

Allergic contact dermatitis in children: common allergens and treatment: a review

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Purpose of review

The following study reviews the recent literature pertaining to allergic contact dermatitis (ACD) in the pediatric population. This study also provides an overview of the most common allergens and discusses various therapeutic modalities.

Recent findings

The pathophysiology of ACD is intricate and multifaceted, resulting in a characteristic, delayed inflammatory response. Although commonly recognized in adults, its existence in the pediatric population was questioned. Recent literature suggests that pediatric ACD exists and is more common than previously recognized. The diagnosis relies on the clinical presentation combined with appropriate use and interpretation of a patch test. Although many studies have investigated ACD in children, few have documented the relevance of positive patch test reactions until recently. The most current prevalence estimates of positive patch test reactions range from 14 to 70% of children patch tested. Although that range is broad, these studies have demonstrated the relevance of positive reactions and confirmed ACD as a disease entity in children.

Summary

ACD is a previously underrecognized disease process in the pediatric population that can manifest as a serious dermatologic challenge for both patients and physicians. This review will address the prevalence, diagnostic methods, frequent allergens and treatment options in pediatric ACD.

Keywords

allergic contact dermatitis, children, contact allergens, contact allergy, patch testing

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Introduction

Recently, reports of allergic contact dermatitis (ACD) in children have been rising, possibly reflecting an increased incidence, increased detection through more frequent patch testing or both. Once correctly diagnosed and avoidance strategies are implemented, many cases of contact dermatitis are self-limited or more easily treated. However, as the morbidity from contact dermatitis depends on the ability to avoid repeated or continued exposure, the patient may experience chronic or recurrent episodes of dermatitis if the source is not correctly identified.

Epidemiology

Positive patch test rates in children have been reported in a range between 14 and 70%, with a significant subset demonstrating clinical relevance (contact allergy) [1–3,4[•]]. Two early reports on the United States-based data suggested sensitization rates in asymptomatic children of 20.3–24.5% [5]. New evidence suggests that the prevalence of contact allergy (ACD with a clinically correlating positive

patch test) in childhood is underestimated and either is similar to or may exceed rates observed in the adult population [4[•],6,7^{••}]. Heine *et al.* [8] demonstrated, in a large multicenter study of 75 971 patients, almost equivalent rates of sensitization in children and adolescents as compared with adults, although the most common allergens identified differed between age groups. The North American Contact Dermatitis Group (NACDG) confirmed this in their United States pediatric population [9^{••}].

Clinical presentation

As ACD may be difficult to distinguish clinically and histopathologically from other eczemas, a high index of suspicion is necessary to make the diagnosis. The classic presentation is a pruritic, eczematous plaque localized to the site of allergen exposure. Geometric or linear patterns or involvement of unusual focal skin areas, such as the earlobes, or the weight-bearing areas of the feet may also suggest a contact as a cause (Table 1) [10].

The chronicity of the dermatitis may also affect the presentation. For example, acute ACD (i.e. poison ivy

Table 1 Location clues for diagnosis

Distribution of eruption	Suggested allergen source
Hairline, tops and behind ears Eyelids	Hair products: dyes; shampoo; conditioners; styling products Aerosolized, applied or transferred products: cosmetics; nail products: hardeners, polish; fragrances; hair dyes; lotion applied to hands; metal particles from objects handled
Earlobes, necklace line Axillary vault Axilla – sparing the vault Peri/infraumbilical Linear streaks on extremities Feet – dorsum Feet – weight-bearing surfaces	Metal jewellery, fragrances Deodorants Clothing/textile dyes Metal snaps in pants, belt buckles Poison ivy, poison oak, phytophoto Products used to make shoe uppers: leather, rubber, dyes Products used to make insoles/soles

and poison oak) may be edematous, erythematous, intensely pruritic and can become vesicular with crusts or serous drainage – usually in the linear distribution of where the plant was in contact with the skin. However, if the plant was burned and the allergen aerosolized, the clinical picture would be a more generalized dermatitis. Chronic ACD (i.e. nickel and fragrances) can be insidious and present as localized lichenification or with more generalized reactions. Occasionally, generalized eczematous responses (auto-eczematization) develop and can cause diagnostic confusion. These auto-eczematization reactions have been reported in up to 50% of nickel ACD [11] and are thought to represent increased stimulation from circulating activated T-cells [12]. Given this variable presentation, ACD should remain in the differential diagnosis of chronic dermatitis cases that do not respond to standard treatments.

Patch testing in children

Positive patch test (sensitization) rates in children have been reported as high as 67% [13•]. However, a positive patch test is not equivalent to the incidence or prevalence of ACD, as not all positive tests have clinical relevance. Patch testing remains the gold standard and a valuable testing tool in the diagnosis of ACD in children. That being said, however, there is no Food and Drug Administration-approved commercially available patch test tool designated for patients less than 18 years of age. There are also some specific challenges to testing in the pediatric age group, such as their limited back size and potentially decreased willingness to participate or potential for increased susceptibility to irritant reactions in the very young [14••]. Insightful clues that heighten the index of suspicion for ACD and fulfill the criteria for pediatric series investigation are further discussed by Jacob *et al.* [15••].

With children, the frequency of positive results and the most common allergens may differ as well. The differences in the frequency of positive reactions for a given allergen among different age groups likely reflect differences in the age of exposure and the frequency, type and

length of exposure required to induce sensitization to specific chemicals [5]. In addition, cultural practices and regional variation may have an impact. For example, in one study, Buckley *et al.* [16] found that, in a UK population, positive patch tests to fragrance were infrequent in the first few decades of life and increased gradually after 20 years of age to peak in the seventh decade of life in women and the eighth decade of life in men. They hypothesized that fragrance sensitivity resulted from repeated environmental exposure and age-related susceptibility factors in their tested population.

Most important contact allergens in childhood

As has been described in adults, children are most frequently sensitized to those allergens that are ubiquitous to their environments and thus incur numerous repeated contacts, such as nickel and fragrances. The top 10 allergens found in internationally reported pediatric patch test data are listed in Table 2 [1,7••,17–25].

Nickel is by far the most common allergen in patch-tested patients of all ages [2,3,4•,26]. Classically, it can present as an eruption on the earlobes or periumbilical areas (common areas for exposure to nickel-containing jewellery or pants snaps and belt buckles) [27,28]; however, facial dermatitis has been reported to musical instruments and cell phones due to nickel [29–32]. Of interest, in 1994, the European Union passed legislation restricting the allowable release of nickel from products with prolonged skin contact to be less than 0.5 µg/cm² per week. This was revised in 2004 for body-piercing postassemblies to less than 0.2 µg/cm² per week, which resulted in statistically significant reduced rates of sensitization to nickel on a par with those noted in Denmark. To date, regulation mandates are not in effect in the USA [33,34••].

Neomycin sulfate has remained second place in the most common culprits in ACD for close to 25 years [35]. It is a topical antibiotic with multiple clinical indications, including use for superficial wounds or burns, and can

Table 2 Top 10 allergens in children

Allergen	Description	Source	Frequent distribution
Nickel	Metal	Jewellery, buckles and snaps, eyeglasses, orthodontics, cell phones, keys, coins	Face/eyelids, earlobes, neck, wrists
Neomycin	Topical antibiotic	Antibiotic ointments, combinations with corticosteroids	Face/eyelids
'Balsam of Peru'/fragrance mix	Fragrance	Perfumes and cosmetics, flavoring agent, toothpaste, lozenges and naturally cross-reacts with tomato and cinnamon	Eyelids/face, neck, mouth/lips
Thimerosal	Preservative	Vaccinations, creams, lotions, mascara	Body/torso
Cobalt	Metal	Jewellery, buttons/snaps, ceramics, cement, vitamin B12	Earlobes, neckline, umbilical area, hands
Chromate	Metal	Tanned leather, matches, cement, paints, green felt	Hands, umbilical area
Thiuram	Rubber accelerant	Elastic waistbands, socks, swimsuits, shoes (soles or insoles), gloves, pesticides	Waistline, feet, hands
Lanolin	Emollient	Emollients, rust-preventive waxes, soaps, lip balms	Hands, any body area with emollient use
Formaldehyde/formaldehyde-releasing products	Preservative	Shampoos, lotions, cosmetics, newsprints, cosmetics, clothing – wrinkle-resistant	Face, ears, hands, trunk
Paraphenylenediamine	Oxidative chemical	Hair dye, printer inks, black henna tattoos	Hairline, ears, hands, tattoo sites

Adapted from [2,7[•],17–25].

be found in many over-the-counter products in the United States [36]. Notably, it is also formulated in combination with other antibiotics, antifungals or corticosteroids, which may lead to observed coreactivity of these chemically unrelated substances [37].

A particularly challenging allergen category to avoid is fragrances. The *Myroxylon pereirae* tree extract (aka Balsam of Peru) is used as a screen for fragrance allergy, due to its wide usage and natural cross-reactivity with other frequently encountered fragrances. Fragrance allergy is common in the pediatric population and emerges with the typical involvement areas as seen in adults – face, neck and axillae, in addition to full systemic contact dermatitis [38]. However, it is also one of the most frequently implicated allergens in isolated hand eczema [39]. In addition to cosmetic products such as lotions, make up or sunscreens, *M. pereirae* or chemicals with a natural cross-reactivity can be used as flavorants in toothpastes and mouthwashes, causing a contact stomatitis or cheilitis that is not the usual presentation for fragrance ACD [40,41]. These allergens (or chemically similar ones) are also used in soft drinks and artificial flavoring such as cinnamon, cloves, curry and vanilla. Although dietary intervention remains controversial, there is evidence that it may help those with significant disease that is not resolving with more typical fragrance avoidance [42].

Thimerosal is a mercury-derived preservative found in multiple products. The most common exposures include otic and ophthalmic (contact lens) solutions, antiseptics and cosmetics, and the reaction is mainly periorbital dermatitis. Low clinical relevance along with high sen-

sitization rates is thought to be related to its presence in vaccines [43–45]. Because the majority of thimerosal positive patch tests have been shown to be clinically irrelevant, the NACDG and other notable patch test experts have removed thimerosal from their standard testing trays [46–48]. The rates of sensitization are also expected to decline as many vaccine manufacturers have removed thimerosal from their preparation [46].

Cobalt is a metal often added to other metals to increase the strength of the composite. It is naturally found in metal ore with nickel and can have nickel contamination in its sources [49,50]. As with nickel, a majority of sensitization exposures result from contact with jewelry, clothing snaps, buttons and metal objects. Furthermore, it can also be found in cosmetic products, joint replacements, ceramics, paints, cement and multivitamins (cobalt is incorporated into the vitamin B12) [51].

Another important metal and frequent cause of ACD is chromate. Leather products (e.g. shoes and belts) are a significant exposure source for both children and adults [52,53]. Vegetable-tanned footwear can be used as an alternative [54]. In addition, other sources include multivitamins, paints and antirust products [55]. Matches also contain chromates and can release it while lit or charred [50].

Thiuram and carbamate function as rubber accelerants (chemicals promoting the transformation of rubber from a liquid to a solid state) and are typically present as additives in many rubber products, from elastic waistbands, socks and swimwear to toys, pacifiers, shoes (insoles and soles), cosmetic applicators and adhesives [56].

Table 3 Top allergens (honorable mentions)

Allergen	Description	Source	Frequent distribution
Disperse dyes	Chemical dye	Clothing, diapers	Axilla, sleeves, trunk, diaper area
Cocamidopropyl betaine	Surfactant	Shampoos, bath gels, soaps	Eyelid, face, neck, scalp
Corticosteroids	Medication	Over-the-counter or prescription anti-inflammatory preparations (topical, oral, i.m. and i.v.)	Site of application or systemic contact dermatitis

i.m., intramuscular; i.v., intravenous. Adapted from [2,7^{••},17–24,57].

Lanolin (aka wool wax alcohols) is derived from the sebaceous excretions of sheep, extracted from wool and used as an emollient for skin barrier protection and repair. It is often added to skin ointments, moisturizers and lip balms and may be a source of allergy through cosmetic and personal hygiene products [57,58].

Formaldehyde and/or the formaldehyde-releasing preservatives [quaternium-15, bromonitropropanediol (Bronopol; Xingning Fine Chemicals Factory Co., Ltd., Guangdong, China), diazolidinyl urea (Germall II; Wuhu Huahai Biology Engineering Co., Ltd., Anhui, China), 1,3-dimethylol-5,5-dimethylhydantoin (DMDM) hydantoin (Glydant; Qingzhou Ailitong Chemicals Technical Co., Ltd., Shandong, China), imidazolidinyl urea (Germall), tris (hydroxymethyl) nitromethane (Tris nitro) and sodium hydroxymethylglycinate] are commonly added to personal hygiene products as antimicrobials to maintain their shelf life (e.g. make-up, shampoos, deodorants and baby wipes). Furthermore, they are found in paper products and clothing labeled wrinkle-resistant [51,60]. Of the various textiles, rayon, corduroy, silk and blended cottons have the highest concentrations of formaldehyde, whereas 100% polyester is believed to have the least [60]. Systemic exposure through cigarette smoke inhalation and the ingestion of certain foods that metabolize into formaldehyde (e.g. aspartame-containing foods, shiitake mushrooms, smoked ham and maple syrup) can result in persistent dermatitis, and some patients have improved their symptoms through dietary avoidance, although this remains controversial [62–64,65[•],66,67].

Para-phenylenediamine (PPD) is commonly used as a permanent hair dye, and related compounds may be found in printer ink and photography products. More recently, it has gained notoriety for its use in adulterating natural henna to make ‘black henna’, a substance increasingly being used to make temporary tattoos [67–69]. Although many parents and consumers believe these tattoos to be temporary, adverse events to them (scarring and sensitization) can be permanent. PPD is the most commonly used ‘permanent hair dye,’ but has been detected in concentrations up to 15.7% in henna tattoo preparations, far exceeding the limit permissible for hair dyes (<6%) [70]. Notably, 25% of those allergic to PPD can also be reactive to semi-permanent dyes found in

dark synthetic clothing [71,72]. One concern with PPD is the potential for lifelong sensitization, and reported systemic contact dermatitis evoked with exposure to cross-reactors such as benzocaine, diuretics (hydrochlorothiazide) and sulfonamide medications [73,74]. Children with a history of localized reactions to black henna tattoos have been reported to have had severe generalized reactions requiring hospitalization and ICU stays after subsequent exposure to hair dye [74,75].

With advances in the recognition and understanding of ACD, new allergens are constantly being identified and a few others deserve honorable mention for their impact (Table 3) [2,7^{••},17–24,57].

Textile dermatitis is often a result of the dyes used to color clothing or the resins that lend a ‘wrinkle resistant’ quality as mentioned earlier. In children, the aniline dyes found in clothes, undergarments, seatbelts, diapers and glasses frames have been frequently reported to cause ACD [76–79]. Because of their sensitization potential, disperse blue dyes 106 and 124 are often selected for screening in pediatric patch testing [80]. It is important to note that many individual colors can make up a hue, and the direct application of the patient’s suspected garment may be applied as a component of the patch test [80].

Cocamidopropyl betaine (CAPB) is derived from coconut oil and is a commonly used surfactant in foaming cleansers, appearing in many no tears shampoos, bath foams and soaps [81]. Recently, there is evidence that impurities from the CAPB preparation, such as amidoamine [82,83] and 3-dimethylaminopropylamine (DMAPA) [84,85], may be the true sensitizers. With improved (less contaminated) manufacturing, sensitization to products containing this ingredient may be reduced in the near future [86].

Corticosteroids are synthetic analogues of hormones used for their anti-inflammatory properties. Emerging studies [87,88] have identified them as causes of ACD in 0.2–6% of patients. There are five classes of corticosteroids (A, B, C, D1 and D2) designated based on their differing chemical structures (most notably involving carbon 6/9 and carbon 16/17 substitutions) [89,90]. Due to over-the-counter usage of class A steroids, their sensitization potential and ACD prevalence exceed all the other

Table 4 Topical corticosteroids

Structural class	Class A	Class D2	Class B	Class D1	Class C
Cross-reactions	Cross-reaction between A and D2		Cross-reaction between D2 and budesonide (B)		
Allergenic potential. [88]	+++++	++	++++	+++	+
Examples	Low potency Hydrocortisone Tixocortol pivalate Systemic Methylprednisolone	Mid-potency Hydrocortisone valerate Lower mid-potency Hydrocortisone butyrate Prednicarbate	Potent Budesonide Fluocinonide Upper mid-potency Triamcinolone 0.1% Mid-potency Halcinonide Lower mid-potency Desonide Fluocinolone	Ultra-potent Clobetasol propionate Betamethasone dipropionate Potent Betamethasone valerate Upper mid-potency Fluticasone propionate Mometasone furoate	Potent Desoximetasone Mid-potency Clocortolone pivalate

Adapted from [26,89–102].

structural classes – A (5.72%), B (4.80%), D1 (3.54%), D2 (2.13%) and finally C (1.10%) [91].

Treatment

The central tenets of ACD management are to accurately identify the causative allergen and to implement avoidance measures. If patch testing fails to detect the causative allergen and the diagnosis of ACD is still strongly considered, a detailed diary of the patient's daily activities may help discover patterns of exposure. When the appropriate allergen is identified, the patient must be educated on potential sources of exposure and cross-reacting chemicals, as well as offered suggestions for avoidance [103^{*}]. This may be especially difficult in households with small children affected, as the products that are used by the parents and siblings may also need to be considered as sources for allergen exposures.

For cases in which avoidance alone has not improved the ACD, topical or systemic therapies are available. Emollients can be added after a bath in an effort to retain hydration and restore the barrier function of the skin. Barrier repair also decreases pruritus and reduces visible scaling and dryness [104]. Physical barrier creams may be useful in cases in which the allergen exposure cannot be avoided, and there is a defined time of exposure; patients may apply the creams before and during the exposure in an effort to decrease absorption.

In regards to medication options, topical corticosteroids are the first-line treatment modality for ACD, but they are not without risk and can cause multiple cutaneous side effects with extensive and long-term use [90]. When selecting a corticosteroid for treatment, it is important to choose one that the patient is not allergic to in terms of the active ingredient (the steroid component) and inactive ingredients in the vehicle [105]. Table 4 lists examples from each class and highlights the potential cross-reactions [92–101].

Topical calcineurin inhibitors (TCIs) are another therapeutic option and should be considered when steroid-sparing agents are required. These agents can be used for certain areas, such as the face, axilla and groin, which are more susceptible to steroid-induced atrophy. The currently available TCIs are tacrolimus ointment, pimecrolimus cream and cyclosporine ophthalmic emulsion; the first two have both shown efficacy in the treatment of ACD when compared with vehicle controls [106,107], and notably both have been implicated as causal agents in ACD [108].

When the dermatitis is particularly severe (e.g. bullae), widespread, involving the mucous membranes or continuing to progress despite topical therapy, systemic agents may be considered. Oral H1-antihistamines are an adjuvant therapy that may relieve pruritus and also cause drowsiness that may help with sleep disturbances from pruritus. Systemic corticosteroids may be employed and are generally started at 1 mg/kg per day [109]. For those requiring multiple courses of systemic steroids, other 'steroid-sparing' systemic immunosuppressive agents can be considered to allow for lower oral corticosteroid doses; these include cyclosporine, methotrexate and azathioprine, which all require laboratory monitoring and close follow up.

Conclusion

ACD is a multifaceted and complex disease with many diagnostic and therapeutic challenges. Until recently, the practice of patch testing in North American children was largely undiscovered for several reasons: lack of a Food and Drug Administration indicated commercially available patch test tool for pediatric populations, lack of a published pediatric standard screening series, no published studies from the United States sites on patch testing-affected children and lack of a review in a United States-based journal of the international pediatric patch test data. Hopefully, these recent additions to

the literature, taken as a whole, might result in a paradigm shift.

References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:

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Additional references related to this topic can also be found in the Current World Literature section in this issue (pp. 000–000).

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