

Patch Tests in Children: A Review of 13 Years of Experience in Comparison with Previous Data

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Abstract: The true prevalence of allergic contact dermatitis (ACD) in children remains unknown. Our aim was to compare the results of patch tests in children with suspected ACD between two different periods of time and identify possible changes in emerging allergens. We compared contact allergens, gender, age distribution, and personal history of atopic dermatitis (AD), in correlation with the positivity of patch tests, between two equal periods of time (232 children tested during 1980–1993, period A, and 255 children during 1994–2007, period B) in the same region and in the same institution. Patch test positivity was 47.8% in period A, and 60% in period B ($p = 0.083$). The most common allergens in period A were: nickel sulfate (16.3%), cobalt chloride (8.6%), fragrance mix (7.3%), potassium dichromate (4.3%), and thimerosal only (1.7%). In period B, the allergen distribution was as follows: nickel sulfate (21.56%), thimerosal (18.03%), cobalt chloride (12.9%), potassium dichromate (9.4%), and fragrance mix (4.7%). Girls were more likely to have a positive patch test compared with boys, with reactions in 53% of girls and 39% of boys in period A ($p = 0.003$), and 61% of girls and 58% of boys in period B ($p = 0.691$). Twenty-nine per cent of patients with positive results had a personal history of AD in period A and 44% in period B ($p = 0.015$). Differences in the positivity of allergens between different time periods reflect changes in habits, of allergens exposure or preventive measures.

Allergic contact dermatitis (ACD) is increasing in childhood, presumably due to higher levels of exposure to environmental allergens. The rate of positive patch test results varies as a result of different selection criteria for patch testing. Allergen exposure also varies, resulting from different social and regional practices (1). In industrialized countries, increases in ACD are occurring

in parallel with increases in the number of potential sensitizers (2). Children are commonly exposed to a variety of allergens at a much younger age, partially due to exposure to cosmetics, body piercing, and through participation in sports and hobbies.

The aim of this study was to determine the most common contact allergens among children with

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suspected allergic dermatitis, and to compare the results between two different and equal periods of time (period A during 1980–1993, and period B during 1994–2007) in the same region and institution, to establish the changes over time.

MATERIALS AND METHODS

We carried out two retrospective single-center case studies at the largest hospital for skin diseases in Athens. All patients were under the age of 16 years with suspected ACD, 232 consecutive children (145 girls and 87 boys) during period A (3) and 255 consecutive children (162 girls and 93 boys) during period B. Patients were identified from an existing database of the contact dermatitis clinic. The patient's history and patch test results were reviewed for each individual. In this study, relevance is not mentioned because this information was not available in all medical histories.

Patch testing was performed in a standard manner and reactions were recorded by two dermatologists according to the International Contact Dermatitis Research Group scoring system (4). Allergens were applied to intact skin on the patient's upper back and left for 48 hours. Readings were recorded at 49 and 96 hours. In case of doubtful reactions, the test was repeated. All children were patch-tested with a modified European basic standard series (Trolab, Hermal, Germany), and with additional series as indicated. The concentrations of allergens used were the same as those used for adults in our patch testing center. A personal history of atopic dermatitis (AD) was recorded according to the diagnostic criteria of Hanifin and Rajka.

Pearson chi-squared test (or Fisher exact test, wherever chi-squared test could not be applied) was performed to test for differences in age, test result (positive–negative), and personal history of atopy among male and female patients for both the periods.

RESULTS

During the study period A, a total of 232 children were referred for patch testing and of those, 111 (47.8%) had one or more positive patch test results. During period B, a total of 255 children were referred for patch test investigation and of those, 153 (60%) had one or more positive patch test reactions ($p = 0.083$).

The most common allergens we had in period A were: nickel sulfate (5% in petrolatum (pet.)) 16.3%, cobalt chloride (1% in pet.) 8.6%, fragrance mix (8% in pet.) 7.3%, potassium dichromate (0.5% in pet.) 4.3%, and thimerosal (0.1% in pet.) 1.7%. In period B, the allergen distribution was slightly different: nickel sulfate (5% in pet.) 21.56%, thimerosal (0.1% in pet.) 18.03%, cobalt chloride (1% in pet.) 12.9%, potassium dichromate (0.5% in pet.) 9.4%, and fragrance mix (8% in pet.) 4.7%. Corticosteroids did not elicit any reaction. Irritant reactions were associated with metals especially in atopic individuals. Table 1 shows the most common positive patch tests to the modified basic series among children in both periods.

Gender distribution was examined in correlation with the positivity of patch test results for the two time periods. Girls were significantly more likely to have a positive patch test compared with boys in periods A and B (RR = 1.34, 95% CI: 1.07–1.69).

In period B, the incidence rate of contact allergy increased in all age groups as compared with period A, with the exception of the age group “0–5 years” where we had an important decrease in boys and a stable male: female ratio (Table 2). The hands were the most common site of involvement in period A, whereas in period B, a majority of patients had generalized lesions.

A positive history of AD was found in 31.5% of patients during period A, and 48% of patients during period B ($p < 0.0005$). Twenty-nine per cent of patients

TABLE 1. The Most Common Positive Patch Tests to A Modified Basic Series, Among Children of Period A (232 Children, 87 Boys/145 Girls) and Period B (255 Children, 93 Boys/162 Girls)

Allergens	No. positive patch tests period A			No. positive patch tests period B			p value
	Boys	Girls	Total (%)	Boys	Girls	Total (%)	
Nickel sulfate, 5%	3	35	38 (16.4)	4	51	55 (21.6)	NS
Thimerosal, 0.1%	2	2	4 (1.7)	20	26	46 (18)	<0.001
Cobalt chloride, 1%	10	10	20 (8.6)	9	24	33 (12.9)	NS
Potassium dichromate, 0.5%	6	4	10 (4.3)	9	15	24 (9.4)	<0.05
Fragrance mix, 8%	8	9	17 (7.3)	6	6	12 (4.7)	NS

NS, nonsignificant.

TABLE 2. Gender and Age Distribution in 232 Patients During Period A (1980–1993), and in 255 Patients During Period B (1994–2007)

Age (yrs)	Period A				Period B			
	Boys		Girls		Boys		Girls	
	Tested, n	Positive, n (%)	Tested, n	Positive, n (%)	Tested, n	Positive, n (%)	Tested, n	Positive, n (%)
0–5	12	6 (50)	2	1 (50)	6	1 (17)	2	1 (50)
6–10	21	10 (48)	30	11 (37)	35	24 (68)	39	21 (54)
11–14	28	9 (32)	49	34 (49)	35	21 (60)	57	31 (54)
15–16	26	9 (35)	64	41 (64)	17	8 (47)	64	46 (72)
Total	87	34 (39)	145	77 (53)	93	54 (58)	162	99 (61)

TABLE 3. Patch Test Results in Atopic and Nonatopic Patients During Period A and Period B

Test result	No. patients (%)			
	History of atopy-period A		History of atopy-period B	
	No	Yes	No	Yes
Patch test negative	80 (66.1)	41 (33.9)	47 (46.1)	55 (53.9)
Patch test positive	79 (71.2)	32 (28.8)	86 (56.2)	67 (43.8)
Total	159 (68.5)	73 (31.5)	133 (52.2)	122 (47.8)

with positive patch tests results in period A had a personal history of AD and 44% of patients in period B ($p = 0.015$). In addition, no statistically significant difference in the prevalence of positive patch test results between period A and period B was found between atopic and nonatopic patients (Table 3).

Occupational contact dermatitis was diagnosed in children aged between 13 and 16 years especially in period A and most of them were hairdressers. In period B, occupational contact dermatitis was diagnosed in children aged 16 years and most of them were hairdressers as well.

DISCUSSION

Allergic contact dermatitis is an acquired eczematous skin disease mediated by a type IV immune mechanism. Patch testing is a realistic and credible method for the identification of sensitizing allergens. Allergic contact dermatitis in childhood has important repercussions for the patient and may affect decisions regarding future occupation in adulthood (5). The early patch test diagnosis of contact allergy is associated with improved quality of life, increased response to treatment, and decreased prediagnostic cost of treatment (5,6).

In this study, the comparison of a large number of patch tests over two time periods allows a relatively comprehensive assessment of positive allergens in

children and an estimation of the evolution of contact allergy over time. Because the information concerning relevance was incomplete, our incidence rates are contact sensitization rates and not allergic contact dermatitis rates.

The overall incidence rate of positive patch test results in children increased from 47.8% to 60% ($p = 0.083$). In a United Kingdom (UK) study, contact allergy increased over the beginning of the past decade from 32.6% to 49% towards the middle of that decade (7). In France, contact allergy has been reported as high as 67% in the latter part of the same decade (8). It is thought that the increased rates may be due to increases in utilization of personal health products in everyday life that contain certain allergens and the fact that children are becoming exposed to a wider variety of allergens at a younger age (1,2). An alternative explanation is improved selection of children who undergo patch testing. In this study, we observed that girls were diagnosed to have positive patch test significantly more than boys (34%), especially in the group of 15–16 years of age, and this result is in accordance with other studies (5,9–13).

Sensitization to nickel sulfate 5% was increased in period B (from 16.4% to 21.6%, $p = \text{NS}$). Nickel was the most common contact allergen in children younger than 16 years. This is similar to findings in many other studies (2,9,13–16). The trend for ear and body piercing at younger ages, may be the main nickel source in girls and this was reflected in the results of positive tests. Nickel is the most common sensitizer in Europe and North America, though the prevalence varies from country to country (1,5,13–17). Boys can become sensitized from body piercing, which is very popular among teenagers, as well as through everyday exposure. A predominance for nickel sensitization in girls was observed in both time periods and this is in absolute accordance with other studies (1,17).

There was a significant increase in the rate of positive patch tests to thimerosal 0.1% in period B. Thimerosal was not patch-tested in our basic standard series before 1987. Thimerosal was ranked in the top four allergens

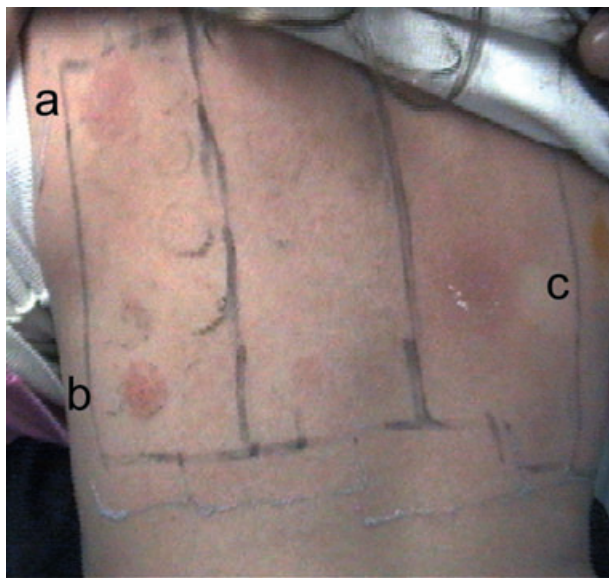


Figure 1. Positive patch test to potassium dichromate (A), above left, cobalt chloride (B), below left, and mercapto-benzothiazole (C), below right, in a child with shoe dermatitis.

among children in several studies (15–17). Sensitization to thimerosal may be related to the use of vaccines and antiseptics containing this substance (18). However, the clinical relevance of positive patch tests to thimerosal is low (19,20). For this reason, it is now excluded from many standard screening recommendations (19). In our opinion, in countries where the positivity is high, such as Greece, it should still be evaluated.

Allergy to cobalt chloride 1% was slightly increased in period B. The majority of positive patch test was associated with co-sensitization to nickel in the same patient. This may be attributable to the fact that these metals are commonly associated. Pure cobalt allergy was uncommon, and this result is in accordance with other reports (2,13).

Contact allergy to potassium dichromate 0.5% was doubled in period B (from 4.3% in period A to 9.4% in period B, $p < 0.05$). The most common cause of chromate allergy in adults is cement. In children, leather found in shoe uppers, which is traditionally chrome-tanned, can be the main source of chrome and can explain foot dermatitis (21,22). In addition, in Greece, parents prefer leather shoes for their children (Fig. 1).

As compared with results of period A, children had a lower rate of positive patch tests to fragrance mix 8% in period B. This finding, which is consistent with other reports (16), is very promising, as fragrance allergy was very common in the past. The policies of the cosmetic and toiletry industry and the production of a variety of fragrance-free products

appears to have resulted in diminution of exposure to fragrances in the younger population.

In period A, the hands were the most common site of involvement, whereas in period B, a more generalized pattern was observed. This can be explained by the fact that in period B, we had more severe cases in association with AD.

This report is consistent with other evidence that contact allergy is common in children with AD as well as in those without AD. The relationship between atopy and contact allergy is not very well established. Some older studies report lower rates of contact allergy in atopic patients (23), whereas others indicate a similar prevalence of contact allergy in patients with AD and nonatopics (1,24). Atopy, according to many reports, is a predisposing factor for contact hypersensitivity resulting from the damaged epidermal barrier and the subsequent increased penetration of allergens (5,25). In our study, the rate of positive patch tests in atopics increased from 29% to 44% in period B ($p < 0.0005$), and this may reflect the overall increase of AD in children (26). In a recent study from the Netherlands, 55% of children with allergic patch test reactions had AD (14). We found no difference in the distribution of allergens among atopic and nonatopic patients and this observation is not new (4,25).

In period A, occupational contact dermatitis was diagnosed in children aged between 13 and 16 years and the majority were hairdressers. In period B, occupational contact dermatitis was diagnosed in children aged 16 years and most of them were hairdressers as well. The finding of occupational contact dermatitis in teenagers has also been documented by Lewis et al. (27). This suggests that patch testing can be a useful tool in the choice of future occupations in such children.

In conclusion, as sensitization rates to different allergens show great variation over time, it is important to consider performing period patch test evaluation.

REFERENCES

1. Beattie PE, Green C, Lowe G et al. Which children should we patch test? *Clin Exp Dermatol* 2007;32:6–11.
2. Akyol A, Boyvat A, Peksari Y et al. Contact sensitivity to standard series allergens in 1038 patients with contact dermatitis in Turkey. *Contact Dermatitis* 2005;52:333–337.
3. Katsarou A, Koufou V, Armenaka M. Patch test in children: a review of 14 years experience. *Contact Dermatitis* 1996;36:70–71.
4. Wilkinson DS, Fregert OS, Magnusson B et al. Terminology of contact dermatitis. *Acta Derm Venereol* 1970;50:287–292.
5. Clayton TH, Wilkinson SM, Rawcliffe C et al. Allergic contact dermatitis in children: should pattern of dermatitis determine referral? A retrospective study of 500 children

- tested between 1995 and 2004 in one U.K. centre. *Br J Dermatol* 2006;154:114–117.
6. Rajagopalan R, Anderson RT, Sarma S et al. An economic evaluation of patch testing in the diagnosis and management of allergic contact dermatitis. *Am J Contact Dermat* 1998;9:149–154.
 7. Rajagopalan R, Anderson R. Impact of patch testing on dermatology specific quality of life in patients with allergic contact dermatitis. *Am J Contact Dermat* 1997;8:215–221.
 8. Shah M, Lewis FM, Gawkrödger DJ. Patch testing in children and adolescents: five years experience and follow-up. *J Am Acad Dermatol* 1997;37:964–968.
 9. Onder M, Adisen E. Patch test results in a Turkish paediatric population. *Contact Dermatitis* 2008;58:63–65.
 10. Lazarov A. European Standard Series patch test results from a contact dermatitis clinic in Israel during the 7-year period from 1998 to 2004. *Contact Dermatitis* 2006;55:73–76.
 11. Militello G, Jacob SE, Crawford GH. Allergic contact dermatitis in children. *Curr Opin Pediatr* 2006;18:385–390.
 12. Fernandez Vozmediano JM, Armario Hita JC. Allergic contact dermatitis in children. *J Eur Acad Dermatol Venereol* 2005;19:42–46.
 13. Hogeling M, Pratt M. Allergic contact dermatitis in children: the Ottawa hospital patch testing clinic experience, 1996 to 2006. *Dermatitis* 2008;19:86–89.
 14. De Waard-van der Spek FB, Oranje AP. Patch tests in children with suspected allergic contact dermatitis: a prospective study and review of the literature. *Dermatology* 2009;218:119–125.
 15. Hammonds LM, Hall VC, Yiannias JA. Allergic contact dermatitis in 136 children patch tested between 2000 and 2006. *Int J Dermatol* 2009;48:271–274.
 16. Zug KA, McGinley-Smith D, Warshaw EM et al. Contact allergy in children referred for patch testing: North American Contact Dermatitis Group data, 2001–2004. *Arch Dermatol* 2008;144:1329–1336.
 17. Wantke F, Hemmer W, Jarisch R et al. Patch test reactions in children, adults and elderly. *Contact Dermatitis* 1996;34:316–319.
 18. Katsarou A, Lambrinopoulou K, Armenaka M. The positivity of thimerosal in Greece. *Contact Dermatitis* 1999;41:291–292.
 19. Breithaupt A, Jacob SE. Thimerosal and the relevance of patch–test reactions in children. *Dermatitis* 2009;19:276–277.
 20. Wantke F, Demmer CM, Gotz M et al. Contact dermatitis from thiomersal: 2 years experience with ethyl mercuric chloride in patch testing thiomersal sensitive patients. *Contact Dermatitis* 1994;30:115–117.
 21. Chowdhuri S, Ghosh S. Epidemio-allergological study in 155 cases of footwear dermatitis. *Indian J Dermatol Venereol Leprol* 2007;73:319–322.
 22. Trattner A, Farchi Y, David M. Shoe contact dermatitis in Israel. *Am J Contact Dermat* 2003;14:12–14.
 23. De Groot AC. The frequency of contact allergy in atopic patients with dermatitis. *Contact Dermatitis* 1990;22:273–277.
 24. Vender RB. The utility of patch testing children with atopic dermatitis. *Skin Therapy Lett* 2002;7:4–6.
 25. Giordano-Labadie F, Rance F, Pellegrin F et al. Frequency of contact allergy in children with atopic dermatitis: results of a prospective study of 137 cases. *Contact Dermatitis* 1999;40:192–195.
 26. Mohammedamin RS, van der Wouden JC, Koning S et al. Increasing incidence of skin disorders in children? A comparison between 1987 and 2001. *BMC Dermatol* 2006;6:4.
 27. Lewis VJ, Statham BN, Chowdhury MMU. Allergic contact dermatitis in 191 consecutively patch tested children. *Contact Dermatitis* 2004;51:155–156.