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# Clinically Relevant Patch Test Reactions in Children—A United States Based Study

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> Abstract: Allergic contact dermatitis in the pediatric population is more common than previously recognized, with recent prevalence estimates of positive patch test reactions in the range of 14-70% of children patch tested. The aim of this study was to confirm the prevalence of clinically relevant allergic contact dermatitis in children at two referral centers and determine the most common contact allergens. We performed a retrospective case series analysis of 65 symptomatic children (35 girls and 30 boys) aged 1– 18 years old who were patch tested over a 5-year period for recalcitrant dermatitis. Positive patch test reactions were noted in 54 of the 65 children (prevalence rate of 83%) to 80 different allergens. Fifty children (77%) had positive reactions which were determined to be of "definite" or "probable" current clinical relevance. We conclude that the diagnosis of allergic contact dermatitis to specific relevant allergens is common in children referred for patch testing and that contact allergy should be considered in all children with recalcitrant dermatitis. With this article, we review the literature and present a US based study regarding the clinical relevance of positive patch test reactions in children.

Allergic contact dermatitis (ACD) was once thought to be rare in children. This can be attributed to the low frequency of patch tests performed on children (compared with adults) and by the fact that in clinical practice, manifestations of ACD are often attributed to morphological look-alikes such as atopic dermatitis or irritant dermatitis (1). However, a review of studies published over the past decade suggests that ACD in children may be more common than previously realized.

It is important to note that prevalence of positive patch tests in population based studies is different from the prevalence of ACD (positive patch test with clinical correlation) in patients referred for patch testing. Among children with suspected contact dermatitis referred for patch testing, positive patch test rates have ranged from 14% to 70%. Of these, about 56–93% were of current relevance (2–8).

For comparison, there are at least four populationbased patch test studies of unselected pediatric patients (sample size 85–1, 146 patients per study, two in the United States) (2,9–11). In this population, positive patch test rates ranged from 13–24%, considerably lower than the rates observed in patients selected for suspected contact dermatitis. The largest

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of these studies and the only one to provide specific relevance information found the prevalence of past or current relevant reactions to be 7%, with a higher risk seen in females (11). The most common sensitizers were nickel (8.6%, relevance 69%) and fragrance mix (1.8%, relevance 29%) (11).

Several important large-scale European and South American comprehensive patch test studies have documented sensitization rates to particular allergens in symptomatic children. For example, in the United Kingdom, Buckley et al (12) investigated the frequency of contact allergy to fragrance mix in relation to patients' decade of age and, of 23,846 patients tested, 8.4% of the females and 6.4% of the males had positive reactions to fragrance mix. The frequency of fragrance allergy was found to be low in the first two decades of life (2.5-3.4%), with gradual increase in females after the age of 20 with a peak in the 60s (12). Notably, in this study, the youngest patients found to be sensitized were 2 years of age.

Furthermore, Roul et al (13) presented a 3-year study of 337 French children from ages 1 to 15 years which assessed the relevance of the European standard series in patch testing of children. A positive patch test rate of 66% was found, in addition to a notable "peak incidence among children less than 3 years of age" (13). The authors noted the allergens with the highest clinical relevance were nickel, fragrance, rubber chemicals (mercaptobenzothiazole and thiuram), and methylchloroisothiazolinone/methylisothiazolone. Because of the difficulty in interpreting relevant exposures in this age group, particularly in patients with atopy, they recommended that an abbreviated series of patch tests be used for pediatric patients.

Duarte et al (14) patch tested 1,027 Brazilian patients with a suspicion of contact dermatitis to the 30 allergen Brazilian Study Group of Contact Dermatitis standard series. In this cohort, 102 patients (93 girls and 9 boys) were between 10 and 19 years of age; 56% had positive patch test results (14). The most frequent allergens in this adolescent index group were nickel (31%) and tosylamide-formaldehyde resin (12%) (14).

A more recent retrospective patch test case study on 114 children (66 girls and 48 boys) from ages 3 to 15 years (median 11.5) with uncontrolled or deteriorating dermatitis by Beattie et al (15) in the United Kingdom demonstrated that 61 children (54%) had positive reactions that were of current, possible, uncertain or past clinical relevance. They concluded that the prevalence of ACD among children, in particular to nickel and rubber allergy, appeared to be increasing, and that, while this may reflect exposure trends, patch testing should be carried out more frequently. The diagnosis of ACD in children, as in adults, relies on the clinical judgment of the treating physician combined with appropriate use and interpretation of the patch test. While many studies have investigated ACD in children, very few have documented the relevance of positive patch test reactions; and, to our knowledge, no study has documented rates of relevant reactions in US children. We report a retrospective review of the positive patch tests and relevancies in the children evaluated between May 2001 and May 2006 at two US academic patch test referral centers.

#### **METHODS**

We carried out a retrospective case study of 65 symptomatic children (35 girls and 30 boys) from ages 1 to 18 years (median 10 years), who had patch testing performed between May 2001 and May 2006. Recalcitrant or deteriorating atopic dermatitis and localized recalcitrant dermatitis were indications for patch testing to be performed with individually customized allergen batteries. With the exception of patients 31 and 33, all children over 8 years of age had been tested with the North American Contact Dermatitis Group (NACDG) Standard series, and to selected exposure-targeted supplemental allergens, in addition to the patient's own personal care products and medicaments.

Patch tests were performed using standard allergens (Chemotechnique Diagnostics, Vellinge, Sweden) applied to Finn Chambers<sup>™</sup> (Allerderm<sup>™</sup>, Phoenix, AZ) for subjects tested at the University of Pennsylvania or IQ chambers<sup>™</sup> (Chemotechnique Diagnostics) for those tested as at the University of Miami. Tests were then taped with Hypafix<sup>™</sup> (Smith & Nephew Inc., St. Petersburg, FL) to clinically normal skin on the back for 48 hours and read at 48 and 96 hours. Patients 5 years old or younger were read at 48, 72, and 96 hours.

Clinical relevance was assigned by the patch testing physician as follows: "Definite" if the allergen was found to be present in the patient's environment, the dermatitis corresponded to point(s) of contact with the allergen, and the dermatitis significantly improved upon isolation of the allergen or recurred with re-challenge (positive use test). "Probable" relevance was assigned, if the same criterion as above was met, but no follow-up information was available and thus improvement status or re-challenge could not be assessed. In the event that only one of the criteria was met, the positive reaction was assigned a "possible" relevance. Lastly, "past" was assigned to a positive patch test if the allergen was found in the child's past environment and "unlikely" if it could not be found in the current or past environment.

Author/country	Yrs	No. patients tested	Positive patch test prevalence (%)	Age range, yrs (median) ( <i>mean</i> )	Top allergens	No. positives	Prevalence (%)
Fernandez	1990-2000	96	54	0-15 (10.57)	Thimerosal	18	19
Vozmediano	1990 2000	70	54	0 15 (10.57)	Mercury	16	17
et al (5)					Nickel	15	16
Spain					Cobalt	6	6
opum					Thiuram	4	4
					Colophony	4	4
					Fragrance mix	3	3
					Potassium dichromate	3	3
Romaguera and	1992–1997	141	50	4–14	Nickel sulfate	27	19
Vilaplana (24)	1002 1000		20		Cobalt chloride	16	11
Spain					Thimerosal	12	8.5
~ F					Metallic mercury	9	6.4
					Fragrance mix	6	4.3
					Carba mix	6	4.3
					Thiuram mix	6	4.3
					Para-phenylenediamine	4	2.8
					Potassium dichromate	4	2.8
Lewis et al (7)	1993-2003	191	41	< 16	Nickel	N/A	13
United Kingdom	1990 2000	191		10	Fragrance mix	N/A	9
e inter Hingaein					Thiuram	N/A	9
					Cobalt	N/A	8
					Para-phenylenediamine	N/A	6
					Tixocortol pivalate	N/A	5
					Myroxylon pereirae	N/A	5
Roul et al (13)	1995–1997	337	67	1-15	Nickel	80	23.7
France	1995 1997	557	07	1 15	Fragrance mix	32	9.5
1 funce					Wool wax alcohols	29	8.6
					Potassium dichromate	27	8
					Balsam of Peru	16	4.7
					Neomycin	12	3.6
					MBT/thiuram	7/4	3.3
					Cobalt	9	2.7
					PTBF	8	2.4
					Thimerosal	7	2.1
					Kathon CG	3	0.9
Seidenari et al (4)	1995-2001	1094	52.1	0.6-12 (5.4)	Neomycin	N/A	13.2
Italy	1990 2001	102.	0211	010 12 (011)	Nickel	N/A	10.9
itting					Wool alcohols	N/A	10.1
					Thimerosal	N/A	10.1
					Propolis	N/A	4.8
					Kathon CG	N/A	4.2
					Potassium dichromate	N/A	3.8
					Fragrance mix	N/A	3.5
					p-Tert-butylphenolformaldehyde	N/A	2.6
					Mercaptobenzothiazole	N/A	2.5
					Disperse red	N/A	2.3
					Para-phenylenediamine	N/A	2.1
					Balsam of Peru	N/A	2.1
Heine et al (6)	1995-2002	285	52.6	6-12	Thimerosal	N/A	18.2
Germany	1775 2002	200	52.0		Benzoyl peroxide	N/A	16.5
					Nickel sulfate	N/A	10.3
					Cobalt chloride	N/A	8
					Fragrance mix	N/A	6.1
					Compositae mix	N/A	4.2
					Propylene glycol	N/A	4
					Neomycin	N/A	3.7
					Potassium dichromate	N/A	3.7
					i otassium alemoniate	1 1/ / 1	5.1

### **TABLE 1.** Positive Patch Test Reactions in Children Referred for Patch Testing 1990–2002 (International Data)

Author/country	Yrs	No. patients tested	Positive patch test prevalence (%)	Age range, yrs (median) ( <i>mean</i> )	Top allergens	No. positives	Prevalence (%)
Heine et al (6)	1995-2002	2175	49.7	13–18	Thimerosal	N/A	14.3
Germany					Benzoyl peroxide	N/A	8
					Nickel sulfate	N/A	16.7
					Cobalt chloride	N/A	4.6
					Fragrance mix	N/A	6
					Compositae mix	N/A	3.1
					Propylene glycol	N/A	2.3
					Neomycin	N/A	0.7
					Potassium dichromate	N/A	1.9
Duarte et al (14)	1996-2001	102	56	10-19	Nickel	33	32
Brazil	1990 2001	102	20	10 15	Tosylamide-formaldehyde	13	13
					Thimerosal	11	11.9
					Cobalt	9	110
					Balsam of Peru	5	5
					Fragrance mix	5	5
					Para-phenylenediamine	4	4
Giordano-Labadie	1997–1998	114	43	0.3-16 (4.5)	Nickel	17	14.9
et al (25)	1997-1998	114	45	0.5-10 (4.5)	Lanolin/Amerchol L-101	7	6.1
France					Fragrance mix	5	4.4
Tance					Potassium dichromate	3	2.6
					Balsam of Peru	3	2.6
					Neomycin	3	2.6
Wohrl et al (3)	1997-2000	79	49	1-10 (7.5)	Nickel	27	34.2
Austria	1997-2000	19	49	1-10 (7.5)	Thimerosal	14	17.7
Lustria					Fragrance mix	10	12.7
					Cobalt chloride	5	6.3
					Amalgam	4	5.1
					Balsam of Peru	3	3.8
Kohl et al (26)	1998–1999	70	48.6	1-15 (7.8)	Cosmetics	21	30
	1996-1999	70	46.0	1-13 (7.8)		16	23
Belgium					Topical drugs Metals	10	23 20
D	1000 2002	114	54	2.15(11.5)	Rubber	5 22	7
Beattie et al (15)	1999–2002	114	54	3-15 (11.5)	Nickel		19
United Kingdom					Rubber chemicals*	11	10
					Fragrance mix	8	7
					Wool alcohol/amerchol	8	7
					cobalt	6	5
					Balsam of Peru	3	3
					Sorbitan sesquioleate	3	3
					Potassium dichromate	2	2

#### TABLE 1. (Continued)

\*Mercapto mix, mercaptobenzothiazole, carba mix, thiuram combined.

#### RESULTS

We reviewed the more recent studies on children referred for patch testing for suspected ACD (11 studies, sample size 70–2,175 patients) and found a positive patch test rate of 41–67%, with variable assignment of relevance (Table 1). The most common allergens across these studies, in order of frequency, were the following: nickel sulfate, fragrance mix, cobalt chloride, thimerosal, *Myroxylon pereirae* (balsam of Peru), potassium dichromate, neomycin, lanolin, thiuram mix, and para-phenylenediamine.

On review of our data, we found positive reactivity to eighty different allergens in 54 of 65 children, which corresponded to a positive patch test prevalence rate of 83% (Table 2). The positive patch test reactions were distributed over the entire age range, with the number of cases and ages in years as follows: 20 (1–6), 17 (7–12), and 17 (13–18). Fifty of the 65 children (77%) had at least one positive patch test that was determined to be of "definite" or "probable" current clinical relevance. The 10 most common allergens in order of frequency in our population were nickel sulfate, thimerosal, *Myroxylon pereirae*, cocamidopropyl betaine, neomycin, carbamates, cinnamic aldehyde, cobalt chloride, disperse blue 106, and formaldehyde. Allergens detected in three or more patients are listed in Table 3 with their assigned relevancies.

#### DISCUSSION

Previously it was believed that children had fewer chemical exposures and relative immune naivety (16).

Case	Age	Sex	Location	Positive				
1†	1	М	Generalized	<i>Myroxylon pereirae</i> <sup>‡</sup> , Fragrance mix 1 <sup>‡</sup> , Nickel sulfate <sup>‡</sup> , Propylene glycol <sup>¶</sup>				
2†	1	М	Generalized	Fragrance mix 1 <sup>‡</sup> , Menthol <sup>‡</sup> , Paraben mix <sup>§</sup> , Octyl gallate <sup>††</sup> , Carba mix <sup>††</sup>				
3†	1	М	Perioral	Paraben mix <sup>‡</sup> , Budesonide§				
4†	2	М	Generalized	Formaldehyde <sup>‡</sup> , Bronopol <sup>‡</sup> , <i>Myroxylon pereirae</i> <sup>‡</sup> , Sodium Benzoate <sup>‡</sup> , Isopropyl myristate <sup>‡</sup> , Geraniol <sup>¶</sup> , Thimerosal <sup>††</sup>				
5†	3	М	Eyelids, hands	Lanolin‡, Amerchol L-101‡, Sorbitan sesquioleate‡, Cobalt chloride§, BHT¶, Propylene glycol¶				
6†	3	М	Torso, ankles, flexural areas	Cocamidopropyl betaine <sup>‡</sup> , Disperse blue 106¶, Para-phenylenediamine¶				
7†	3	М	Hands, feet	n,n-diphenylguanidine‡, Sorbitan sesquioleate‡, <i>Myroxylon</i> <i>pereirae</i> §, Cinnamic aldehyde§, Cetyl alcohol§, Paraben mix¶ Ethylenediamine dihydrochloride¶				
8†	3	F	Generalized	Imidazolidinyl urea <sup>‡</sup> , Propylene glycol <sup>¶</sup> , Benzalkonium chloride <sup>††</sup>				
9†	3	М	Hand, feet, umbilicus	Cocamidopropyl betaine <sup>‡</sup> , Nickel sulfate <sup>‡</sup> , Cinnamic aldehyde <sup>¶</sup> , Geraniol <sup>¶</sup>				
10†	3	F	Extremities, trunk	Formaldehyde‡, Quaternium-15‡, Imidazolidinyl urea‡, Disperse blue 3‡, Disperse blue 124‡, Disperse blue 153‡, Sorbitan sesquioleate‡				
11† 12†	4 4	F M	Face, arms, legs Perioral	Tosylamide formaldehyde resin‡, Neomycin sulfate¶ Menthol‡, Diazolidinyl urea‡, Nickel sulfate§, Benzoyl peroxide¶				
13†	5	F	Perioral	Cocamidopropyl betaine <sup>‡</sup> , Thimerosal <sup>†</sup> <sup>†</sup>				
14*	5	F	Eyelids	Disperse blue 106§, Neomycin sulfate**				
15†	5	F	Groin	Diazolidinyl urea§, P-tert-butyl-phenol formaldehyde resin**				
16†	5	М	Hand, eyelid	Formaldehyde <sup>‡</sup> , Imidazolidinyl urea <sup>‡</sup> , Tosylamide formaldehyde resin <sup>‡</sup> , Sodium benzoate <sup>§</sup> , Methyldibromoglutaronitrile-phenoxyenthanol <sup>¶</sup> , Phenylmercuric acetate <sup>††</sup>				
17†	6	F	Eyelids, flexural surfaces, hands	Myroxylon pereirae <sup>‡</sup> , Dodecyl gallate <sup>††</sup> , Sorbitan sesquioleate <sup>¶</sup> , Neomycin sulfate <sup>¶</sup> , Carba mix <sup>¶</sup>				
18*	6	F	Medicament testing	Neomycin sulfate¶, Bacitracin¶, EMLA**				
19†	6	М	Eyelids, antecubital fossa	Potassium dichromate§, Disperse blue 106§, Carba mix¶, Mercaptobenzothiazole¶				
20†	6	F	Generalized	Myroxylon pereirae‡				
21†	7	М	Hands	Formaldehyde <sup>‡</sup> , Octyl gallate <sup>¶</sup> , Thimerosal <sup>††</sup> , Disperse blue 106 <sup>††</sup>				
22†	7	М	Eyelids, perioral	Fragrance mix 1 <sup>‡</sup> , <i>Myroxylon pereirae</i> <sup>‡</sup> , Cinnamic aldehyde <sup>‡</sup> , Cinnamic alcohol <sup>‡</sup> , Benzyl salicylate <sup>‡</sup> , Benzoic acid <sup>‡</sup> , Cocamidopropyl betaine <sup>¶</sup> , Sodium omadine <sup>††</sup>				
23†	7	F	Left eye	Diazolidinyl urea <sup>‡</sup> , Tosylamide formaldehyde resin <sup>‡</sup>				
24†	8	М	Face	Fragrance mix 1 <sup>‡</sup> , Ethyleneurea melamine formaldehyde <sup>††</sup>				
25†	9	F	Generalized	Carba mix§, Cobalt chloride¶				
26†	9	F	Generalized	Disperse blue 124 <sup>‡</sup> , Dimethylaminopropylamine <sup>§</sup> , Iodopropynyl butylcarbamate <sup>¶</sup> , 4-Chloro-3-cresol <sup>††</sup>				
27†	9	M	Hands, feet	Formaldehyde <sup>‡</sup> , Quaternium-15 <sup>‡</sup>				
28†	9	F	Gums, hives	Nickel sulfate <sup>‡</sup> , Cobalt chloride <sup>‡</sup> , Palladium <sup>‡</sup> , Thimerosal <sup>††</sup>				
29†	9	F	Face	Formaldehyde§, Bronopol§, Carba mix¶				
30*	9	M	Gums	Nickel sulfate§, Cobalt chloride§, Palladium¶, Gold††				
31†	9	F	Hands	Neomycin sulfate <sup>‡</sup> , Cocamidopropyl betaine <sup>‡</sup> , Cinnamic aldehyde <sup>¶</sup> , Benzalkonium chloride <sup>††</sup> , Disperse yellow 3 <sup>††</sup> , Benzoyl peroxide <sup>††</sup>				
32†	10	М	Hand, foot	Neomycin sulfate§, Disperse blue 106¶, Disperse yellow 9¶, Hydroquinone monobenzylether¶, Thimerosal††				
33*	10	F	Retroauricular (cochlear implant site)	Negative				
34*	10	F	Thighs/buttocks	Disperse blue 124¶, Nickel sulfate**, Thimerosal††, Cobalt chloride††				
35†	10	М	Feet	Ethyl acrylate <sup>‡</sup> , Methyl methacrylate <sup>‡</sup> , Cocamidopropyl betaine <sup>§</sup> , Amidoamine <sup>§</sup> , Abitol <sup>§</sup> , Para-phenylenediamine <sup>¶</sup> , Alpha tocopherol <sup>††</sup> , Dodecyl gallate <sup>††</sup>				

**TABLE 2.** Patient Data with Relevancies

TABLE 2. (	Continued)
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Case	Case Age Sex		Location	Positive				
36†	11	F	Hands, feet	Mercaptobenzothiazole‡, Mercapto mix‡, Cetyl alcohol§, Thiuram mix¶, Cocamidopropyl betaine¶, Potassium dichromate¶				
37†	11	М	Right index finger	Colophony <sup>‡</sup> , Bacitracin <sup>‡</sup> , Thimerosal <sup>††</sup>				
38†	12	F	Generalized	Negative				
39*	12	M	Hand/foot	Negative				
40†	12	F	Legs	Cobalt chloride <sup>‡</sup> , Nickel sulfate <sup>‡</sup> , <i>Myroxylon pereirae</i> <sup>‡</sup> , Cinnamic alcohol <sup>‡</sup> , Cinnamic Aldehyde <sup>‡</sup> , Fragrance mix 1 <sup>‡</sup>				
41†	13	F	Avilla abast book					
41† 42*	13	г М	Axilla, chest, back Mouth	Nickel sulfate§, Gold††				
42* 43†	13	F	Face, neck, hairline	Negative				
431 44*	13	г М	Diffuse $( > > feet)$	Triamcinolone acetonide <sup>‡</sup> , Disperse Blue 106¶, Thimerosal <sup>††</sup> Negative				
44 · 45*	13	F	Back and arms	Negative				
46†	13	F	Generalized	Bronopol§, Disperse blue 153¶, Reactive blue 238¶, p-tert-butyl-formaldehyde resin††				
47*	13	М	Feet	Potassium dichromate§				
48†	13	M	Hands, legs	<i>Myroxylon pereirae</i> <sup>‡</sup> , Para-phenylenediamine <sup>‡</sup> , Cocamidopropyl betaine <sup>§</sup> , Propylene glycol <sup>§</sup> , Carba mix <sup>¶</sup>				
49†	13	F	Face	Myroxylon pereirae <sup>‡</sup> , Hydroxycitronellal <sup>¶</sup> , Neomycin sulfate <sup>¶</sup> , Octyl gallate <sup>†</sup> <sup>†</sup> , Carba mix <sup>¶</sup>				
50†	13	М	Oral ulcers	Cinnamic alcohol <sup>‡</sup> , Copper <sup>¶</sup> , Neomycin sulfate <sup>††</sup> , Iodopropynyl butylcarbamate <sup>††</sup> , Alpha tocopherol <sup>††</sup> , Thimerosal <sup>††</sup>				
51†	13	F	Neck	Cinnamic aldehyde <sup>‡</sup> , Sesquiterpene lactone mix <sup>‡</sup> , Compositae mix <sup>‡</sup> , Ylang-ylang oil <sup>§</sup> , Sorbic acid <sup>§</sup> , Ethylenediamine dihydrochloride <sup>§</sup> , Nickel sulfate <sup>¶</sup>				
52*	14	F	Hand/foot	Negative				
53†	15	F	Hands	Nickel sulfate <sup>‡</sup> , Cocamidopropyl betaine <sup>‡</sup> , Disperse blue 106 <sup>††</sup>				
54*	15	F	Perioral	Thimerosal††				
55*	15	F	Gums	Negative				
56†	15	F	Face, arms, neck	Nickel sulfate <sup>‡</sup> , Tixocortol <sup>‡</sup> , Cinnamic aldehyde <sup>§</sup>				
57†	15	М	Feet	Potassium dichromate <sup>‡</sup> , Neomycin sulfate <sup>§</sup>				
58*	16	Μ	Wrists, legs, feet	Negative				
59†	16	M	Eyelids, lips	Polyoxethylenesorbitan monooleate <sup>‡</sup> , Sorbitan monooleate <sup>‡</sup> , Chloroxylenol <sup>§</sup> , Nickel sulfate <sup>¶</sup>				
60†	16	М	Arms, torso, eyelids	Nickel sulfate§, Alpha tocopherol¶				
61†	16	F	Back, periumbilical	Nickel sulfate <sup>‡</sup> , Cobalt chloride <sup>‡</sup>				
62*	17	M	Feet	Negative				
63*	17	F	Eyelids	Negative				
64*	17	F	Elbows, legs, fingers	Para-phenylenediamine§, Ammonium persulfate¶				
65*	18	F	Photodistributed	Benzalkonium chloride††				

\*University of Pennsylvania

†University of Miami

<sup>‡</sup>Definite, §Probable, ¶Possible, \*\*Past, ††Unlikely

Review of the literature and our retrospective data, however, demonstrate that ACD in children may, in fact, be quite common (17). A few studies noted an early peak in prevalence in children under the age of 3 (4,13,18), while others found generally increasing prevalence through adolescence (16,19–21).

In our study, patch tests were customized to the individual patients based on their exposure histories and physical presentations. Our data corroborated the findings of the prior international studies reviewed in Table 1, as eight of the "top 10" allergens noted also ranked in our top 15 allergens. Furthermore, our data demonstrated notable allergen prevalence concordance with the most recent NACDG adult data on six of these "top 10 allergens" (22). Nickel, a metal, was found to be

our most frequently identified allergen with 11 children having definite or probable clinical relevance. The second most frequent metal was cobalt. Of note, five out of the seven patients (71%) allergic to cobalt, also demonstrated sensitivity to nickel. Relevant exposures to these metals included orthodontic braces, coin rolling, school chairs, and ballet balance bars.

Thimerosal was found to be the most prevalent allergen with the least clinical relevance. The positive reactions to this allergen were probably secondary to vaccine exposure, an exposure which is expected to decrease over time as fewer vaccines are being preserved with this agent. *Myroxylon pereirae*, a complex botanical mixture used as a screen for fragrance contact dermatitis, was the third most prevalent allergen with nine children

		Frequency	Prevalence (%)	Relevance				
Rank	Allergen positive			Definite	Probable	Possible	Past	Unlikely
1	Nickel sulfate <sup>‡</sup> 5% pet.	14	17.5	7	4	2	1	_
2	Thimerosal 0.1% pet.	10	12.5	_	_	_	_	10
3	Myroxylon pereirae 25% pet.	9	11.3	8	1	_	_	-
4	Cocamidopropyl betaine 1% aq.	9	11.3	5	2	2	_	_
5	Neomycin sulfate 20% pet.	9	11.3	1	2	4	1	1
6	Carbamates†‡	8	10.0	1†	1	5	_	1
7	Cobalt chloride 1% pet.	7	8.8	3	2	1	_	1
8	Disperse blue 106 1% pet.	7	8.8	_	2	3	_	2
9	Cinnamic aldehyde 1% pet.	7	8.8	3	2	2	_	-
10	Formaldehyde <sup>‡</sup> 1% aq.	6	7.5	5	1	_	_	-
11	Fragrance mix 1 14% pet.	5	6.3	5	_	_	_	-
12	Sorbitan sesquioleate 20% pet.	4	5.0	3	-	1	_	-
13	Potassium dichromate 0.25% pet.	4	5.0	1	2	1	_	-
14	Para-phenylenediamine <sup>‡</sup> 1% pet.	4	5.0	1	1	2	_	-
15	Propylene glycol 30% aq.	4	5.0	-	1	3	_	-
16	Cinnamic alcohol 2% pet.	3	3.8	3	-	-	_	-
17	Imidazolidinyl urea $2\%$ pet.	3	3.8	3	-	-	_	-
18	Bronopol 0.5% pet.	3	3.8	1	2	_	_	-
19	Corticosteroids*	3	3.8	2	1	_	_	-
20	Disperse blue 124 1% pet.	3	3.8	2	_	1	_	-
21	Tosylamide formaldehyde resin 10% pet.	3	3.8	2	_	_	_	1
22	Paraben mix 12% pet.	3	3.8	1	1	1	-	-
23	Diazolidinyl urea 2% pet.	3	3.8	1	1	_	-	1
24	DL-Alpha tocopherol 100%	3	3.8	_	_	1	-	2
25	Octyl gallate 0.25% pet.	3	3.8	_	_	1	-	2
26	Benzalkonium chloride 0.1% aq.	3	3.8	-	_	-	-	3

TABLE 3. Clinical Relevance of Positive Reactions

Myroxylon pereirae is balsam of Peru; pet., petrolatum; aq., aqueous.

\*Corticosteroids include one reaction each to tixocortol pivalate 0.1% pet., budesonide 0.1% pet., and triamcinolone acetonide 1% pet. †Carbamates includes carba mix<sup>‡</sup> 3% pet. and n,n-diphenylguanidine 1% pet., as some patients were tested to n,n-diphenylguanidine separately.

 $\ddagger$ These allergens are diluted to half concentration if they are selected for testing in children  $\leq 5$  years old at the University of Miami.

having definite or probable clinical relevance. Exposures to *Myroxylon pereirae* or fragrances were found through body washes, shampoos, and diaper balms.

We noted three "allergens" in particular which deserve special mention. Cocamidopropyl betaine (CAPB), the nonionic surfactant used in No More Tears<sup>TM</sup> formulations and baby washes was found to be highly prevalent in our group of patients with high clinical relevance. As has been previously reported (23), disperse blue and yellow dyes were also found to be highly prevalent in our group and were related to exposures to dyes in clothing apparel. Finally, 3 of the 77 patients were found to have positive reactions to corticosteroids with "definite" or "probable" clinical relevance, underscoring the need to consider these allergens in patients with recalcitrant dermatitis.

The high rate of detection of CAPB, disperse dyes, and cortisones may reflect both the high frequency of use of products and materials containing these ingredients in our population and the ability of our test sites to screen for these allergens. Notably, the 24 component Thinlayer Rapid Use Epicutaneous T.R.U.E. TEST<sup>™</sup> (Allerderm, Phoenix, AZ) does not contain these allergens.

#### CONCLUSION

While contact dermatitis has been thought to be somewhat rare in children, our study and review of the literature indicate that, in fact, ACD is quite common in children referred for patch testing. Additionally, our study demonstrates that the majority (77%) of patch test reactions in the children at our two academic contact dermatitis referral centers were clinically relevant ("definite" or "probable"). While referral bias must be recognized as a potential limitation of this study, one can reasonably conclude from these data that extended exposure-targeted epicutaneous patch testing is a useful tool in the evaluation of children with potential ACD.

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