An Investigation of Contact Allergy in 217 Hong Kong Children with Atopic and Non-atopic Dermatitis

Dr. K. Y. Chan
Private Practice, Hong Kong

ABSTRACT

This study attempts to determine the incidence of contact allergy in children in Hong Kong and to see if any difference in the incidence of contact allergy exists between children with non-atopic and atopic dermatitis. It also attempts to identify the common contact allergens for children in Hong Kong. 217 children under 16 were classified into non-atopic and atopic dermatitis groups and there was no significant difference found between them. Nickel was the most common allergen in both groups. The children with atopic dermatitis were more sensitive to medicament groups. Traditional Chinese medicament was found to be a common contact allergen in Chinese children.

Keywords: contact dermatitis, atopic, non-atopic, children, Hong Kong

INTRODUCTION

There are few data available on the patch testing of children and adolescents because allergic contact dermatitis is considered to occur infrequently in childhood. This is based on two beliefs:

1. that children have less exposure than adults to contact allergens; and
2. that the immune system may be less responsive than an adult's system to contact allergens.

In addition, there are perceived technical difficulties in carrying out patch testing in small children, which may also contribute to the paucity of clinical studies. Several studies have recently demonstrated that sensitization in children is a more frequent event than previously thought. The results vary from 7% to 71% in different studies.[1,2]

The differing values could be due to the use of a selected population for study, the total number of children studied, the different allergens applied, the different concentrations of allergens used, and social and geographic variations.

The objectives of our study were to:
1. establish the incidence of contact allergy in children with atopic and non-atopic dermatitis; and
2. identify the common contact allergens in children with atopic and non-atopic dermatitis.

MATERIAL AND METHODS

Selection of Patients

From March 1998 through August 1998, 236 patients aged from 0-16 years were invited for patch testing. Subjects were entered into the study only after informed consent documents had been signed and copy of which was given to the parents. The subjects were divided into four groups as follows:

- Group A: age 0-8 with non-atopic dermatitis
- Group B: age 9-16 with non-atopic dermatitis
- Group C: age 0-8 with atopic dermatitis
- Group D: age 9-16 with atopic dermatitis

Correspondence address:
Dr. K. Y. Chan
3B, G/F, Roca Centre
North Point MTR Station
467-78 King's Road
Hong Kong

We defined atopic dermatitis according to the criteria set down by the U.K. working party for atopic dermatitis.[3]

The Patch Test

The patch test generally involved two and a half tapes of IQ chambers containing at least 23 allergens being placed on each side of the upper back. Each tape contained 10 chambers. In infants, the test was divided into five halved tapes; one was applied on each side of the upper part of the arms and three on the upper part of the back.

Readings were made two and four days after application. We showed the positive reactions to the patients or parents and asked them to report any new reactions that developed for up to one week after application.

RESULTS

Group A comprised 65 individuals. The group originally consisted of 72 individuals, of whom 68 agreed to have patch testing. There were three cases of failed patch tests. One was loosened after exercise and two individuals asked for patches to be removed because of irritation.

Group B comprised 45 individuals. The group originally consisted of 47 individuals, of whom 45 agreed to patch testing. One did not wish to participate because of the hot climate and one declined because of a sporting activity. No patch test failed in this group.

Group C comprised 59 individuals. The group originally consisted of 67 individuals, of whom 62 came for patch testing. There were three failed patch tests; all complained of skin irritation and asked for patch removal within 24 to 48 hours of application.

Group D consisted of 48 individuals. 50 subjects were asked to participate but two refused because of the hot climate. All patch tests were performed successfully.

The mean age of those in group A and group C were 4.7 and 4.5 years, respectively. The mean age of group B and group D participants were 11.7 and 12.0 years, respectively.

Incidence of Positive Reactions among Non-atopic and Atopic Participants

There were 45 of 110 (40.9%) positive patients among non-atopic patients versus 42 of 107 (39.3%) among atopic participants. This difference was not statistically significant (P=0.8).

Of the children aged from 0-8 years, 23 of 65 (35.4%) non-atopic children had one or more positive reactions whereas atopic children had 24 of 59 (40.7%) yielding a positive reaction. This difference was also not statistically significant (P=0.5, i.e. Group A vs Group C: 35.4 % vs 40.7%.)

In the older group of patients aged from 9-16 years, 22 of 45 (48.9%) non-atopic patients had at least one positive reaction. Similarly, 18 of the 48 (37.5%) atopic patients had such a reaction. This difference was not statistically significant (P=0.2, i.e. Group B vs Group D: 48.9% vs 37.5%).

Incidence of Positive Reactions Related to Age

35.4% of non-atopic children aged 0-8 years versus 48.9% of those aged 9-16 years had a positive reaction. This difference was not statistically significant. (P=0.1, i.e. Group A vs Group B: 35.4% vs 48.9%).

As for the atopic children, 40.7% of those aged 0-8 years versus 37.5% of aged 9-16 years had a positive reaction. This difference was also not statistically significant (P=0.7, i.e. Group C vs Group D: 40.7% vs 37.5%).

Ranking of Positive Test Substances in the European Standard Series (Table 1)

Nickel was found to be the most common allergen (14.7%). The next most common allergen was cobalt chloride (7.4%), followed by fragrance mix (6.5%), potassium dichromate (6%), wool alcohol (4.6%), Balsam of Peru (3.2%), and formaldehyde (3.2%). The ranking of positive tests in the non-atopic and atopic groups was identical, irrespective of age. The next most common positive substances were neomycin sulphate and Paraben mix. Benzocaine and Clioquinol reactions were only found in the younger atopic group (group C).

The positive rubber component Thiuram mix, Mercapto mix, and Black rubber mix reactions were

Table 1. Materials that elicited a positive reaction when patch tested

Allergens tested	All (n=217) Positive	(%)	Non-atopic group (n=110) Positive	(%)	Atopic group (n=107) Positive	(%)
Metals						
Nickel Sulphate 2.5%	32	14.7	15	13.6	17	15.9
Cobalt Chloride 1%	16	7.4	8	7.3	8	7.5
Chromate 0.5%	13	6.0	8	7.3	5	4.7
Fragrances						
Fragrance Mix 8%	14	6.5	8	7.3	6	5.6
Balsam of Peru 25%	7	3.2	4	3.6	3	2.8
Vehicles						
Wool Alcohols 30%	10	4.6	6	5.5	4	3.7
Preservatives						
Formaldehyde 1%	7	3.2	4	3.6	3	2.8
Quaterium 15%	1	0.5	0	0.0	1	0.9
Kathon C G	3	1.4	2	1.8	1	0.9
Paraben Mix 15%	6	2.8	4	3.6	2	1.9
Medicaments						
Neomycin Sulphate 20%	7	3.2	4	3.6	3	2.8
Benzocaine 5%	2	0.9	0	0.0	2	1.9
Clioquinol	1	0.5	0	0.0	1	0.9
Rubber Compounds						
Thiuram Mix	2	0.9	1	0.9	1	0.9
Mercaptobenzothiazole	0	0.0	0	0.0	0	0.0
Mercapto Mix	1	0.5	0	0.0	1	0.9
Black Rubber Mix	1	0.5	0	0.0	1	0.9
Resins						
Epoxy	3	1.4	2	1.8	1	0.9
PTBP Formaldehyde Resin	1	0.5	0	0.0	1	0.9
Colophony	0	0.0	0	0.0	0	0.0
Miscellaneous						
p-phenylenediamine	2	0.9	1	0.9	1	0.9
Primin	0	0.0	0	0.0	0	0.0
Sesquiterpene Lactone	1	0.5	1	0.9	0	0.0
Own Materials						
Bone-setter's Herbs	5	2.3	2	1.8	3	2.8
Hydrocortisone Acetate	2	0.9	0	0.0	2	1.9
Benzoyl Peroxide	3	1.4	2	1.8	1	0.9
Ginger	1	0.9	1	0.9	0	0.0
Garlic	1	0.5	1	0.9	0	0.0

found in group C. The incidence of positive reactions to resins, plants, and dyes were too low to be significant in any of the four groups.

Positive Tests of Own Material

Five individuals showed a positive reaction to traditional Chinese medicaments. The products were Chinese orthopaedic tincture Zheng-Gu-Shui and bonesetter's herbs with unknown exact formulae. These five patients showed positive reactions both in patch testing with IQ chambers and in repeated open application tests (ROATS). A further three patients showed positive reactions to benzoyl peroxide, two showed positive reactions to ginger, and one to garlic. These test substances were patched and applied by ROATS.

Clinical Relevance of Results

The reactions were more often clinically relevant in the two older age groups, (group B and group D). The clinical relevance of nickel sulphate sensitivity was around 70% in group B and group D but only about 20% in the younger children (group A and group C). The clinical relevance of cobalt chloride was low, being about 20% in all four groups. Fragrance mix was clinically relevant in more than 50% of children; no clinical relevance was found for potassium dichromate.

The results of clinical relevance for test substance of own material were high - all five own materials showed 100% clinical relevance.

DISCUSSION

Our study is the first study investigating contact allergy among children and young adults in Hong Kong. We have compared our results with another study of a mixed population in Hong Kong and have found a difference in the ranking of contact allergens.

Incidence of Contact Allergy among Non-Atopic and Atopic Children

One or more positive reactions were found in 40.9% of non-atopic versus 39.3% of atopic children under 16 years of age. Results were very similar between the two groups. There was no significant difference between the younger non-atopic and atopic groups (age 0-8 years; 35.4% vs 40.7%, P=0.5). For the older group (age 9-16 years) there was a slightly lower incidence of positive reactions in the atopic group compared with the non-atopic children (37.5% vs 48.9%, P=0.2), but the difference was not statistically significant. This was probably due to the severity of the atopic dermatitis. Most of the patients in this group suffered from moderate to severe atopic dematitis.

We assessed the disease severity by means of six area six sign atopic dermatitis severity score (SASSAD).[4] A score under 15 was considered to represent mild disease, 15-24 to be moderate, and 25 or above to be severe. Ten children had mild disease, 30 were moderate, and 8 were severe. Cronin found a lower incidence of contact allergy in patients with severe atopic dermatitis.[5] Uehara found similar results[6] - severe atopic dermatitis patients had reduced reaction to DNCB compared with mild atopic dermatitis patients. Furthermore, the majority of these patients who were non-reactive on the first challenge tests had positive reactions on the second challenge tests during a remission of the disease.

Incidence of Contact Allergy in Small Children and Adolescents

For the group with non-atopic dermatitis, 35.4% of those aged 0-8 years versus 48.9% of the older children showed more than one reaction. The difference was not statistically significant (P=0.1). The increased incidence in contact allergy in older non-atopic patients is mainly due to their wider exposure to contact allergens together with their having a more mature immune system compared with the younger patients.

Incidence of Positive Reactions to Individual Substances

Nickel was tested at a 2.5% concentration in a petrolatum vehicle. This was because the 5% concentration might have caused a higher incidence of primary irritant reaction especially in children and patients with atopic dermatitis.[7] Nickel sensitivity was observed in 14.7% of the study group. It caused most reactions in both non-atopic and atopic dermatitis patients, regardless of age group. The greater number of clinically relevant reactions in older children was noteworthy. Values of 72% and 62% for clinical relevance were noted in older non-atopic and atopic dermatitis children compared with only 22% for younger atopic patients. None of the younger non-atopic patients' reactions correlated with their history. Sources of nickel allergy in children include eyeglass frames, belt buckles, and metal fasteners on clothing, watches, and jewellery in older children.

Cobalt sensitivity was seen in 7.4% of the study group and was one of the five most common allergens in all four groups. The usual source of cobalt allergy is metal but it is also found in paint, glass, china, pottery, crayons, and cement. Co-sensitivity was observed between cobalt and nickel. The rate of clinical relevance of cobalt was lower than that for nickel in all groups.

Potassium dichromate sensitivity was observed in 6% of study participants. Although no clinical relevance was noted, we assume that leather shoes, including popular leather athletic shoes, are the most likely source

of sensitization in subjects. Cement is an unlikely source of exposure in children.

Reactions to fragrance mix and Balsam of Peru were observed in 6.5% and 3.2% of study children, respectively. The two were among the five most common allergens in all four groups. However, the lower incidence in younger children might reflect an exposure difference, as greater exposure to cosmetics and fragrance-containing compounds occurs as the children get older. Balsam of Peru may cross-react with the fragrances that are added to cosmetics and may account for a substantial amount of cosmetic allergy in children. The clinical relevance of both fragrance mix and Balsam of Peru sensitivity were higher than the values for cobalt and potassium dichromate.

Neomycin yielded positive reactions in 3.2% of the children studied. Its role as a cause of contact allergy in children seems to be over-rated. The incidence of sensitivity was similar for non-atopic and atopic children. If medicament allergens including neomycin, benzocaine, clioquinol, Bonesetter's herbs, hydrocortisone acetate and benzoyl peroxide were studied as a group, atopic dermatitis children had a greater number of positive reactions compared with the non-atopic children. Co-reactivity is extremely common with bacitracin, even though the two agents are chemically unrelated. Since neomycin is frequently used in topical agents containing corticosteroids, the contact allergy may be partially suppressed and results in failure of the original dermatitis to clear rather than an acute eczematous response. Nevertheless, all of the medicaments described above had more clinical relevance than was expected.

Only four children had positive reactions to rubber compounds: two to Thiuram mix, one to Black Rubber mix, and one to Mercaptobenzothiazole. We were interested to find this low sensitization to rubber compounds as rubber sensitivity has been cited as a frequent cause of childhood foot dermatitis. No clinical relevance was found for the children in our study.

Only 4.6% of children had a positive reaction to wool alcohol. The incidence was similar in all four groups but there was little clinical relevance. Wool alcohol varies in composition depending on its source.

Formaldehyde and Quaternium 15 are extensively used as preservatives in cosmetics, shampoos, glues, and other commercial products. The parabens are the most common preservatives used in cosmetics but these do not commonly cause allergic contact dermatitis. Kathon CG is an important biocide that is used in cosmetics and in industry. The total incidences of positive reactions to these four preservatives were less than 8% and the incidence of clinical relevance was low.

Sensitization to resins was rare. Only one child was found to have a correlated history of sensitization to epoxy due to wearing eyeglass frames. Sensitization to p-phenylenediamine was less frequent and the only child with a possible correlated history was one in contact with photocopying materials. One child was sensitive to Sesquiterpene Lactone mix, which is used to screen for sensitivity to Compositae plants. One six-year-old child with non-atopic dermatitis had a positive reaction to this plant. No clinical relevance could be found and no generalised sensitization was observed after taking chrysanthemum tea.

2.3% of children had a positive reaction to bone-setter's herb. Patch testing as well as repeated open application test was performed and all had positive clinical relevance. One child was sensitive to Zheng-Gu-Shui, which is manufactured in China and is widely available in Hong Kong. Its ingredients are listed on the information leaflet included with the product. Four children were sensitive to bone-setter's herb obtained from different bonesetters. Although the exact formulae of herbs from different providers are not available due to commercial secrecy, Lee has indicated that Myrrh, a gum resin from the stem of Commiphora molmol Engler, is the putative allergen.[8] Because it is so widely used in many over-the-counter traditional Chinese medicines, it is recommended that it should be included in the standard battery of allergens used in Hong Kong.

In Hong Kong, garlic is still employed as an anti-fungal and anti-bacterial agent. Ginger, on the other hand, is used to relieve abdominal 'wind'. We observed one positive reaction to garlic and one to ginger. Repeated open application test was performed by applying the cut surfaces of fresh garlic and ginger to the outer aspect of the arm for two days. Patch testing was also performed by preparing the extract according to the method of Pasricha and Guru.[9] Lee found garlic to be a potent irritant under occlusive conditions and thus it should not be used for patch testing.[8] The extract form is much safer and is recommended when testing for allergic reaction.

Results of Comparable Studies Investigating the Incidence of Contact Allergy in Children

The reported incidence of contact allergy in children varies from 9% to 71%, according to the study.[1,2] This wide variation is due primarily to how the selection of the population to be tested is chosen and secondarily, to the selection of antigens to be tested.[10-18]

Nickel was the most common allergen in almost all studies but other metals like cobalt, chromate, and mercury were also found to be common allergens. Fragrance mix and Balsam of Peru were also often found to be allergens. The most common allergen among own materials was benzoyl-peroxide.

There have been conflicting reports as to the incidence of contact allergy in the atopic state. Increased, normal, or decreased incidence may be due to different criteria being used to select patients, varying definitions of atopic skin disease, the retrospective character of the studies, etc.[5,6,19]

In a study by De Groot, only patients who were 15 years of age or older were selected.[20] For those with atopy, 37% had a contact allergy compared with 52% among the non-atopics. Edman retro spectively studied 3790 consecutive patients with suspected contact dermatitis.[21] Of those with atopy, 36.9% had a contact allergy compared with 44.1% in the non-atopic group. Klas studied 410 suspected contact dermatitis patients and among the atopic group, 52% were found to have definite allergic contact dermatitis compared with 41% in the non-atopic group.[22] The incidences of a positive contact allergen among atopic dermatitis patients in these three studies were similar to our findings.

Suggested Modifications for Future Studies

There were 20 positive reactions relating to medicaments, including 7 for neomycin, 1 to clioquinol, 2 to Benzocaine, 2 to hydrocortisone acetate, 3 to Benzoyl peroxide and 5 to bone-setter's herbs. 12 of 20 reactions were found in atopic patients. We suggest testing with the actual complete product in any patient who has used a topical medicament and found worsening of their dermatitis. Allergic contact dermatitis resulting from topical corticosteroid was until recently, thought to be a relatively rare phenomenon. It usually develops in the setting of chronic dermatitis like atopic dermatitis. In the vast majority of cases, however, the etiologic agent in the topical corticosteroid is a preservative or vehicle component, rather than the corticosteroid itself.

Benzoyl peroxide is a widely used active ingredient in topical acne preparations. It is an irritant but has infrequently been reported as a sensitizer. Bone-setter's herbs are widely used in the local Chinese population and contact dermatitis due to traditional Chinese medicine is common but has rarely been studied. The nature of the ingredients are not specified by the supplier and most of the time, the exact putative ingredient causing the dermatitis cannot be determined. Nevertheless, medicaments including traditional Chinese medicine are considered to be an important series for testing in patients with chronic dermatitis whose condition fails to clear or when a flare-up occurs. The differences in race, geographical situation, habits, and exposure suggest that the European standard battery of allergens is not the ideal test for patients in Hong Kong. We used the European standard allergens only as a reference point and our aim is to develop a standard battery that includes most allergens commonly encountered by local people and that can be used for screening patients with dermatitis in Hong Kong.

Acceptance Rate for Patch Testing

Our study was performed from March through August, which are the spring and summer months in Hong Kong. In spite of the hot and humid climate, the acceptance rate for patch testing was more than 90%. The technical concerns about testing in young children include the restriction of activities for a number of days and the small area of back available for patch testing. However, more than 90% of children in our study tolerated the patches without difficulty and even infants were patch tested by applying the test to the back of the arms as well as the back. The infrequent use of the patch test in children in Hong Kong is due more to the reluctance of dermatologists than to any rejection by patients. Reasons for this reluctance might include a misconception that a low incidence of allergic contact dermatitis occurs in children and in atopic dermatitis patients. The basic principle and technique involved in patch testing are not difficult.

CONCLUSION

Patch testing in children has rarely been studied in our locality. The literature shows varied results because of different study methods. Our observation is that contact allergy is not uncommon in children in Hong Kong. We also found the incidence of contact allergy in children with atopic dermatitis to be similar to that of non-atopic dermatitis children. There was no difference regarding the common allergens between non-atopics and atopics, although medicament group sensitivity was more common among atopic dermatitis patients. No difficulty was encountered in performing patch testing in children. There was difficulty in assessing the clinical relevance of positive reactions. The study of the incidence of allergic contact dermatitis in children is not easy but it is worth doing.

References

1. Angelini G, Meneghini CL. Contact and bacterial allergy in children with atopic dermatitis. Contact Dermatitis 1977;3:163-74.
2. Pevny I, Brennenstuhl M, Razinskas G. Patch testing in children (I) collective test results; skin testability in children. Contact Dermatitis 1984;11:201-6.
3. Williams H, Burney P, Strachan D et al. The U.K. working party's diagnostic criteria for atopic dermatitis. Br J Dermatol 1994;131:383-416.
4. Berth-Jones J. Six area, six sign atopic dermatitis (SASSAD) severity score: a simple system for monitoring disease activity in atopic dermatitis. Br J Dermatol 1996;135(Suppl 48):25S-30S.
5. Cronin E, McFadden JP. Patients with atopic eczema do become sensitized to contact allergens. Contact Dermatitis 1993;28:225-8.
6. Uehara M, Sawai T. A longitudinal study of contact sensitivity in patients with atopic dermatitis. Arch Dermatol 1989;25:366-8.
7. Hjorth N. Contact dermatitis in children. Acta Derm Venereol Suppl (Stockh) 1981;95:36-9.
8. Lee TY, Lam TH. Patch testing of 490 patients in Hong Kong. Contact Dermatitis 1996;35:23-6.
9. Pasricha, J, Guru, B. Preparation of an appropriate antigen extract for patch tests with garlic. Arch Dermatol 1979;115:230.
10. Barros MA, Baptista A, Correia TM, Azevedo F. Patch testing in children: a study of 562 schoolchildren. Contact Dermatitis 1991;25:156-9.
11. Kuiters GR, Smitt JH, Cohen EB, Bos JD. Allergic contact dermatitis in children and young adults. Arch Dermatol 1989;125:1531-3.
12. Ayala F, Balato N, Lembo G, et al. A multicentre study of contact sensitization in children. Gruppo Italiano Ricerca Dermatiti da Contatto e Ambientali (GIRDCA). Contact Dermatitis 1992;26:307-10.
13. Rademaker M, Forsyth A. Contact dermatitis in children. Contact Dermatitis 1989;20:104-7.
14. Goncalo S, Goncalo M, Azenha A, et al. Allergic contact dermatitis in children. A multicenter study of the Portugese Contact Dermatitis Group (GPEDC). Contact Dermatitis 1992;26:112-5.
15. Sevila A, Romaguera C, Vilaplana J, Botella R. Contact dermatitis in children. Contact Dermatitis 1994;30:292-4.
16. Stables GI, Forsyth A, Lever RS. Patch testing in children. Contact Dermatitis 1996;34:341-4.
17. Brasch J, Geier J. Patch test results in school children. Contact Dermatitis 1997;37:286-93.
18. Rudzki E, Rebandel P. Contact dermatitis in children. Contact Dermatitis 1996;34:66.
19. Lammintausta K, Kalimo K, Fagerlund VL. Patch test reactions in atopic patients. Contact Dermatitis 1992;26:234-40.
20. De Groot. The frequency of contact allergy in atopic patients with dermatitis. Contact Dermatitis 1990;22:273-7.
21. Edman B, Moller H. Contact allergy and contact allergens in atopic skin disease. Am J Contact Dermatitis 1992;13:27-9.
22. Klas PA, Corey G, Storrs FJ, Chan SC, Hanifin JM. Allergic and irritant patch test reactions and atopic disease. Contact Dermatitis 1996;34:121-4.