

Pediatric Allergic Contact Dermatitis



Christen Brown, BS^a, JiaDe Yu, MD^{b,c,*}

KEYWORDS

- Pediatric allergic contact dermatitis • Contact dermatitis • Patch testing
- Pediatric allergy • Allergy • Atopic dermatitis

KEY POINTS

- Allergic contact dermatitis is equally prevalent in children and in adults, and patch testing is the gold standard for evaluation.
- Children can develop allergic contact dermatitis at any age, even in infancy.
- Children with atopic dermatitis can develop allergic contact dermatitis to weaker allergens found in eczema therapies.
- Patch testing should be performed to a broad baseline series such as the Pediatric Baseline Series in addition to personal products.

INTRODUCTION

Allergic contact dermatitis (ACD) in children was once thought to be a rare occurrence, but studies have shown that it affects up to 20% of children.¹ Its prevalence and significance within the pediatric population are likely underrepresented because many cases are either undiagnosed or misdiagnosed, unreported, or both.^{2,3} ACD may be difficult to distinguish clinically from atopic dermatitis (AD) because of the high prevalence of AD in children. However, in a systematic review and meta-analysis, there was no significant difference in the prevalence of ACD in patients with and without AD.^{4,5} Untreated, recalcitrant pediatric ACD can have significant negative consequences on the patients' quality of life, and, thus, expedient referrals for patch testing and adequate clinical suspicion are key to treatment of pediatric ACD. This article presents an update on the most recent literature on pediatric ACD and discusses common contact allergens in children, patch testing techniques, special considerations, and best practices relevant to the point of care.

^a Tulane University School of Medicine, 1430 Tulane Avenue, New Orleans, LA 70112, USA;

^b Department of Dermatology, Massachusetts General Hospital, Boston, MA, USA; ^c Harvard Medical School, Boston, MA, USA

* Corresponding author. Department of Dermatology, 50 Staniford Street, Suite 200, Boston, MA 02114.

E-mail address: jiade.yu@mgh.harvard.edu

Twitter: @patchtestyu (J.Y.)

HISTORY OF PEDIATRIC ALLERGIC CONTACT DERMATITIS

In 1931, Straus⁶ first described contact sensitization of infants with an experimental model testing poison ivy in newborns and found that 73% had contact sensitization and developed a delayed type IV hypersensitivity reaction to poison ivy. Subsequent studies investigated the prevalence of positive patch test results in children younger than 5 years of age to determine whether sensitization to contact allergens was as common at a very young age.³ Bruckner and colleagues³ used the TRUE (Thin Layer Rapid-Use Epicutaneous, SmartPractice, Phoenix, AZ) test, and found contact sensitization in 24.5% of asymptomatic children, and, pivotally, determined that half of all sensitized children were younger than 18 months of age, reinforcing the idea that sensitization to contact allergens may begin in infancy and is common in older infants and young children.

EPIDEMIOLOGY OF PEDIATRIC ALLERGIC CONTACT DERMATITIS

The first recent study of pediatric ACD in the United States was published in 2008 from the North American Contact Dermatitis Group (NACDG) based on data collected from 2001 to 2004 in children.⁷ They found no significant difference in the overall frequency of positive patch test reactions in children (51.2%) compared with adults (54.1%); however, the allergens differed between the groups, with children more likely to have reactions to nickel, cobalt, thimerosal, and lanolin, whereas adults were more likely to have reactions to neomycin, fragrance mix, balsam of Peru (BoP), and quaternium 15 (a formaldehyde releaser).⁷ These differences may be explained by differences in age, and frequency and duration of exposure.⁷ Children were also more likely have a comorbid diagnosis of AD than adults.⁷

Since the last NACDG publication in children, the retrospective Pediatric Contact Dermatitis Registry (PCDR) in 2016 reported multicenter data on 1142 children and found that 48% of patients had 1 or more relevant positive patch test.⁸ Common allergens included metals (nickel and cobalt), fragrances, antibiotics (including neomycin and bacitracin), propylene glycol, and cocamidopropyl betaine ([Table 1](#)).⁸

Similar studies have taken place abroad, including the European Surveillance System on Contact Allergies (ESSCA), the largest pediatric ACD study from Europe. The ESSCA collected patch test data from 11 European countries, and 6008 patients aged 1 to 16 years with suspected ACD between 2002 and 2008.⁹ There was a 36.9% positive patch test rate.⁹ The 10 most frequent allergens are shown in [Table 1](#).⁹ Younger children aged 1 to 5 years were more likely to be polysensitized compared with older children aged 6 to 16 years.⁹ Like other global studies,¹⁰ allergen sensitivities varied by geographic region.⁹ There was no difference in prevalence of positive patch test reactions between boys and girls and between children with AD and without.⁹

However, epidemiologic data in children are still incomplete because of underuse of patch testing in children and inconsistent data collection. Work is currently underway at multiple academic centers in the United States to prospectively collect data on pediatric ACD.

PATHOPHYSIOLOGY OF ALLERGIC CONTACT DERMATITIS

ACD is a cell-mediated inflammatory, biphasic response to cutaneous exposure to allergens.^{2,4} During the sensitization phase, the skin is directly exposed to allergens that penetrate the stratum corneum.^{2,11} These allergens are subsequently taken up by antigen-presenting cells that migrate to draining lymph nodes, leading to activation of naive T cells that differentiate into primed effector and memory T lymphocytes.^{12,13} Although there are no clinical manifestations of the sensitization phase,

Table 1
Comparison of Top 10 allergens listed in North American Contact Dermatitis Group, Pediatric Contact Dermatitis Registry, and European Surveillance System on Contact Allergies data

	NACDG	PPT (%)	PCDR	PPT (%)	ESSCA	PPT (%)
1	Nickel sulfate	28.1	Nickel sulfate	22.0	Nickel sulfate	20.9
2	Cobalt dichloride	12.3	Fragrance mix I	11.0	Cobalt dichloride	8.3
3	Neomycin sulfate	7.1	Cobalt dichloride	9.1	Potassium dichromate	5.4
4	BoP	5.7	BoP	8.4	Neomycin sulfate	4.4
5	Lanolin alcohols	5.5	Neomycin sulfate	7.2	MCI/MI	3.2
6	Fragrance mix I	5.2	Propylene glycol	6.8	BoP	3
7	Bacitracin	5.2	Composite mix	6.4	p-Phenylenediamine	2.5
8	Carmine	3.8	Bacitracin	6.2	Fragrance mix I	1.9
9	p-Phenylenediamine	3.3	Formaldehyde	5.7	Lanolin alcohols	1.9
10	Quaternium-15	3.2	Gold sodium thiosulfate	5.7	Thiuram mix	1.7

Abbreviations: BoP, Balsam of Peru; ESSCA, European Surveillance System on Contact Allergies; MCI, methylchloroisothiazolinone; MI, methylisothiazolinone; PPT, positive patch test.

these immune reactions may be ongoing internally for 10 to 15 days.^{14,15} The potency of allergens varies, and a single exposure of the more potent allergens (eg, poison ivy) may be sufficient for sensitization to occur.^{2,11} Conditions that cause disruption of the skin barrier, such as AD or cutaneous injury, predispose toward sensitization.^{2,5,16} The elicitation phase of ACD produces clinical features of the disease. In this phase, reexposure to the sensitized allergen leads to activation and mobilization of primed effector and memory T lymphocytes, producing the localized, erythematous, pruritic, and eczematous eruptions seen in clinical manifestations of ACD.^{12,13} Although the pathogenesis of ACD has not been fully elucidated, cytotoxic T, T-helper (Th)1, Th2, Th17, and Th22 cells have all been implicated in the development of ACD.^{13,17}

OVERLAP OF ATOPIC DERMATITIS AND ALLERGIC CONTACT DERMATITIS

AD is the most common chronic inflammatory skin disease in children, affecting up to 13%.^{16,18,19} Similar to ACD, the pathogenesis of AD is multifactorial and includes a combination of factors such as genetic predisposition, skin barrier defects, environmental triggers, and an errant immune system.^{20,21} AD is primarily mediated by Th2 cells in both the acute and chronic phases, producing pruritic eczematous plaques and patches that make ACD difficult to distinguish from AD.^{12,22} The relationship between AD and ACD has not been definitively elucidated. Historically, it was thought that the predominantly Th2 inflammatory response of AD would result in a lower likelihood of ACD, predominantly Th1 mediated.²³ Uehara and Sawai²³ found that contact sensitivity was suppressed in patients with AD who have extensive skin lesions. Earlier studies found that patients with AD who develop ACD require a larger sensitizing dose or repeated applications before showing clinical manifestations.²⁴ However, some studies have shown that, compared with patients without AD, patients with AD have an increased risk of developing ACD with increased potential to being allergic to multiple, weaker allergens.^{21,24,25} This finding is likely caused by the inherent disruption of the skin barrier in AD that leads to increased penetration of irritants and allergens in emollients and topical medication used by

patients with AD.^{16,26,27} Furthermore, there is also evidence that disruption of the skin barrier (in particular tight junctions) may lead to the expression of danger signals (inflammasomes, toll-like receptors, C-type lecithin receptors, neuropeptide receptors, and so forth) that may lead to cutaneous sensitization to less potent allergens.^{28–30}

More recently, in a retrospective case review of 1142 children, patients with AD were more likely to react to allergens found in their skin care products (eg, cocamidopropyl betaine, wool alcohol [lanolin], tixocortol-21-pivalate, and Compositae-related allergens).²⁵ These data are significant in that they present a challenge to clinicians who must consider the possibility of superimposed ACD in patients with AD. The study also showed that children who presented for patch testing, and who also had an underlying history of AD, tended to be (1) younger than their counterparts without AD, (2) more likely to present with generalized dermatitis, (3) have prolonged duration of dermatitis compared with those without, and (4) that Asians and African Americans with ACD were also more likely to have concurrent AD.²⁵ Thus, although the nature of the relationship between ACD and AD continues to be debated, there are increasing data in the literature that show that ACD can coincide with and exacerbate the clinical course of AD.

PHYSICAL EXAMINATION CLUES TO ALLERGIC CONTACT DERMATITIS IN CHILDREN

Given the high prevalence of AD in children and the overlapping clinical features of ACD and AD, differentiating between them can be a challenge. There are key clinical findings that may suggest ACD: if a patient's dermatitis (1) worsens despite usual treatment and/or changes distribution; (2) becomes recalcitrant to current treatments; (3) presents in unusual locations, such as predominantly the head and neck, hand or foot, eyelid, groin, perioral, or periorbital; (4) commences in adolescence with no history of childhood eczema; (5) requires immunosuppressive systemic medication; and (6) rebounds after cessation of therapy.^{16,31} In some circumstances, patients can be sensitized to the active ingredients in their topical therapies, leading to rebound of their dermatitis.^{16,31} A helpful algorithm for patch testing in children has been published that may be used to guide clinical decision making.¹²

The location of rash and clinical history may provide clues to specific allergens. According to the NACDG, the most common sites for pediatric ACD are the face, generalized scattered distribution pattern, and extremities (arms and legs).³² Facial dermatitis in children may be caused by common personal care products such as shampoos, soaps, and face creams, which may contain preservatives, fragrances, and surfactants.^{33,34} Often, more than 1 allergen can contribute to dermatitis in the same distribution (eyelids, periorbital), such as benzoyl peroxide in acne wash and diethylthiourea, the rubber accelerator found in equipment (goggles, masks, wetsuits) used in water sports.³⁵ Hand dermatitis in children may be associated with various sources, ranging from a popular homemade toy called slime, which is made with common household products, including glues, detergents, and soaps, to personal care products such as moisturizers, hand soap, and nail polish.^{33,36} Dermatitis of the extremities may be a result of shin guards used in contact sports, which contain allergens such as neoprene rubbers or glues.^{12,33} Dermatitis affecting diaper areas is another method to differentiate ACD from AD in children, because this region is usually spared in AD.^{11,37} Face dermatitis could result from electronic devices that contain nickel, cosmetics, spray-on fragrances, or common personal care items such as face washes and moisturizers.^{33,37}

PATCH TESTING SERIES FOR CHILDREN

Patch testing is the gold standard for diagnosis of ACD, but, despite the increasing prevalence of children with ACD, testing is less used in children. The PCDR showed that, although patch test evaluations occur in children as young as 7 months, and that most providers customize their patch tests to patient history, most providers patch tested fewer than 10 patients annually.⁸ In the most recent study by the NACDG in adults from 2015 to 2016, more than 5597 adults were tested.³⁸ However, over 8 years, only 883 children were tested by the NACDG, a difference of nearly 25-fold.³⁸ The discrepancy in patch testing between adults and children may be caused by barriers that limit patch testing capabilities in the pediatric population, including lack of consensus on allergens to patch test in children, misdiagnosis of ACD, logistical challenges, and general knowledge gap on how to patch test in children.

In 2017, The TRUE test was approved by the US Food and Drug Administration in children aged 6 to 18 years.^{38,39} The TRUE test is a commercially available patch test kit containing 35 allergens, and 1 study found that it detects only 67% of the most common allergens.³⁸ Some prevalent allergens in children, such as methylisothiazolinone (MI), propylene glycol, and cocamidopropyl betaine, are not included in the TRUE test. Clinicians also are unable to add or subtract allergens from the TRUE test, making customization based on patient history impossible. Although the TRUE test is a reasonable screening test for patients suspected of having ACD, more comprehensive testing is necessary to avoid missing relevant allergens.

To facilitate comprehensive patch testing in children, an expert consensus-derived baseline patch test series for children aged 6 to 18 years was published in 2017.³⁹ The panel includes 38 allergens prevalent in children older than 6 years, and integrates data published by the PCDR and NACDG.^{8,32,39} The Pediatric Baseline Series includes high-yield allergens in children in patches that could easily fit on the back of a 6-year-old.³⁹ Furthermore, the Pediatric Baseline Series is constantly reevaluated in order to add and remove allergens based on changing prevalence data.³⁹ Ultimately, baseline series such as this serve as a foundation for increasing the diagnostic yield of patch testing in children and detecting emerging allergens in children.

Regionally specific pediatric series are also used in both Australia and Europe. The Australian Pediatric Baseline panel includes 30 allergens based on local prevalence data.⁴⁰ The European Academy of Allergy and Clinical Immunology proposed a patch test series in children that included only 9 allergens, with an optional 12 additional allergens available to be used according to history and exposure.⁴¹ Because exposure and allergen prevalence differ between the United States, Australia, and Europe, use of regional baseline series is generally recommended.

PATCH TESTING PROCEDURE

The process of patch testing in children requires cutaneous application of allergens on the patient's back and avoiding the spine because of movement.^{33,37} In addition to the back, patches can be placed on the thighs if the back is not clear for patch testing or if additional space is needed.³⁷ Although the number of allergens that can be tested is limited by the child's size, it has been estimated that 80 allergens can comfortably fit on an average 8-year-old³⁷ (Fig. 1). Hypoallergenic adhesive tape, such as Scanpor (SmartPractice, Phoenix, AZ) is applied over the patches to avoid dislodging.³⁷ In smaller children, the number of patches used should be judiciously selected and based on exposure history.^{33,34,37} Because younger children may be more susceptible to irritant reactions, shorter occlusion time, such as 24 hours instead of the standard 48 hours, has been proposed, although clinical studies have yet to determine whether

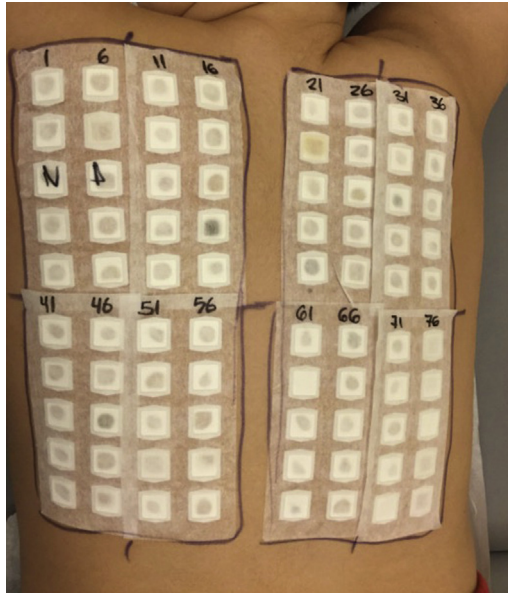


Fig. 1. Eighty patches are easily placed on the back of an 8-year-old.

this significantly affects outcomes. Children 13 years of age or older may be patch tested under the same guidelines as adults, with removal of patches and an initial reading at 48 hours, and a second or final reading at 96 hours.^{33,37} This final reading is the most clinically relevant reading, with one-third of negative allergen tests at the initial 48-hour reading becoming positive at 96 hours.^{33,42} Final reading times may vary from 72 hours to 120 hours, and there is currently no evidence to suggest which time frame is superior, and all may be acceptable. The International Contact Dermatitis Research Group established a standardized grading system for evaluation of patch tests that is widely used.^{33,42,43} This grading system entails 6 reaction categories: negative reaction (–); doubtful reaction characterized by faint erythema only (+/–); weak positive reaction with nonvesicular erythema, infiltration, and possible papules (+); strong positive reaction with vesicular erythema, infiltration, and papules (++); and extreme positive reaction with intense erythema and infiltration, coalescing vesicles, and bullous reaction (+++).³³

Optimal reading times depend on specific allergens. Metals (nickel, cobalt, gold, chromate, palladium), medications (neomycin, topical corticosteroids, caine mix), and certain preservatives and glues (methylchloroisothiazolinone [MCI]/MI, epoxy resin) can be associated with late reactions^{33,44} and should be considered for delayed reading at 7 to 10 days after patch test application.^{45,46} In comparison, some allergens may have early positive reaction readings that disappear at later readings. Fragrances and preservatives are prominent on day 5 but may disappear by day 7.^{33,42}

False-positive and false-negative reactions can occur, and there are many variables that contribute to the strength and clinical relevance of reactions. False-positive reactions are produced when allergens are applied at high irritant concentrations or when patch testing occurs on skin with active dermatitis.^{33,34} A phenomenon called angry-back syndrome occurs when false-positive reactions occur adjacent to large true-positive reactions, inducing adjacent skin inflammation and irritation.^{34,47} In the setting of angry-back reactions, it is recommended that

patch testing be repeated avoiding the strong positive reactions. Importantly, a positive reaction does not always signify a relevant reaction because a positive reaction may have no bearing on the current dermatitis but may be of past relevance. It is important that clinicians incorporate patient history and knowledge of the allergen's likely sources when making an assessment of clinical relevance.⁴⁸ Clinical relevance based on positive patch tests depend on current or past exposures,^{33,34} and there are 3 categories of relevance. Clinical relevance is definite if the patch test or use test with the offending product is positive.^{33,34,42} Clinical relevance is probable if the patch test is positive, the offending allergen is present in known cutaneous exposures, and the clinical presentation aligns with that exposure.^{33,34} Clinical relevance is possible if the patch test is positive and the patient has been in contact with materials that may have contained the allergen.^{34,44} False-negative reactions may occur when inadequate allergen concentrations are used, when patients are concurrently on immunosuppressive therapy, or when patients have recently been exposed to ultraviolet light in the setting of sun tanning or phototherapy.³³

Top 10 Allergens in Children

The top 10 allergens from the PCDR among pediatric patients with suspected ACD are listed in [Table 2](#).⁸ One European study assessed the prevalence of allergens in supposedly hypoallergenic/tested/safe cosmetics designed for children younger than 1 year and found that 85% contained potential allergens.⁴⁹

Nickel is a ubiquitous metal and is the most common cause of pediatric ACD worldwide.^{50,51} One study estimated that 1.1 million children are sensitized to nickel, but this

Allergen Type	Allergen	Sources
Metal	Nickel sulfate	Jewelry, toys, clothes, belt buckles, electronics
	Cobalt dichloride	Pigmented cosmetics, jewelry, dental casting alloys
	Gold sodium thiosulfate	Jewelry, dental implants
Fragrances	Fragrance mix I Myroxylon pereirae (BoP)	Cosmetics, personal hygiene products
Preservatives	Formaldehyde and releasers • Quaternium-15 • Diazolidinyl urea • DMDM hydantoin • Imidazolidinyl urea • Bronopol MI and MCI	Personal hygiene products, cleaning supplies
		Household cleaners, hair conditioners, fabric softeners
Emollients	Wool (wax) alcohols/lanolin	Emollients, baby and bath oils, hand sanitizers
Topical medication	Neomycin sulfate Bacitracin	Topical antibiotics

Abbreviation: DMDM, 1,3-dimethylol-5, 5-dimethyl hydantoin.

may be an underestimation.⁵¹ Because nickel is common in children's items such as earrings, toys, clothes, belts, and electronics, early exposure to the metal creates opportunity for lifelong sensitization.^{52,53} Pediatric-specific data from the NACDG showed that 23.7% of children had positive patch testing to nickel between 1994 and 2014.⁵⁰ Girls were significantly more likely to have nickel allergy compared with boys, and jewelry was deemed the most common exposure associated with nickel allergy. Notably, the temporal and environmental contexts of nickel exposure may have some influence on sensitization. One study showed that less sensitization to nickel occurred if metal dental braces were placed before ear piercing.⁵² Avoidance strategies include education that enables patients to recognize materials high in nickel content, and wearing jewelry alternatives, including sterling silver, pure yellow gold, platinum, or plastic earrings (alternatives that have little to no nickel content).⁵³ Patients can also check whether an object releases nickel by using the dimethylglyoxime test kits. If an object releases nickel, the test solution turns pink. Cobalt is found in blue-pigmented cosmetics, jewelry, and dental casting alloys.³⁷ Cobalt is often found with nickel and therefore cosensitization is common. Gold is found in jewelry and some dental implants.⁵⁴

Fragrance allergens (fragrance mix 1, BoP) are commonly found in cosmetics and personal hygiene products. Israeli researchers found increasing rates of fragrance allergy in children, which they attributed to children using a wider range of cosmetics earlier in life.⁵⁵ Younger children who may not yet apply cosmetic products to their own skins may be prone to contact allergy and react to fragrances by proxy of transmission from adults.⁵⁵ Misleading marketing terms that present products as being natural or unscented may contain fragrances and contribute to increasing rates of contact sensitization in young children.

Neomycin is a common topical antibiotic used to treat cutaneous infections and sold over the counter in the United States. It is also used as eye and ear drops in children.^{2,56} It is frequently used with bacitracin, which is therefore a cosensitizer with neomycin, having similar rates of positive patch test reaction.

Lanolin (wood alcohols) is an allergen found in emollients, baby and bath oil, hand sanitizers, and creams.⁵⁷ It is derived from sheep wool,^{58,59} and it is a mixture of sterols, fatty alcohols, and fatty acids with varied composition.⁶⁰ Given its emollient properties and its prevalence in common hygiene products, ACD can develop after repeated exposure and is particularly common in damaged skin affected by AD.^{26,60} Although lanolin alcohol 30% petrolatum is the standard patch test agent used in diagnosing lanolin contact allergy, some studies have shown that additional patch testing with lanolin derivatives may enhance identification of patients with lanolin contact allergy.^{58,61,62} One derivative of note, Amerchol L101 50% pet., is a mixture of mineral oil and 10% lanolin alcohols.^{63,64} Studies have found more positive reactions to Amerchol L101 than to lanolin alcohol alone.^{58,61,64,65} Testing to Amerchol L101 is recommended in pediatric patients.

Formaldehyde and MI are preservatives commonly used to prolong the shelf-life of cosmetic and household products and prevent bacterial, fungal, and viral growth.³⁷ MI was introduced into the United States market in the 1980s in a 3:1 MCI/MI formulation, but this formulation was gradually replaced by MI alone because of concerns for contact allergy from MCI.^{66,67} Thus, high concentrations of MI in particular have become ubiquitous in consumer products over the past decade and can be found in various personal care products, including shampoos, hair conditioners, moisturizers, soaps, and nail polish.^{36,68,69} It is also found in household products, including laundry detergents and fabric softeners, and surface disinfectants as well as residential wall paints and glues.⁷⁰⁻⁷³ The American Contact Dermatitis Society (ACDS) named MI the contact allergen of the year in 2013 because of rapidly increasing prevalence.⁶⁷ After

nickel, it is now the second most common cause of ACD in adults and children.³⁷ In the United States and Europe, it has replaced potentially carcinogenic preservatives such as formaldehyde.⁶⁶ Thus, although MI is known to be a sensitizer and common cause of ACD in adults, cases of pediatric ACD caused by MI are increasing because of its common use in care products for babies and children.⁶⁶ MI was found in wet wipes but has been removed because of published cases.^{74–76} Recently, an epidemic of hand rash was caused by children making slime using laundry detergent, glues, and soap, all of which may contain MI.^{37,73,77,78} MI sensitization is often underdiagnosed in the United States because it is still tested in combination with MCI when using the TRUE test, suggesting a need for MI to be tested singly to prevent missing this important allergen.⁶⁶

Formaldehyde is one of the oldest and most widely used preservatives. It is a ubiquitous allergen that is difficult to avoid given its common placement in many consumer products, including cosmetic, household, and industrial products.^{79–81} Thus, it was named as the ACDS Allergen of the Year in 2015.⁸² In addition to formaldehyde, preservatives that release formaldehyde, such as quaternium-15, imidazolidinyl urea, diazolidinyl urea, bronopol, and 1,3-dimethylol-5, 5-dimethyl hydantoin (DMDM) hydantoin, are frequently found in personal care products.^{79,82,83} One study found that these releasers are among the most frequent allergens in children who underwent patch testing because of ACD, further highlighting the necessity of paying attention to all preservatives included within cosmetic, household, and industrial products on labels.⁸⁴

Emerging Allergens

New potential allergens are constantly being introduced to consumers, whereas older known allergens are used less frequently, such as MCI. Therefore, it is important to keep track of and test for emerging allergens in children.

Hydroperoxides of limonene and hydroperoxides of linalool are two emerging pediatric fragrance allergens that were found to be positive in 13% and 17.9% of children, respectively, in 1 study.⁸⁵ Limonene and linalool are naturally occurring fragrances that rapidly oxidize into their respective hydroperoxides, which are more allergenic than the reduced forms.⁸⁵ It is estimated that 60% to 70% of sensitizations to linalool and 70% of sensitizations to limonene were not detected by positive patch test reactions when tested for fragrance allergy alone (fragrance mixes I and II, BoP).^{86,87} These fragrances are commonly used in soaps, shampoos, perfumes, and household cleaning products.⁸⁶ Limonene has been identified in 88 of 91 essential oils that have caused ACD, and linalool has been identified in 82 of 91 essential oils that have caused ACD.^{86,87}

Isobornyl acrylate, an acrylate derivative found in glucose sensors or insulin sets used in the management of type 1 diabetes, is another emerging allergen that should be considered in children.⁸⁸ Although medical devices have significantly improved glycemic control and quality of life, cases of adhesive-driven ACD have been reported in association with certain brands of continuous glucose monitors.^{89–92} It is thought that isobornyl acrylate leaches through the adhesives to cause sensitization,⁹³ and this process may be exacerbated by occlusion and sweating.⁸⁸ Therefore, it is recommended that isobornyl acrylate should be tested in every suspected case of ACD caused by medical device adhesives or glues to avoid missing sources of sensitization.⁸⁸ These findings also highlight the need for increased transparency from manufacturers regarding the agents used to create these medical devices. Isobornyl acrylate was named ACDS Contact Allergen of the Year in 2020.⁹⁴

Acetophenone azine, a biocide found in foam, including sneakers and shin pads, has emerged as a source of ACD presenting in the distribution of the shin and foot, especially in athletes.^{95,96} Recently, Darrigade and colleagues⁹⁵ reported on 6 male

children, aged 7 to 14 years, who presented with shin and plantar dermatitis related to wearing shin pads that contained acetophenone azine. Avoidance strategies for acetophenone azine include wearing leather-inlay soles and using polyurethane shin pads.⁹⁵ Of note, many of the children reported in this study had been misdiagnosed as experiencing exacerbation of AD or experiencing recalcitrant hyperkeratotic plantar foot dermatitis.⁹⁵ Therefore, it is important to consider patch testing acetophenone azine in children presenting with shin and/or foot dermatitis.⁹⁷ Acetophenone azine is an important emerging allergen and will be the ACDS Contact Allergen of the Year in 2021.⁹⁸

Counseling, Education, Avoidance

Accurate diagnosis with patch testing, avoidance of potential allergens, and future preventive measures are the 3 pillars of pediatric ACD management and treatment.^{25,37} Providers should counsel on avoidance and prevention strategies with both the patient and all relevant caretakers,³⁷ along with initiating treatments that will suppress inflammation (with topical corticosteroids, compresses, topical immunomodulators).⁹⁹ National organizations have provided resources to aid with patient counseling. The ACDS offers services to help providers and patients identify common sources of allergens.¹⁴ One such service, the Contact Allergen Management Program (CAMP), is a Web-based resource that assists patients in the management of ACD and aids in identifying which personal care products are safe to use.¹⁰⁰ After patch testing identifies allergens the patient may react to, physicians can generate a personalized list of products that are free of the identified allergens.¹⁰⁰ The patient is also provided with allergen search codes that are tied to the patient's specific allergy profile.¹⁰⁰ Each allergen is linked to synonyms and cross-reactors, and this resource is designed to populate safe alternatives to each allergen.¹⁰¹

It must be noted that patch testing is not possible in all patients because of barriers to access and availability of patch testing.⁸ Patch testing can also be complicated by having a full-body rash leading to no clear skin for placement of patches, angry-back reaction during patch testing, and false-negatives caused by the use of systemic immunosuppressants at the time of patch testing. Hill and colleagues¹⁰² proposed the option of using a preemptive avoidance strategy (PEAS) in patients who do not have access to patch testing or are highly reactive to patch tests. PEAS is defined as preemptively avoiding the top offending allergens in pediatric ACD in the absence of patch testing.^{99,102} The top 10 allergens identified in PEAS were fragrance mix I, BoP, neomycin sulfate, bacitracin, lanolin, formaldehyde, MI, bronopol, propylene glycol, and MCI/MI.¹⁰³ The study consisted of a systematic review of 5 studies reporting data on rates of positive patch tests in pediatric patients and estimated that between one-quarter and one-third of these patients theoretically would have had their relevant allergens avoided had they applied the PEAS in careful selection of pediatric personal care products.¹⁰² It is thought that using PEAS for children without access to patch testing may provide an early opportunity for intervention in ACD.¹⁰² Recently, Brankov and colleagues¹⁰³ performed a meta-analysis of the most recent data released by the NACDG and PCDR to create a list of the top 25 allergens with high clinical relevance to be considered when using PEAS. New to the list were glucosides, which are found in several products ranging from shampoo to sunscreen, and are marketed at children.¹⁰³

SUMMARY

ACD can be a physically, psychologically, and economically burdensome disease that has ramifications for both pediatric patients and their caregivers. Children can become

sensitized to allergens at an early age, and it is important to have high clinical suspicion of ACD in children of all ages who have recalcitrant dermatitis despite appropriate treatment or who present with dermatitis in an atypical distribution. Accurate and early diagnosis, avoidance, and prevention are key to successful management and treatment of pediatric ACD. There is currently a multicenter North American prospective pediatric ACD registry to gather cases of pediatric ACD from major academic centers across the United States, Canada, and Mexico. Initiatives such as this contribute to elucidating the true prevalence of ACD in children as well as identifying ever-changing trends of allergen sensitization in children. Continued collection of prevalence data is necessary to help guide physician decision making, patient education, and potential industry and governmental response to emerging and evolving contact allergens in children.

CLINICS CARE POINTS

- Allergic contact dermatitis is prevalent in children and those with atopic dermatitis.
- Patch testing with too limited a series may miss important allergens.
- Patch testing in young children (< 8 years old) require shorter contact time due to risk of irritation.

DISCLOSURE

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