Review

Patch-test results in children and adolescents: systematic review of a 15-year period*

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Abstract: The number of studies on patch-test results in children and adolescents has gradually increased in recent years, thus stimulating reviews. This paper is a systematic review of a 15-year period devoted to studying the issue. Variations pertaining to the number and age groups of tested children and/or adolescents, the number of subjects with atopy/atopic dermatitis history, the quantity, type and concentrations of the tested substances, the test technique and type of data regarding clinical relevance, must all be considered in evaluating these studies, as they make it harder to formulate conclusions. The most common allergens in children were nickel, thimerosal, cobalt, fragrance, lanolin and neomycin. In adolescents, they were nickel, thimerosal, cobalt, fragrance, potassium dichromate, and Myroxylon pereirae. Knowledge of this matter aids health professionals in planning preventive programs aimed at improving children's quality of life and ensuring that their future prospects are not undermined.

Keywords: Adolescent; Allergens; Child; Dermatitis; Dermatitis, allergic contact; Dermatitis, contact; Patch-tests

INTRODUCTION

The increase in the number of published studies on patch-test results in children and adolescents has contributed vast knowledge on the subject and shown that contact sensitization (or contact allergy) and allergic contact dermatitis (ACD) are not uncommon in childhood or adolescence, contrary to what was believed.[1]

Most of these studies were based on selected populations: children and adolescents with suspected ACD, many with a diagnosis of atopic dermatitis (AD). There are few studies that examine the general population.[2,3] Many papers present contact sensitization frequency data, without data on the positive tests' clinical relevance or conclusions on ACD frequency.[2,4,5] The higher frequency of positive patch-tests in children aged under 3 years has indicated that contact sensitization may occur early in life. The association between atopy and ACD has been studied and still presents controversial results.[2]

Dermatologists, pediatricians and allergologists pursue a valuable interest in identifying the substance causing ACD, differentiating it from other dermatoses and identifying the possible coexistence of AD and ACD in patients.

Nowadays, children and adolescents frequently use cosmetics (fragrances, makeup, nail polish, etc.) and adornments (Henna tattoo, jewelry, piercing, etc.) that can be sources of potential allergens.[6-10] Therefore, it is justifiable to expect a higher number of positive reactions to patch-tests among these age groups.

The objective of this study is to perform a systematic review, gathering and synthesizing information about patch-test results in children and adolescents published during a 15-year period, thus enhancing our knowledge.

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MATERIALS AND METHODS

A literature search to find descriptors for this systematic review was undertaken via six databases: BVS COCHRANE, BVS LILACS, BVS IBECS, BVS MEDLINE, Web of Science and PUBMED. It used the following terms: patch-test, contact sensitization, contact allergy, contact hyper sensitization, allergic contact dermatitis, and contact eczema. Filters were placed for age (children and/or adolescents aged up to 19 years; classification adopted by the World Health Organization), study period (January 1997 to May 2012) and language (Portuguese, English and Spanish). A study was selected with patients aged up to 20 years, taking into account the sample size (n=2340) and lack of Asian studies in this review.

Seventy articles were picked out. All the data about the subjects' characteristics and patch-test results from 48 articles were recorded and catalogued in specific forms, which were divided into three categories:

1. Studies with selected samples (34): patients with suspected ACD.
2. Studies with no selected samples (2): children and/or adolescents with no suspected ACD.
3. Studies with selected (9) and non-selected (3) samples with specific focus.

Categories 1 and 2 include articles presenting samples of at least 50 children and/or adolescents, in addition to data on the frequency results of tested substances. Category 3 includes specific articles, with greater flexibility regarding the data.

STUDIES IN SELECTED SAMPLES: PATIENTS WITH SUSPECTED ALLERGIC CONTACT DERMATITIS

1.Country, period, number of centers and delineation of studies

The data were organized according to the study period intending the evaluation of the tests results temporal evolution (Table 1).

Twenty-two studies were carried out in Europe, five in the USA, one in the USA and Canada, one in Canada, two in Brazil, two in Asia and one in Africa.[11-44]

Only three studies were performed in more than three centers; twenty-four were carried out at only one center.[11-44]

Regarding the delineation, twenty-six studies were based on retrospective data, while eight were prospective.[11-44]

2.Research subjects: sample size and selection, age, sex, atopy history, dermatitis location and duration

The number of patients was below 200 in 20 studies and a maximum of 100 in 10.[11-44]

In the 34 studies, tests were carried out in patients with suspected ACD but half of these involved a significant percentage of patients (over 30.0%) with AD or atopy history.[12,13,15,19-22,25,26,29,31,33-35,41,43,44] In 13 studies, there was monitoring of Hanifin and Rajka criteria for this diagnosis.[45] In some studies, all subjects with suspected ACD presented an AD diagnosis, compared with only a small percentage in others (below 30.0%).[14,28,32,38,39] In 2 studies, patients presented chronic recalcitrant eczematous dermatitis or severe AD.[32,35]

Children and adolescents of varying ages and age groups were examined; one study included exclusively children aged 3-36 months[33], whereas another included adolescents.[25]

Regarding gender, females were predominant in 25 studies and males were predominant in 2.[11-44]

As for dermatitis evolution prior to testing, a study revealed that 80.0% of dermatitis cases had durations of over three months.[25]

The body sites most affected by dermatitis were: the face and hands, followed by the feet, generalized dermatitis, the legs and neck.[14-16,18-20,23-26,29,39]

3.Technique:

Batteries were used in six pediatric studies: 17 substances for children under 5 years;[21] 30 substances for children under 10 years;[22] pediatric series of 30 substances in another three studies[33,34,36] and a series of 10 substances.[40] Others used adult standardized batteries.[11,12,15-21,23-26,29-32,35,37,38,41,43,44]

The number of substances tested varied. Approximately 50.0% of these studies assessed 22-40 substances.[11,12,15,17-23,25,27,28,30,33,36-38,41,44] In one study, 25-185 substances (mean: 92) were evaluated; the number was 48 or 66 in another, and 65 in one other.[29-31] The smallest number of tested allergens was 10.[40]

Furthemore, the concentrations of some substances were also diverse: nickel (most studies: 5.0%, some: 2.5%), thimerosal (most: 0.1%, some: 1.0% and 0.05%), fragrance mix I (most: 8.0%, some: 5.0%, 7.0%, 14.0%), potassium dichromate (most: 0.5%, some: 0.25%), cobalt (most: 1.0%, one study: 0.5%),[40] Kathon CG (2.0% and 0.5%).[13,22,23,25,27,31-33,40-42]

Most studies followed the ICDRG (International Contact Dermatitis Research Group) testing criteria.[46] One study reduced the test occlusion time to 24 hours in 11 centers[23] and three increased it to 72 hours.[12,22,27] Another study implemented only a 48-hour reading.[29] There was no active sensitization and the number of irritant reactions was small in the Manzini study.[12]

Data about the tests' clinical relevance are presented below.

Table 1 : Patch-test results in selected groups of children and adolescents with suspected allergic contact dermatitis (34 selected groups)

Author Country	Data Collection, years	Nº of children and adolescents tested	Age	Adolescents and children with >1 positive reaction (%)	Relevance* of positive tests (%)	Two most common allergens Frequency of positive reactions
Goon et al.[11] Singapore	1986-2003	2340	< 20 years	45.4	Calculated per substance	Nickel 40.0% Thimerosal 15.0%
Manzini et al.[12] Italy	1988-1994	670	6 months-12 years	42.0	not reported	Thimerosal 12.2% Nickel 7.7%
Brash et al.[13] Germany	1990-1995	416	6-15 years	40.9	not reported	Nickel 15.9% Thimerosal 11.3%
Fernandez et al.[14] Spain	1990-2000	96	< 15 years	54.2	57.7	Thimerosal 21.0% Mercury 19.0%
Shah et al.[15] UK	1991-1995	83	6-16 years	49.0	100.0	Nickel 14.0% Fragrance mix I 7.2%
Romaguera et al.[16] Spain	1992-1997	141	< 14 years	50.0	calculated per substance	Nickel 19.1% Cobalt 11.3%
Lewis et al.17 UK	1993-2003	191	< 16 years	41.0	51.7	Nickel 13.0% Fragrance mix I 9.0%
Onder et al.[18] Turkey	1993-2005	360	2-16 years	32.0	30.5%	Nickel 46.0% Cobalt 9.5%
Milingou et al.[19] Greece	1994-2007	255	<16 years	60.0	not reported	Nickel 21.6% Thimerosal 18.3%
Kuljanac et al.[20] Croatia	1994-2009	412	4-18 years	26.0	not reported	Nickel 25.4% Thimerosal 17.8%
Roul et al.[21] France	1995-1997	337	1-15 years	67.0	not reported	Nickel 23.7% Fragrance mix I 9.5%
Seidenari et al.[22] Italy	1995-2001	1094	7 months-12 years	52.1	70.0	Neomycin 13.2% Nickel 10.9%
Heine et al.[23] Germany	1995-2002	2460	6-12 years 13-18 years	52.6 49.7	not reported not reported	Thimerosal 18.2% Nickel 16.7%
Clayton et al.[24] UK	1995-2004	500	< 16 years	27.0	61.0	Nickel 33.0% Fragrance mix I 18.0%
Duarte et al.[25] Brazil	1996-2001	102	10-19 years	56.0	100.0	Nickel 31.0% Tosylamide 12.0%†
Hogeling et al.[26] Canada	1996-2006	100	4-18 years	70.0	55.8	Nickel 26.0% Cobalt 14.0%
Wöhrl et al.[27] Austria	1997-2000	79	1-10 years	62.0	not reported	Nickel 34.2% Ethylmercury 25.3%‡
Giordano et al.[28] France	not reported	137	4 months-16 years	43.0	100.0	Nickel 14.9% Fragrance mix I 4.4%
Beattie et al.[29] UK	1999-2002	114	3-15 years	54.0	54.0	Nickel 20.0% Fragrance mix I 7.2%
Hammonds et al.[30] USA	2000-2006	136	3-18 years	61.0	53.0	Nickel 22.0% Cobalt 17.0%
Zug et al.[31] USA, Canada	2001-2004	391	0-18 years	65.7	51.2§	Nickel 28.3% Cobalt 17.8%
Jacob et al.[32] USA	2001-2006	65	1-18 years	83.0	77.0	Nickel 17.5% Thimerosal 12.5%
Fortina et al.[33] Italy	2002-2008	321	3-36 months	62.3	calculated per substance	Nickel 26.8% Potassium dich.9.0% |

Table 1 (continued): Patch-test results in selected groups of children and adolescents with suspected allergic contact dermatitis (34 selected groups)

Author Country	Data Collection, years	Nº of children and adolescents tested	Age	Adolescents and children with >1 positive reaction (%)	Relevance* of positive tests (%)	Two most common allergens Frequency of positive reactions
Moustafa et al.[34] UK	2002-2008	110	2-18 years	44.0	44.0	Drugs 15.4% Nickel 10.0%
de Waard-van der Spek et al.[35] Netherlands	2003-2008	79	1-18 years	51.0	calculated per substance	Nickel 21.5% Potassium dich. 6.0% |
Jacob et al.[36] USA	2004-2006	69	6 months-18 years	95.6	76.7	Nickel 23.3% Cocamido 23.3%¶
Stoskute et al.[37] Lithuania	not reported#	194	3-17 years	55.0	not reported	Nickel 18.0% Cobalt 13.8%
Belhadjalli et al.[38] Tunisia	2005-2006	63	mean: 69 months	39.7	38.2§	Nickel 24.7% Potassium dich. 7.9% |
Sarma et al.[39] India	2005-2008	70	1-15 years	80.0	60.7	Paraben 43.0% Potassium dich. 27.0% |
Czarnobilska et al.[40] Poland	2007	229	7 years 16 years	43.8 52.6	not reported not reported	Nickel 30.2% Thimerosal 27.8%
Kobata[41] Brazil	2007-2009	62	2-12 years	61.0	70.0	Nickel 27.4% Thimerosal 17.7%
Czarnobilska et al.[42] Poland	2008-2009	196	7-8 years 16-17 years	67.0 58.1	not reported not reported	Nickel 35.9% Thimerosal 37.6%
Jacob et al.[43] USA	2008-2009	102	6-18 years	76.2	not reported	Nickel 29.7% p-tert-Butylphenol 16.8%**
Herro et al.[44] USA	not reported††	101	6-18 years	78.0	not reported	Nickel 31.0% Lanolin 18.0%

*Relevance: current and/or past; †tosylamide formaldehyde resin; ‡cloreto ethylmercuric chloride; §calculated from number of tested patients; | potassium dichromate; ¶cocamidopropyl betaine; #published in 2005; **p-tert-Butylphenol formaldehyde resin;††published in 2011.

4.Response to patch-tests

• Relationship with age

Seven studies showed no difference in contact sensitization regarding age[23,26,29,30,32,33,39] but three found a greater frequency of positive tests in older age groups: 11-15 years, 12 years,15-16 years.[11,19,24] In addition, two studies showed higher sensitization rates in children aged over 5 and 6.[28,35] Despite the link found between increased contact sensitization indicators and older ages, three studies revealed higher sensitization rates among children under 3.[12,21,22]

• Relationship with gender

Three studies showed a significant difference regarding the relationship between contact sensitization frequency and gender: two with a higher frequency among girls [19,24] and one among boys.[33] However, there were five studies that revealed no differences in this respect.[13,22,26,30,39] In addition, five studies demonstrated differences concerning only certain allergens: nickel (more frequent among girls), nickel and cobalto and other substances.[14,16, 28,29,42]

• Relationship with atopy

There was no statistically significant difference regarding contact sensitization among atopic and non-atopic patients in nine studies.[14,20-22,25,26,28,31,33] In contrast, four studies did reveal a significant difference.[13,24,39,44] In three studies, all the patients under study had AD, thus making assessment impossible, though one of them showed higher sensitization rates in severe AD (60.9%) than in the moderate (37.5%) and mild (30.0%) forms.[28,32,38] One study compared a group of children and adolescents with AD to a healthy group of adolescents (asymptomatic), demonstrating contact sensitization frequencies of 55.0% and 15.0%, respectively.[37] Other studies presented data on atopy,

without statistical data on the association.

• **Relationship with body sites affected by dermatitis**

The body sites most frequently affected by dermatitis in patients with positive tests were: the trunk, followed by the face, hands, feet and generalized dermatitis.[12,14,22,24,33]

• **Relationship with allergen sources**

There was a significant association between mercapto mix and plantar eczema in one study.[24] Footwear was considered a source of rubber derivatives, formaldehyde, potassium dichromate and metallic mercury.[14,15,19] Sports equipment was regarded as sources of rubber derivatives, while "natural" cosmetics were considered sources of propolis. [17,22]

• **Relationship with the first site of dermatitis**

One study showed that the initial site of the most common dermatitis in positive tests was the palm region (33.0%), followed by the plantar region (29.0%) and legs (29.0%). But there was no statistically significant difference in the relationship between the first site of dermatitis and the positive result of contact testing.[24]

Two studies reported that the initial dermatitis site did not match any specific allergen.[24,26] Except for the involvement of the ears, which is characteristic of sensitization by nickel, no other body site has been related to a specific allergen.[12]

• **Relationship with occupation and polysensitization**

The few reports regarding occupation were on: hairdressers, construction workers, health professionals and metallurgical workers. [14-16,19,23]

Six studies presented data on polysensitization, with the following, respective frequency rates: 42.0%, 29.6%, 19.6%, 17.8% of children undergoing tests; and 54.0%, 51.0% of positive test cases. [12,17,22,26,29,33]

• **Percentage of patients who had at least one positive reaction**

Frequency rates ranged from 26.0% to 95.6%.

Thirteen studies revealed rates of below 50.0%, 17 studies had frequencies ranging from 50.0% to 70.0%, and 5 reported a frequency of over 70.0%.[11- 44] There was the total of 35 studies as one study separated these frequencies: children and adolescents.

• **Percentage of patients with clinical relevance of positive tests**

Among the studies containing data on the clinical relevance of positive tests, fifteen revealed a frequency above 50.0%, of which five had an 100.0% relevance in cases of positive tests. Frequency relevance varied from 30.5% to 100.0%. Four studies did not take this frequency from all positive tests; calculations were made based on the number of positive tests for each substance assessed. Two studies presented the relevance calculated only from the total number of patients undergoing tests (not from positive tests), while twelve studies presented no data on the matter.[11-44]

• **Frequency of the most common allergens**

The most common allergens in children were nickel, thimerosal, cobalt, fragrance mix I, lanolin and neomycin. In adolescents, they were nickel, thimerosal, cobalt, fragrance mix I, potassium dichromate, and balsam of Peru (Myroxylon pereirae).[11-44]

Nickel was the most frequent allergen in 29 studies and was placed among the 10 most common allergens in the 34 studies, with frequency varying from 7.76% to 46.0%.[12,18]

There were reports of positive reactions for cobalt as well as nickel in 68.0% and 71.0% of cases.[26,32] Pure sensitization for cobalt was uncommon.[11,25]

Thimerosal was the most frequent substance in four studies and classed among the 10 most common allergens in 29 studies. Its frequency varied from 0.9% to 37.6%.[33,42]

Fragrance mix I was among the 10 most frequent allergens in 28 studies, cobalt in 27 studies, neomycin in 18, potassium dichromate in 15, lanolin in 12, balsam of Peru in 12, para-Phenylenediamine in 10, formaldehyde and rubber derivatives in 8, colophony in 7, quaternium-15 and p-tert-Butylphenol in 6.[11-44]

Neomycin was the most common allergen in 1 study, paraben mix also in 1 and drug allergens (lanolin, quinoline mix, gentamycin, tixocortol pivalate) in another. Kathon CG, tosylamide formaldehyde resin, gold thiosulfate, disperse dyes, cocamidopropylbetaine, tixocortol pivalate, propolis and paraben mix, were also among the 10 most frequent allergens in some studies.[12,17,22,25,26,30,32,33,34,36,38,39,43]

Amerchol L-101 and plant allergens were ranked among the most common allergens in 1 study.[34] Cocamidopropylbetaine was tested in 3 studies and the allergy contact frequency varied from 7.2% to 23.3%.[32,33,36]

In studies that tested tixocortol pivalate, the frequency of positive reactions (among the most frequent allergens) varied from 5.0% to 7.9%.[17,43,44]

STUDIES IN NON-SELECTED SAMPLES

A European study was carried out in 40 schools where most students had a history of AD and hand eczema. They assessed 1,146 adolescents aged 12-

Table 2: Patch -test results in children and adolescents without suspected allergic contact dermatitis (two unselected groups)

Author Country Nº of centers	Data collection years	Nº of children and adolescents tested	Age	Adolescents and Children with >1 positive reaction (%)	Relevance* of positive tests (%)	Three most common allergens. Frequency of positive reactions
Mortz et al.[45] Denmark 40 centers	1995-1996	1146	12-16 years	15.2	47.7	Nickel 8.6% Fragrance mix I 1.8% Cobalt 1.0% Thimerosal 1.0%
Bruckner et al.[46] USA 1 center	not reported†	85	6 months-5 years	24.5	not reported	Nickel 12.9% Thimerosal 9.4% Kathon CG 2.4%‡ Neomycin 1.2%

*Relevance: current and/or past; †published in 2000; ‡methylchloroisothiazolinone/methylisothiazolinone

16 years using the TRUE test and nickel in three concentrations (Table 2).[47]

An American study evaluated 95 asymptomatic children of both sexes, aged between 6 months and 5 years, via the TRUE test.[48]

Response to patch-tests

In the European study, there were significantly more female adolescents with positive tests. No association emerged between contact sensitization and AD, though there was a significant association between contact sensitization and hand eczema. Reactions to two or more allergens were reported in 14.9% of the adolescents. The relevance frequency of positive tests was 47.7%.[47]

In the American study, 45.0% of children with positive tests were aged under 18 months.[48]

Patients with at least one positive reaction to the patch-test had the following frequency rates: 15.2% of adolescentes and 24.5% of children undergoing tests.[47,48]

The most common allergens in these two studies were nickel. Nickel, cobalt, thimerosal, and p-tert-butylphenol were among the six most frequent allergens.[47,48]

STUDIES IN SELECTED SAMPLES (9) AND NON-SELECTED SAMPLES (3) WITH SPECIFIC FOCUS

Preservatives were tested in 811 children (566 with AD) and 7.27% of the children had at least one positive reaction to a preservative: imidazolidinylurea, diazolidinylurea, paraben mix, formaldehyde, quaternium 15, Euxyl K 400, Kathon CG (methylcloroisothiazolinone/methylizothiazolinone), butylated hydroxyanisole. Kathon CG was the most frequent and quaternium 15 entailed no positive reactions, thus emphasizing the importance of patch-tests for preservatives in children with eczema and/or AD.[49]

An investigation of 2,482 children and adolescents (0-19 years) showed a frequency variation for fragrance mix of 2.5-3.4%, with a lower frequency among those aged 0-9 years.[50]

Allergy to cosmetics occurred in 21 (30.0%) children out of 70, aged 1-15 years, followed by topical medication, metals and rubber derivatives.[51]

One study demonstrated a higher proportion of very strong reactions (3+) to the para-phenylenediamine in patch-tests among children aged up to 14 years, compared with other age groups and other tested allergens (nickel, fragrance mix I and Kathon CG). It was suggested that the concentration of para-phenylenediamine for testing should be reduced for children with a history of allergy to hair dyes and/or Henna tattoos.[52]

In a study of 641 children with AD diagnoses, the contact sensitization frequency to AD topical treatments was 6.2%. The risk factors associated with contact sensitization to AD topical treatments were: disease seriousness (more frequent in moderate to severe AD), early AD onset (before 6 months) and sensitization mediated by IgE. The most frequent sensitizers were antiseptics (chlorhexidene) and emollients (particularly vegetal protein extracts and fragrances). The authors suggested including antiseptics and emollients in the contact test battery for children with AD and suspected ACD. In addition, they recommended using emollients devoid of fragrances and vegetal protein extracts.[53]

The ISAAC (International Study of Asthma and Allergies in Childhood) undertook a study of 143 children, concluding that every case of recurrent chronic dermatitis in children requires differential diagnosis of ACD with other dermatoses (AD, etc.), even if they are predominantly located in the flexural areas.[54]

A multicentric study of 111 children with hand eczema revealed frequencies of 46.8% (contact allergy) and 36.0% (ACD). Nickel, fragrances and Kathon CG were the most common allergens. It was recommended that patch-testing be performed on any child with chronic hand eczema.[55]

One study tested 1,255 children with suspected ACD, using propolis at 20.0%. The frequency for positive reactions was 5.9% of cases. It was suggested that propolis should not be used as a constituent of topical products for children.[56]

In another study, 1,098 children were tested with 30 substances, including dyes: 5 disperse dyes in 964 and 7 disperse dyes in 134 children. Further, 4.6% had positive tests, involving at least 1 disperse dye, the most common being: disperse yellow 3, disperse orange 3, disperse blue 124, disperse red 1 and p-dimethylaminoazobenzene.[57]

Two studies of non-selected samples tested only metals, while one tested just nickel and fragrance mix.[58-60] A study showed that children with pierced ears were more likely to react to nickel that those without, revealing a nickel frequency of 20.0%.[60] The frequency of positive tests for fragrance mix I in children aged under 18 months was low.[59] Another study showed that 18.2-29.6% of positive reactions to patch-tests for nickel would not be detected with only a 48-hour reading.[58]

DISCUSSION

Contact testing seems to be as important in children (even those aged under 3 years) as in adolescents, since contact sensitization occurs in every age group, though sensitization frequencies vary according to the specific age group.[12,21,22,48] Importantly, age-related variations occur only in relation to some allergens.[14,31,40,42]

Females were predominant among the tested patients but there was no consensus regarding contact sensitization and gender.[19,22,24,26,30,33,39]

The association between atopy and contact sensitization remains a point of contention.[13,14,20-22,24-29,31-33,37-39,44]

ACD diagnoses depend on correct technique procedures and reading and interpretation of patch-tests. In some studies, there was variation in the occlusion period and reading, which may have influenced patch-test results (false-positives and false-negatives).[12,13,22,23,27,29]

In the thirty-four studies on selected samples, contact sensitization frequency varied from 26.0% to 95.6% and in the two studies on non-selected samples, the range was 15.2-24.5%, showing that the rate changed according to the type of sample assessed.[11-44,47,48] Studies with frequencies of over 70.0% used more extensive batteries; one was composed of 65 allergens.[32,36,39,43,44] In two studies, samples were composed 70.0% and 50.0% respectively of children with a history of AD.[32,36,44] In the three studies with lower frequencies for positive tests, the batteries used were less extensive.[20,24,38] In two of these, 43.0% and 100.0% of the patients had AD.[20,38]

Some substance concentrations varied, which may have affected the frequency of contact sensitization.

Nickel revealed significant frequency variation: 7.76-46.0% in thirty-four studies across selected samples; and 8.6-20.0% in three studies of non-selected samples.[12,18,58-60] Most tested nickel at 5.0% but three assessed it at 2.5%.[31,40,42] The sensitization frequency for thimerosal varied from 0.9% to 37.6%. Its lowest frequency occurred in a study where the concentration was 0.1% whereas its highest frequency occurred when tested at 1.0%.[13,33,42] In four studies, the concentration was 0.05%.[13,25,27,41] Most studies deemed that thimerosal had no clinical relevance.

Regarding studies with propolis, sensitization frequency varied from 0.74% to 16.5% in selected samples but the substance was tested at 10.0% in one study and at 20.0% in two.[12,22,42,56]

Drawing on studies involving disperse dyes in children, the frequency of positive reactions varied as follows: disperse blue 106 (2.98-16.3%); disperse blue 124 (1.27-3.1%); disperse red 1 (0.72-2.8%) and disperse yellow 3 (0.54-1.9%).[32,33,36,57]

Some authors have recommended using pediatric batteries including emollients, antisseptics, preservatives, propolis and fragrance mix II, as well as smaller chambers in the adhesives of childrens' tests.[12,21,28,42,49,53,61]

Nickel was the most frequent allergen in children and adolescents, followed by thimerosal, fragrance mix I, cobalt, neomycin, potassium dichromate, lanolin, para-phenylenediamine, formaldehyde and rubber derivatives.[11-44]

The clinical relevance of positive tests is important in interpreting patch-test results, as this enables the differentiation of ACD and contact sensitization.[10,46] Important data on clinical relevance include: type (current, past), frequency calculated for positive tests and frequency calculated for each substance.

It is important the physician, the parents and the patient interests in relating a substance identified in the test to the patient's current dermatitis

and to the allergen source, not limited only to the identification of contact sensitization, thus making possible the ACD treatment and the recurrence prevention.[62] Furthermore, monitoring patients after patch-testing is important as regards clinical relevance and treatment evaluation.[15,28,34,36]

Patch-tests are an effective method for identifying the causative agent of ACD, inducing the type IV immune reaction in children and adolescents, as it comes about in adults.[63,64,65] Experience is necessary to undertake selection of patients and substances relevant to these patients' problems.[66] The conclusion was that a clinic specialized in patch-testing can detect more ACD cases than a non-specialized one.[67]

Preventive measures can be taken, as has occurred in many countries.[68,69] Furthermore, educational programs can be implemented and directed towards physicians, pregnant women, children and their families, in order to provide guidance on the importance of avoiding contact with allergens in childhood, especially metals and fragrances in atopic children.[37,44,70]

CONCLUSION

The most common allergens in children were nickel, thimerosal, cobalt, fragrance mix, lanolin and neomycin. In adolescents, they were nickel, thimerosal, cobalt, fragrance mix, potassium dichromate, and Myroxylon pereirae. The following also featured among the 10 most frequent allergens in some studies, representing emerging allergens: Kathon CG, tosylamide formaldehyde resin, gold thiosulfate, disperse dyes, cocamidopropylbetaine, tixocortol pivalate and propolis. This knowledge is important when considering preventive measures.

Since they make it difficult to draw conclusions, variations in the following factors must be taken into account when evaluating the studies: the number and age groups of children and/or adolescents tested, the number of subjects with a history of atopy/atopic dermatitis, the quantity, type and concentration of tested substances, the test techniques and type of data with clinical relevance.

Given the difficulty in comparing the results of the study on patch-tests due to regional differences regarding exposure to allergens, as well as the aforementioned factors, an evidence-based, standardized database is needed.❑

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