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Cross-sectional evaluation of the pediatric baseline series in detection of contact sensitization in children

To the Editor: The first expert consensus-derived pediatric baseline series (PBS) was published in 2018 for detection of pediatric allergic contact dermatitis (ACD) in the United States.[1] Previously, only the US Food and Drug Administration–approved Thin-Layered Rapid Use Epicutaneous (TRUE) Test (Smart Practice, Phoenix, AZ) was recommend for use in children age 6 to 17 years.[2] Using data collected from the Prospective Pediatric Contact Dermatitis Registry, we evaluated the ability of the PBS to diagnose pediatric ACD compared with the TRUE Test.

Patch test results of children (age 0-17 years) from the Massachusetts General Hospital (MGH), Brigham and Women's Hospital (BWH), and the University of Missouri between January 2016 and March 2020 were entered into an online registry housed at MGH. Children were tested to extended baseline series containing allergens in the PBS and TRUE Test. A previously described method to evaluate the hypothetical positive patch test (PPT) yield of the TRUE Test and PBS was used.[3] The number of patients who would have had all of their PPTs detected using allergens in the TRUE Test or PBS were compared (Fig 1).

One hundred and eight children (MGH, 63; BWH, 7; Missouri, 38) were tested; there were 44 boys (40.7%) and 64 girls (59.3%). The mean (±SD) age was 9.5 ± 4.7 years. Eighty-one patients (75%) had ≥1 PPT; 39.5% (32/81) would have had all of their PPTs detected by the PBS compared with 18.5% (15/81) by the TRUE Test ($P < .01$). If tested only with the PBS, 13.6% of subjects (11/81) would not have had any of their potential allergens detected compared with 18.5% (15/81) with the TRUE Test alone ($P = .39$). When stratified by age, the PBS was significantly better than the TRUE Test in the ability to detect all PPTs in children 6-12 years old ($P = .02$). The hypothetical yield to detect all PPTs was greater for the PBS than the TRUE test in children 0-5 and 13-17 years old, although there was no statistical difference. This is potentially attributed to the smaller sample sizes in these age groups. The top 50 allergens eliciting a PPT among our cohort is shown in Table I.

Hydroperoxides of linalool and limonene were among the most commonly identified allergens in our cohort (23.1% and 9.6% of patients, respectively), but they were not components of the PBS or TRUE Test. Hydroperoxides of linalool and limonene are emerging sensitizers in children, and fragrance

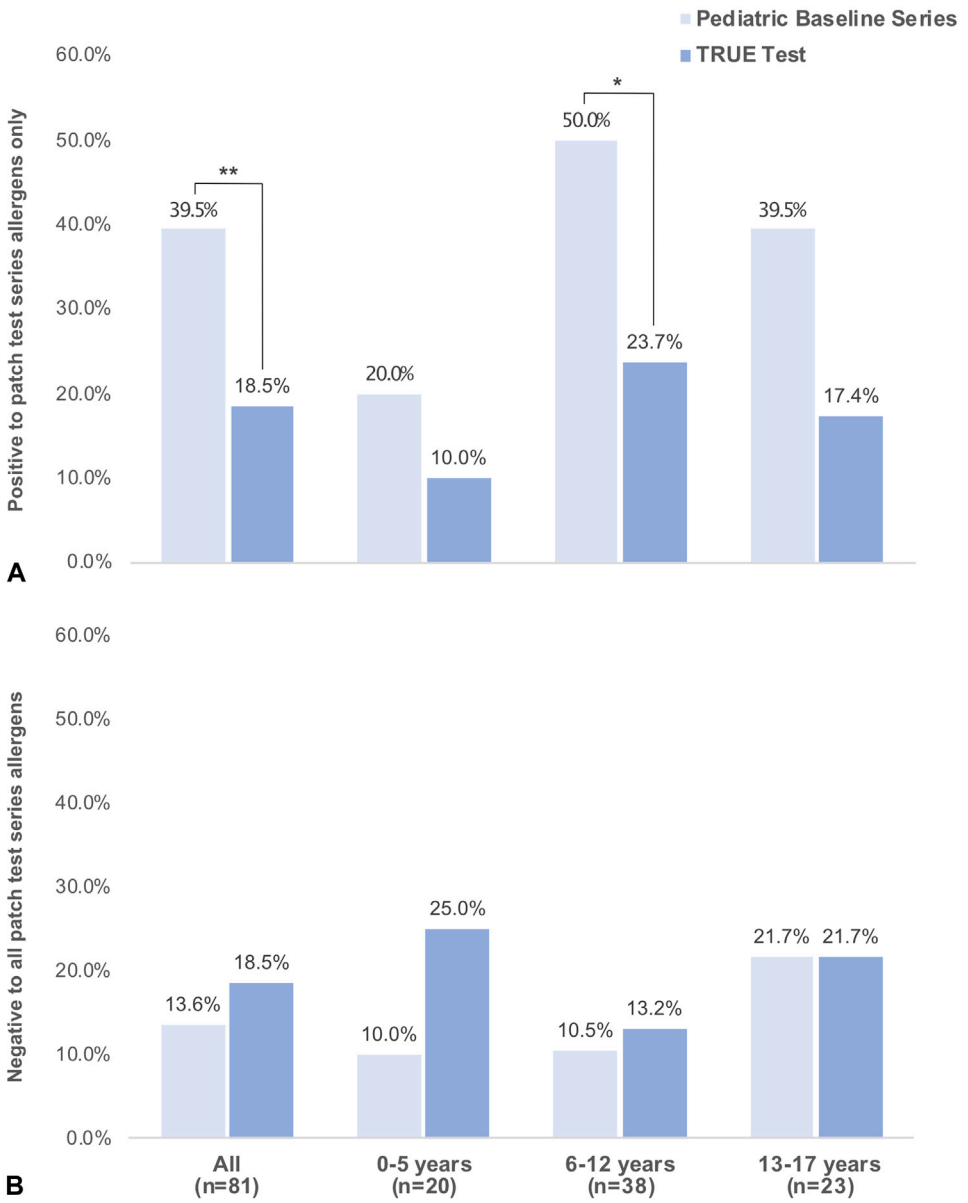

Fig 1. Comparison of the Pediatric Baseline Series and TRUE Test (Smart Practice, Phoenix, AZ). (**A**) Proportions of children who would have had all of their positive patch test reactions detected by the Pediatric Baseline Series vs TRUE Test allergens. (**B**) Proportions of children who did not have any potential allergens detected by the Pediatric Baseline Series vs TRUE Test allergens. *P* values for χ^2 tests comparing the hypothetical positive patch test yields by allergens in the Pediatric Baseline Series versus the TRUE Test are represented by asterisks as follows: $^*P < .05$ and $^{**}P < .01$. Statistical analyses were performed using SAS 9.4 (SAS Institute Inc, Cary, NC); $P < .05$ was considered statistically significant.

allergy could be potentially missed if these allergens are not tested.[4] If both hydroperoxides were added to the PBS, it would have detected all PPTs in 48.1% of patients (an increase from 39.5%).

The PBS was found to be a more comprehensive series than the TRUE Test for diagnosis of pediatric ACD, specifically in the 6-12-year age group. This finding was a result of the inclusion of additional common allergens in the PBS, such as methylisothiazolinone, propylene glycol, cocamidopropyl betaine, propolis, and iodopropynyl butylcarbamate, that are not present in the TRUE Test.[3,5] Our findings support the use of a more comprehensive baseline series for patch testing in children.

Table I. Patch test results of the top 50 allergens

		Age groups, years							
Allergen	**Series**	**All (0-17) PPT (%)**	**N**	**(0-5) PPT (%)**	**n**	**(6-12) PPT (%)**	**n**	**(13-17) PPT (%)**	**n**
Hydroperoxides of linalool	NA*	12 (23.1)	52	1 (100)	1	8 (27.6)	29	3 (13.6)	22
Nickel sulfate	PBS,† NA, T‡	20 (18.5)	108	9 (39.1)	23	7 (13.5)	52	4 (12.1)	33
Dandelion extract	Custom§	2 (18.2)	11	2 (33.3)	6	0 (0)	5	0 (0)	0
Methylisothiazolinone	PBS, NA	17 (15.7)	108	1 (4.3)	23	14 (26.9)	52	2 (6.1)	33
Carmine	PBS	2 (14.3)	14	1 (11.1)	9	1 (20)	5	0 (0)	0
Cobalt chloride	PBS, NA, T	16 (14.8)	108	5 (21.7)	23	7 (13.5)	52	4 (12.1)	33
Fragrance Mix I	PBS, NA, T	14 (13)	108	4 (17.4)	23	8 (15.4)	52	2 (6.1)	33
MCI/MI	PBS, NA, T	13 (12)	108	0 (0)	23	10 (19.2)	52	3 (9.1)	33
Amerchol L101	PBS, NA, T	11 (10.2)	108	3 (13)	23	5 (9.6)	52	3 (9.1)	33
Ammonium persulfate	Custom	2 (10)	20	1 (20)	5	1 (33.3)	3	0 (0)	12
Hydroquinone	Custom	1 (10)	10	1 (20)	5	0 (0)	3	0 (0)	2
Hydroperoxides of limonene	NA	5 (9.6)	52	0 (0)	1	3 (10.3)	29	2 (9.1)	22
Benzoyl peroxide	NA	4 (7.7)	52	0 (0)	1	1 (3.4)	29	3 (13.6)	22
Balsam of Peru	PBS, NA, T	8 (7.4)	108	2 (8.7)	23	6 (11.5)	52	0 (0)	33
Cocamidopropyl betaine	PBS, NA	8 (7.4)	108	5 (21.7)	23	2 (3.8)	52	1 (3)	33
Benzophenone-4	Custom	4 (7.4)	54	1 (5)	20	1 (4.3)	23	2 (18.2)	11
Amidoamine	PBS	4 (7.1)	56	2 (8.7)	23	1 (4.3)	23	1 (10)	10
Methyldibromo glutaronitrile	NA, T	7 (6.6)	106	2 (9.5)	21	4 (7.7)	52	1 (3)	33
Neomycin	PBS, NA, T	7 (6.5)	108	1 (4.3)	23	5 (9.6)	52	1 (3)	33
Polymyxin B	Custom	2 (6.1)	33	1 (11.1)	9	1 (6.7)	15	0 (0)	9
1,3 diphenylguanidine	Custom	2 (6.1)	33	0 (0)	9	1 (6.7)	15	1 (11.1)	9
Bacitracin	PBS, NA, T	6 (5.6)	108	2 (8.7)	23	4 (7.7)	52	0 (0)	33
Propylene glycol	PBS, NA	6 (5.6)	108	1 (4.3)	23	3 (5.8)	52	2 (6.1)	33
Chlorhexidine digluconate	Custom	2 (4.7)	43	1 (7.1)	14	1 (5.6)	18	0 (0)	11
Formaldehyde	PBS, NA, T	5 (4.6)	108	3 (13)	23	2 (3.8)	52	0 (0)	33
Sorbitan sesquioleate	Custom	2 (4.5)	44	1 (6.7)	15	1 (5)	20	0 (0)	9
Tocopherol	NA	4 (3.8)	106	2 (9.5)	21	2 (3.8)	52	0 (0)	33
Potassium dichromate	PBS, NA	4 (3.8)	106	3 (14.3)	21	1 (1.9)	52	0 (0)	33
Bronopol	PBS, NA, T	4 (3.7)	108	2 (8.7)	23	2 (3.8)	52	0 (0)	33
Iodopropynyl butylcarbamate	PBS, NA	4 (3.7)	108	1 (4.3)	23	3 (5.8)	52	0 (0)	33
Propolis	PBS, NA	4 (3.7)	108	0 (0)	23	2 (3.8)	52	2 (6.1)	33
Black rubber mix	T	2 (3.7)	54	1 (5)	20	1 (4.3)	23	0 (0)	11
Gold sodium thiosulfate	NA, T	3 (3.5)	85	0 (0)	10	1 (2.3)	44	2 (6.5)	31
Disperse blue 126/160	NA, T	3 (3.5)	85	0 (0)	10	3 (6.8)	44	0 (0)	31
Textile mix	NA	2 (3.2)	62	0 (0)	6	1 (3.1)	32	1 (4.2)	24
Butylhydroxytoluene	Custom	1 (3)	33	0 (0)	9	0 (0)	15	1 (11.1)	9
p-Phenylenediamine	NA, T	3 (2.8)	106	1 (4.8)	21	0 (0)	52	2 (6.1)	33
Sodium benzoate	Custom	1 (2.3)	44	1 (6.7)	15	0 (0)	20	0 (0)	9
Hydrocortisone-17-butyrate	PBS, T	1 (2.2)	46	1 (4.3)	23	0 (0)	20	0 (0)	3
Benzalkonium chloride	Custom	1 (2.2)	45	0 (0)	15	0 (0)	20	1 (10)	10
Benzyl alcohol	NA	2 (2.1)	96	1 (6.3)	16	0 (0)	49	1 (3.2)	31
Carba mix	PBS, NA, T	2 (1.9)	108	1 (4.3)	23	0 (0)	52	1 (3)	33
Compositae mix	PBS, NA	2 (1.9)	108	0 (0)	23	2 (3.8)	52	0 (0)	33
Decyl glucoside	PBS, NA	2 (1.9)	108	0 (0)	23	1 (1.9)	52	1 (3)	33
Diazolidinyl urea	PBS, NA, T	2 (1.9)	108	1 (4.3)	23	0 (0)	23	1 (1.6)	62
Quaternium-15	PBS, NA, T	2 (1.9)	108	0 (0)	23	1 (1.9)	52	1 (3)	33
Ethylenediamine chloride	NA, T	2 (1.9)	106	1 (4.8)	21	0 (0)	52	1 (3)	33
2-hydroxyethyl methacrylate	NA	2 (1.9)	105	1 (6.7)	15	0 (0)	47	1 (2.3)	43
Cocamide diethanolamide	Custom	1 (1.9)	54	1 (5)	20	0 (0)	23	0 (0)	11
Benzyl salicylate	NA	1 (1.9)	52	0 (0)	1	0 (0)	29	1 (4.5)	22

MCI/MI, Methylchloroisothiazolinone/methylisothiazolinone; *N*, total number of patch tests performed; *n*, number of patch tests in a subgroup; *PBS*, Pediatric Baseline Series; *PPT*, positive patch test.

*Allergens in the North American-80 Comprehensive Series (Chemotechnique, Vellinge, Sweden).

†Allergens in the Pediatric Baseline Series.

‡Allergens in the TRUE Test panels 1.1, 2.1, 3.1 (SmartPractice, Phoenix, AZ).

§Allergens not represented in PBS, T, or NA series.

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Noncompliance with surgical margin guidelines is associated with histologic margin positivity: A retrospective case-control study

To the Editor: Variable recurrence and metastasis rates are noted following standard surgical excision (SSE) with postoperative margin assessment for cutaneous squamous cell carcinoma (cSCC).[1-4] The National Comprehensive Cancer Network (NCCN) cSCC guidelines postulate that this variability could be due to differences in margin sizes and whether clear histologic margins are achieved. The NCCN recommends 4-6-mm surgical margins for low-risk cSCC.[3] This study aims first to determine whether NCCN guideline–compliant surgical margin (GCM) selection and margin documentation are associated with improved tumor clearance and second to examine the factors associated with GCM.

Using an single-institution cSCC registry approved by an institutional review board, a retrospective Brigham and Women's Hospital (BWH) T stage–matched cohort of 462 patients with cSCC BWH stage of T2b or less and undergoing SSE with curative intent by dermatologists or nondermatologists was generated. The primary study endpoint was a negative histologic margin after SSE. Patient data, including demographic, tumor, treatment, and outcome data, were collected. Surgical margins were defined as the margin of normal-appearing skin incorporated into the excision design. Pathologic or histologic margins were defined as the microscopic presence or absence of malignant cells at the specimen margin. Margin compliance was graded according to NCCN guidelines[3] and stratified into 3 groups: (1) NCCN GCM, (2) NCCN guideline noncompliant margins, and (3) no documentation of surgical margins. Factors associated with GCM and positive histologic margins after excision were studied. Factors associated with positive histologic margins on excision were determined using stepwise logistic regression matched for surgical specialty and BWH stage. Data were managed using REDCap electronic data capture and analyzed using JMP Pro 14 (SAS Institute, Cary, NC). ANOVA and χ^2 testing were used to determine statistical significance; $P < .05$ was considered statistically significant.

Dermatology and nondermatology cohorts (n = 231 each) were well matched by mean patient age of 71.3 versus 72.6 years old ($P = .269$), gender being 39% versus 47% female ($P = .074$), mean tumor diameter of 1.4 cm (±SD 0.7 cm) versus 1.5 cm (±SD 1.3 cm; $P = .242$), and BWH stage, which was identical for dermatologists and nondermatologists with each cohort consisting of 78% T1 (n = 180), 22% T2a (n = 5), and 0.4% T2b (n = 1). Table I shows factors associated with margin documentation status and factors associated with positive pathologic margins after excision, matched for specialty and BWH T stage. Table II shows multivariate logistic regression modeling of factors associated with positive pathologic margins on excision after matching for specialty and BWH T stage. Positive histologic margins (incomplete tumor excision) occurred in 6.4% of all cases, including 2% of SSEs performed by dermatologists and 11% of SSEs performed by nondermatologists. Regardless of surgical specialty,