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Contact allergy to hydroperoxides of limonene and linalool in a pediatric population

To the Editor: Allergic contact dermatitis (ACD) is recognized to contribute to 20% of pediatric atopic dermatitis cases. Fragrances are the most common allergens for children with and without atopic dermatitis.[1] Limonene and linalool are 2 common fragrances found in hair and skin products, detergents, perfumes, and 90% to 97% of essential oils.[2,3] Both limonene and linalool rapidly oxidize upon contact with air to become the hydroperoxides of limonene and linalool, which are significantly more allergenic than the reduced forms. Previous studies have determined the optimal concentration for testing to hydroperoxides of limonene and linalool to be 0.3% and 1.0%, respectively.[2,3]

Approximately 60% to 70% of sensitizations to limonene and linalool are undetected by fragrance testing alone (testing to fragrance mixes [FMs] 1 and 2, and Balsam of Peru [BoP]).[2,3] Despite their ubiquity and high allergenicity rates in adults, to our knowledge, no study has evaluated the rates of contact allergy to hydroperoxides of limonene and linalool in pediatric patients.

This retrospective medical record review was approved by the Partners Healthcare institutional review board and included patients younger than 18 years who had patch testing at Massachusetts General Hospital and Brigham and Women's Hospital between January 1, 2007, and March 20, 2019.

Of the 124 children, 54 (43.5%) were tested with hydroperoxides of limonene and 28 (22.6%) with hydroperoxides of limonene and linalool (Table I). In patients tested with hydroperoxides of limonene, positive reactions were observed in 7 (13.0%; 95% confidence interval, 5.4-24.9). Positive reactions to hydroperoxides of linalool were observed in 5 of 28 patients tested (17.9%; 95% confidence interval, 6.1-36.9) (Table II).

Table I. Pediatric patients undergoing patch testing (N = 124)

Characteristics	Value
Total patients identified with any patch testing	N = 124
Sex, n (%)	
Female	74 (59.7)
Male	50 (40.3)
Race, n (%)	
White	87 (70.2)
Asian	10 (8.1)
Hispanic	7 (5.6)
Black	7 (5.6)
Other or not recorded	13 (10.5)
Age at patch test, y, mean ± SD	11.0 ± 4.5
Age at patch test, range	10 months to 17 years
Type of patch testing, n (%)	
Tested to hydroperoxides of limonene and linalool	28 (22.6)
Modified ACDS Core Series	14 (11.3)
Pediatric Core Series	6 (4.8)
Fragrance Series	6 (4.8)
North American Standard Series	2 (1.6)
Tested to hydroperoxides of limonene, not of linalool	26 (21.0)
Modified ACDS Core Series	16 (12.9)
Bakery Series	10 (8.1)
Tested to hydroperoxides of linalool, not of limonene	0 (0)
Tested to neither hydroperoxides of limonene nor linalool	70 (56.5)
Thin-Layer Rapid Use Epicutaneous (TRUE) Patch Test*	25 (20.2)
North American Series	21 (16.9)
North American Comprehensive Series†	7 (5.6)
Modified American Contact Dermatitis Society Core Series	7 (5.6)
Metal Series†	4 (3.2)
Custom selected antigens	4 (3.2)
North American Photopatch Series†	2 (1.6)

*SmartPractice, Phoenix, AZ.
†Chemotechnique Diagnostics, Vellinge, Sweden.

Nine patients tested positive to 1 or both hydroperoxides. Of these 9, 5 (55.6%) did not respond to other fragrance allergens (FM1, FM2, BoP). All 9 (100%) patients had a history of atopy, and 5 (55.6%) had a history of AD.

A minority of pediatric patients in this cohort were tested to hydroperoxides of limonene or linalool (43.5% and 22.6%, respectively). Of the children tested to 1 or both hydroperoxides, 13.0% and 17.9% of patients had positive results for hydroperoxides of limonene and linalool, respectively. Although true

Table II. Testing to hydroperoxides of limonene and linalool

Characteristics	Tested to hydroperoxides of limonene, n (%) (n = 54)	Tested to hydroperoxides of linalool, n (%) (n = 28)
Atopy history	47 (87.0)	25 (89.3)
Atopic dermatitis	27 (50.0)	17 (60.7)
Dermatitis location		
Hand	5 (9.3)	4 (14.3)
Leg	2 (3.7)	1 (3.6)
Face	18 (33.3)	12 (42.9)
Patch testing reaction*		
No reaction	41 (75.9)	19 (67.9)
Doubtful reaction	6 (11.1)	4 (14.3)
+	5 (9.3)	5 (17.9)
++	1 (1.9)	0 (0)
+++	1 (1.9)	0 (0)
Positive reaction	7 (13.0)	5 (17.9)

*Doubtful reaction included cases of macular erythema only (+/-) or unclear reaction (?). The + symbol designates weak nonvesicular reaction with indurated erythema and possibly papules. The ++ symbol designates strong edematous or vesicular reaction. The +++ designates extreme spreading bullous or ulcerative reaction.

allergic contact dermatitis requires soluble protein antigens associated with allergenic haptens to engender a type IV hypersensitivity response, the hydroperoxides of limonene and linalool are oily terpenes, which may produce irritant reactions on patch testing, especially in patients with atopy. In adults, the optimal concentration of hydroperoxides of limonene and linalool has been determined through testing consecutive patients to various dilutions.[4] The optimal concentration in children remains to be determined.

This study presents an important insight into the allergenicity of these hydroperoxides in children, although they are tested infrequently. Importantly, more than half of patients with a positive reaction to either hydroperoxide did not react to other commonly tested fragrance allergens, including FM1, FM2, and BoP. Had these patients not been tested to hydroperoxides of limonene and linalool, an important fragrance allergy would have been missed, leading to incomplete allergen avoidance and continued allergic contact dermatitis. These data underscore the importance of including these hydroperoxides in both adult and pediatric patch testing, given that fragrances are among the most common allergens.[5]

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Characteristics of physicians with dermatology board certification by the American Board of Physician Specialties

To the Editor: The American Board of Medical Specialties (ABMS) and American Osteopathic Association (AOA) are nationally recognized organizations that collaborate with member boards, including the American Board of Dermatology and the American Osteopathic Board of Dermatology, to offer specialty board certification. The American Board of Physician Specialties (ABPS) is another organization offering board certification to physicians in various specialties, including dermatology. Given little data exist, we evaluated the characteristics of physicians with ABPS dermatology board certifications (DBCs).

From July to August 2019, the ABPS board-certified physician membership database was queried. Physician characteristics, such as sex, medical training, and ABMS/AOA board certification status, were obtained from internet searches. The University of Connecticut Health Center Institutional Review Board exempted this study.