard series in 608 patients tested from 1990 to 1997 at Massachusetts General Hospital. Am J Contact Dermatitis 1998;9:207-11.

30 Suneja T, Belsito DV. Thimerosal in the detection of clinically relevant allergic contact reactions. J Am Acad Dermatol 2001;45:23-7.